

Zimmer / Zeman / Hammer / Goldbach / Allekotte

Protecting and Enforcing Life Science Inventions in Europe

under EPC and EU Law
– From Antibodies to Zebrafish –

Second Edition

C.H.BECK · Hart
Nomos · Helbing Lichtenhahn

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Preface to the second edition

Eighteen years have passed since the first edition of this book was published in 1997. This period has witnessed rapid development in the life sciences. Many biotechnology companies then on the cutting edge of research and development no longer exist, while others have taken their place to push that edge yet further. The sequencing of the human genome, completed several years after the first edition of this book appeared, has ushered in a new era of therapeutics, based not only on the elucidation of the many new genes made available, but also on the genes belonging to any one particular individual. The result has been the dawn of personalized medicine. Biologics now make up a significant proportion of today's blockbuster drugs and of these, many are antibody-based therapeutics. Embryonic stem cells bear the potential to raise the standard of health in society, while simultaneously challenging that society with serious ethical questions. Advances in the genetic engineering of plants are rapidly changing our answers to one of the most ancient and fundamental questions of human survival: What do we and our children eat? Finally, transgenic animals have become indispensable tools in modeling diseases which threaten our health. Yet how do we strike an ethically defensible balance between our desire for better health and potential animal suffering?

These and other issues continue to occupy both researchers and Legislators at the beginning of the 21st century. Legislators and Boards of Appeal in the European Patent Office have invested considerable effort over the last two decades to adjust the law and practice governing life science inventions to the rapidly changing technological landscape. The number of changes in law and its interpretation during this period stands as testament to what an active field life science research continues to be. Motivated by these changes since this book's first edition, and encouraged by repeated inquiries from friends and colleagues around the world, we felt the time had come for an updated edition of our handbook on patenting in the life sciences.

Despite the many developments mentioned above, the basic nature and intended audience of our book remain unchanged. As for the first edition, the present second edition is intended as a practical handbook to assist those active in the life sciences who are interested in converting the fruits of their research into protective, enforceable rights in Europe. This book does not intend to present an exhaustive account of all legal developments and decisions within the life science field; other existing books admirably meet this call. Rather, we intend to convey a sense of the requirements for patentability as well as the issues influencing patent enforcement by presenting illustrative examples of relevant decisions and claims. In this way, we intend this book to serve as a starting point for those readers who may not have attorney training, but still require general

guidance as to the factors influencing patent protection for life science inventions, and examples of claim language used to capture them. As in the first edition, each section of the book contains both generic and specific examples of claim language to this end.

At the same time, the content of the second edition differs in several important aspects from its predecessor. In December 2007, the EPC-2000 went into force. The EPC-2000 represented the most comprehensive overhaul of the European Patent Convention since its inception in 1973, and included the incorporation of many new material provisions relevant to the life sciences. In fact, many major changes in the EPC related to the European Directive 98/44/EC on the Legal Protection of Biotechnological Inventions. This Biotech Directive was not yet in force when the first edition went to press, and was only implemented in the EPC in 1999. Such fundamental statutory changes would alone have warranted an update of any book based on the old provisions of 1973.

Where the first edition focused primarily on biotechnological subject matter, the present edition addresses the broader field of life sciences. This includes a more detailed treatment of chemistry, particularly as relevant to small molecule therapeutics not offered in the first edition.

A further important difference between this second edition and its predecessor is the choice to now omit all treatment of German national law and practice. While Germany indeed continues to lead the European pharmaceutical market, Applicants increasingly prefer obtaining patent protection in Germany via a European patent application examined and granted centrally in the European Patent Office. By virtue of the simple volume of cases handled by the EPO, this office has become the clear trendsetter in the development of new case law relating to life science inventions. Under these circumstances an exclusive focus on Europe in the present edition seemed appropriate.

Finally, this second edition adds a chapter on the enforcement of patent rights throughout Europe. It is said that the real value of a patent becomes clear only when it is enforced. True to this notion, the new chapter addresses issues of enforcement both within and – especially important in Europe where borders are so close together – between European states. It is our hope that this new chapter will provide a helpful impression of the scope in which a patent may be enforced against a putative infringer, as well as the factors to consider so that such enforcement has the best chances of succeeding.

The further development of life science technology and law will not cease with the publication of this second edition; the field is in constant flux, and this flux is a good thing. For the purposes of preparing the present manuscript, however, we were forced to draw a line, beyond which further developments could no longer be considered. We drew this line at August 1, 2014. Legal developments and case law after this date could not be taken into account in this edition.

The present book thus represents a practical snapshot of the legal landscape surrounding the patenting and enforcement of life science inventions in Europe up to late 2014. It is our hope that this book will assist the interested reader with his or her entry into this exciting field.

Munich, September 2014

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Jens Hammer
Klara Goldbach
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Abbreviations

Art.	Article
BeckRS	Beck-Rechtsprechung (Beck-Case Law)
BIE	Bijblad bij De Industriële Eigendom (since March 2010: Berichten Industriële Eigendom)
BGH	Bundesgerichtshof (German Federal Court of Justice)
CJEU	Court of Justice of the European Union
CPVO	Community Plant Variety Office
CPVR	EU Regulation on Community Plant Variety Rights
EC	European Community
EMA	European Medicine Agency
RGZ	Entscheidungen des Reichsgerichts
EPC	European Patent Convention
EPO	European Patent Office
EU	European Union
EWCA	England and Wales Court of Appeal Decisions
EWHC	England and Wales High Court of Justice Decisions
FSR	Fleet Street Reports
GRUR	Gewerblicher Rechtsschutz und Urheberrecht (Intellectual Property and Copyright Law)
GRUR Int.	Gewerblicher Rechtsschutz und Urheberrecht – International Part
GRUR-RR	Gewerblicher Rechtsschutz und Urheberrecht – Rechtsprechungs – Report (Case Law Report)
Guidelines	Guidelines for Examination in the EPO
IIC	International Review of Industrial Property and Copyright Law, Since 2004: International Review of Intellectual Property and Competition Law
InstGE	Entscheidungen der Instanzgerichte zum Recht des geistigen Eigentums (Decisions of courts concerning intellectual property)
JW	Juristische Woche (Journal)
LS	Die Leitsatzkartei des deutschen Rechts (Catalog of headnotes from German law)
MSPC	Supplementary Protection Certificate for Medicinal Products
OJ EPO	Official Journal of the EPO
OJL	Official Journal of the European Union (L series)
PCT	Patent Cooperation Treaty
PE	Pediatric Extension
RGZ	Entscheidungen des Reichsgerichts
PSPC	Supplementary Protection Certificate for Plant Protection Products
RGZ	Entscheidungen des Reichsgerichts in Zivilsachen (Decisions by the former Supreme Court in civil cases)
RPC	Reports of Patent, Design and Trade Mark Cases
Rule	Rule from Implementing Regulations to the EPC on the Grant of European Patents
Sec.	Section
SPC	Supplementary Protection Certificate

TRIPS		Agreement on Trade-Related Aspects of Intellectual Property Rights
UKHL		United Kingdom House of Lords Decisions
UPOV		International Union for the Protection of New Varieties of Plants
WIPO		World Intellectual Property Organization

A. Life Science Matter

A.I. Summary of historical development

Life science inventions are among the first inventions for which patent applications were ever filed. Patent No. 3 granted by the Patent Office in Finland in 1843 for a novel method for producing yeast cells, and the French patent granted in 1873 for an improved yeast production method by Louis Pasteur are early examples of life science patents. The enactment of the first German patent law in 1877, which was directed to inanimate technical matter, likewise provided possibilities to protect life science matter. Since then, the development towards the present broad range of possibilities for the protection of life science matter, including in particular biotechnological matter, has made vast progress.

Under the EPC, which came into force in 1978, it was possible from the very beginning to protect life science matter. In the following years, the European Patent Office (EPO) progressively broadened the spectrum of protectable subject-matter. One landmark decision is the well-known decision **T 19/90 (Oncomouse/HARVARD)** acknowledging that animals are, in principle, not excluded from protection under the EPC. Further decisions of the Enlarged Board of Appeal of the EPO, including decision **G 1/98 (Transgenic plant/NOVARTIS II)**, **G 1/04 (Diagnostic methods/-)**, **G 2/06 (Use of embryos/WARF)**, **G 1/07 (Treatment by surgery/MEDI-PHYSICS)**, **G 2/07 (Broccoli/PLANT BIOSCIENCE LTD.)**, **G 1/08 (Tomatoes/STATE OF ISRAEL)**, and **G 2/08 (Dosage regimen/ABBOTT RESPIRATORY)** show the progress made as well as the importance of life science matter for the development of the case law and practice of the EPO.

The EPO now provides a broad range of possibilities for protection of all kinds of innovations in the rapidly developing field of life sciences and biotechnology, under which Applicants can obtain patents relating, for example, to plants, plant cells, seeds and roots, animals and parts thereof, microorganisms and cell lines, nucleic acids and proteins, and even parts of the human body.

With the adaptation of the EPO Implementing Regulations to the EU Biotech Directive, the EPO further strengthened its position to adapt to developing technologies, enabling patent protection in the ever-developing field of life sciences and biotechnology.

In April 1995, the Council Regulation on Community Plant Variety Rights came into force, providing uniform protection for plant varieties throughout the European community. For animals, no corresponding industrial property right is presently available. The Council Regulations concerning the creation of a supplementary protection certificate (SPC) for medicinal products and for plant

protection products, enabling the extension of patent terms for these products, furthermore proves that inventions in the life science and biotechnology field are of high commercial importance, warranting such special means for the extension of the duration of patents, not available in other technical fields.

A.II. Definition of life science matter

There is no legal definition of the term “life science matter” in the EPC or EU Regulations. In the field of biotechnological inventions, the term “biological” first was defined by the German Federal Supreme Court in its decision *Rote Taube*. The European Patent Convention initially contained no definitions for “life science matter” or “biotechnological matter”. With the implementation of new rules in 1996, the EPO partially addresses this lack of definitions by providing a definition for the term “biological material”. With the adaptation of the Implementing Regulations to the EU Biotech Directive, Rules 26 to 30 EPC now provide definitions for the field of biotechnology, in particular for the terms “biotechnological inventions”, “biological material” and “plant variety” as well as for “essentially biological processes” and “microbiological processes”. Rules 28 and 29 EPC define exceptions to patentability in the life science field, while Rule 29 EPC additionally addresses inventions concerning the human body and its elements.

B. Legal Provisions

Inventions in the life sciences can be protected under the European Patent Convention (EPC). Under certain circumstances, the term of protection for medicinal products and plant protection products is extendable by a Supplementary Protection Certificate (SPC). An SPC covering a medicinal product for pediatric use may be extended even further.

Furthermore, plant varieties which are not susceptible to protection under the laws mentioned above can be protected under the Council Regulation on Community Plant Variety Rights (CPVR).

The compilation of the relevant provisions of the laws for protecting life science matter and the relevant provisions defining the scope of protection as shown in Annexes 1 to 8 is based on the presently valid versions of the

European Patent Convention (EPC 2000),

Directive 98/44/EC on the Legal Protection of Biotechnological Inventions (Biotech Directive),

Regulation (EC) No. 469/2009 concerning the Creation of a Supplementary Protection Certificate for Medicinal Products of 2009 (MSPC),

Regulation (EC) No. 1610/96 concerning the Creation of a Supplementary Protection Certificate for Plant Protection Products of 1996 (PSPC),

Regulation (EC) No. 2100/94 on Community Plant Variety Rights of 1994 (CPVR), and

Directive 2004/27/EC amending Directive 2001/83/EC on the Community Code relating to Medicinal Products for Human Use (Bolar Directive).

B.I. European Patent Convention (EPC)

In addition to the relevant articles of the EPC reproduced in Annex 1, Annexes 2 to 5 refer to rules of the EPC which are important for inventions in the life sciences.

Art. 52(1) EPC sets out the substantive requirements for patentability, namely novelty, inventive step and industrial application, whereas paragraph (2) refers to subject-matter which is not regarded as patentable. In the context of this book, only the exclusion of discoveries and mathematical methods is of interest. Several rules of the EPC specifically deal with the patentability of biological matter and the delimitation of an “invention” versus a discovery (see Rules 26, 27 and 29 EPC, which are shown in Annex 2).

Art. 53 EPC specifies those inventions which are excluded from patentability, namely inventions which are contrary to “ordre public” or morality (paragraph

(a)), plant or animal varieties and essentially biological processes for the production of plants or animals (paragraph (b)), and methods for treatment of the human or animal body by surgery or therapy and diagnostic methods practiced on the human or animal body (paragraph (c)). Microbiological processes or the products thereof as well as products, in particular substances or compositions, for use in any method of paragraph (c) are, however, patentable.

The terms denoting the groups of animals excluded from patentability under Art. 53(b) EPC previously had different meanings in the three official languages of the EPC. Specifically, the English version of Art. 53(b) EPC (1973) mentioned “animal varieties”, as opposed to “Tierarten” in German and “races animales” in French. Amendment of the German version of this provision in the EPC 2000 to read “Tierrassen” was intended to align these meanings (the corresponding English and French terms were not amended).

With respect to the novelty requirements set out in Art. 54 EPC, the date of filing within the meaning of paragraphs (2) and (3) of Art. 54 EPC can also be a validly claimed priority date of an earlier other application (Art. 89 EPC).

According to Art. 54 EPC, paragraph (3), only earlier European patent applications, but not earlier (non-European) national patent applications, are comprised in the state of the art. Under Art. 153(5) EPC, earlier international (PCT) patent applications for which the EPO is a designated office are also considered as state of the art if certain prerequisites are met.

The disclosures listed in Art. 55 EPC are considered as non-prejudicial only if they occurred less than half a year prior to the filing date of a European patent application.

The knowledge of the hypothetical skilled person is the standard for evaluating the inventive step under Art. 56 EPC.

According to Art. 57 EPC, it is sufficient that the invention can be industrially produced or used in order to fulfill the industrial application requirement.

Art. 82 EPC stipulates that a European patent application has to be unitary. This means that the subject matter of all claims must be linked by a single common concept which is both novel and inventive.

Art. 83 EPC requires an enabling disclosure of the invention. Special formal requirements for nucleotide and amino acid sequences are provided in Rule 30 EPC (see Annex 3). Rules 31, 32, 33 and 34 EPC relate to the deposit and release requirements for biological material (see Annex 4).

Art. 84 EPC states, *inter alia*, that the claims be clear and concise and be supported by the description. The form and content of the claims are set out in Rule 43 EPC (see Annex 5).

Arts. 87 to 89 EPC basically correspond to the provisions of Art. 4 of the Paris Convention, directed to the right of priority.

Art. 69 EPC defining the scope of protection of a European patent is to be interpreted by the “Protocol on the Interpretation of Article 69 of the Convention” (Annex 1). According to Art. 164(1) EPC (see Annex 1), the “Protocol

on the Interpretation of Art. 69 of the Convention” shall be an integral part of the EPC.

Art. 64(2) EPC sets out that the protection conferred by a patent which is directed to a process, extends to the products directly obtained by such process.

As regards the effect of a European patent, Art. 2(2) EPC specifies that the European patent shall have the same effect and be subject to the same conditions as a national patent in each of the contracting states in which the European patent is granted.

B.II. EU Law

This chapter addresses the relevant EU regulations which have to be considered when patenting life science matter.

B.II.1. EU Biotech Directive and its Implementation into the EPC

The EU Biotech Directive (Directive 98/44/EC) was created to harmonize the protection of biotechnological inventions of the different EU member states. In particular, it was intended to clarify the difficulties in determining the differences between inventions and unpatentable discoveries, the patentability of elements of human origin, the scope of protection by a patent relating to a biotechnological invention, and the right to use a biological deposit in addition to written descriptions as a means of disclosure.

The EPO has implemented the EU Biotech Directive, although it is not a member of the EU and thus was not obligated to do so.

The EPO amended its rules in 1999 to take the EU Biotech Directive into account. The respective rules are shown in Annex 2.

B.II.2. EU Regulations Concerning the Creation of a Supplementary Protection Certificate (SPC) for Medicinal Products (MSPC), Pediatric Extension of Duration for Medicinal Products (PE) and Plant Protection Products (PSPC)

The MSPC allows an extension of the term of protection of a basic national or European patent with respect to a specific medicinal product falling under the scope of the basic patent and covered by an authorization to place the product on the market as a medicinal product. Such authorization is granted by a competent national authority or the European Medicines Agency (EMA). The basic patent may protect a medicinal product, or a process for its preparation or its use.

A further pediatric extension of duration (PE) is possible if the medicinal product's suitability for children has been tested.

The relevant Articles of the MSPC and PSPC are shown in Annex 7.

Art. 1 MSPC defines the products for which a supplementary protection certificate (SPC) can be requested and the types of patents on which an SPC can be based.

Art. 4 MSPC provides that the SPC extends only to the product covered by the market authorization which includes any use as a medicinal product covered by the first marketing approval, and any other use covered by subsequent marketing approvals granted before the expiration of the SPC.

Art. 13 MSPC stipulates that the SPC becomes effective upon expiration of the basic patent. The maximum duration is five years. A medicinal product for pediatric use may further be extended by six months.

The CJEU has developed a large body of case law dealing with the requirements for obtaining an SPC and the scope of protection thereof. An overview of the most pertinent cases is given in C.II.1.

As a consequence of the MSPC and the PSPC, Art. 63 EPC was amended and now reads as shown in Annex 1.

B.II.3. Council Regulation on Community Plant Variety Rights (CPVR)

The relevant provisions of the Regulation (EC) No. 2100/94 on Community Plant Variety Rights (CPVR) are listed in Annex 8.

Art. 5 CPVR defines the object of Community plant variety rights whereas Arts. 6 to 10 CPVR relate to the substantive protection requirements.

Art. 63 CPVR refers to the exceptions for registration as regards the denomination of a plant variety.

Art. 52 CPVR partly corresponds to Art. 11 of the revised UPOV Convention (see Annex 8).

There is no provision on the scope of protection in the CPVR.

The CPVR is discussed in more detail in section C.II.2. below.

B.II.4. EU Bolar Directive

The Bolar exemption set out in Art. 10(6) of Directive 2004/27/EC is listed in Annex 9.

C. General Aspects on Protection

C.I. Protection under the EPC

Articles 52 to 57 EPC provide the legal framework regarding the principles of protecting life science inventions at the EPO. Rules 26 to 34 and 41 to 50 of the Implementing Regulations to the EPC indicate important aspects for life science applications (such as rules relating to biological material) as well as general aspects relating to formal requirements for European patent applications.

C.I.1. Non-patentable matter

Art. 52(1) EPC outlines that European patents shall be granted for any inventions, in all fields of technology, provided that they are new, involve an inventive step and are susceptible of industrial application. Art. 52(2), (3) EPC further defines subject-matter which is not to be regarded as inventions, including discoveries and mathematical methods, schemes, rules and methods for performing mental acts, as well as programs for computers. In the life science field the question of such non-patentable matter is of concern regarding patents for products occurring in nature as well as for inventions relating to the processing of data, for example in the health care field.

C.I.1.a. Discoveries

According to Art. 52(2)(a) EPC, discoveries are not regarded as inventions. This topic is of relevance particularly with respect to inventions claiming a previously unrecognized substance (of any type) occurring in nature.

In decision **T 272/95 (Relaxin/HOWARD FLOREY INSTITUTE)**, the Board of Appeal held that the then valid

Rule 23(e)(2) EPC (1973) [corresponding in principle to current Rule 29(2) EPC], however, defines which biological material originating from the human body may be patented. It states that:

- (2) An element isolated from the human body or otherwise produced by a technical process including the sequence or partial sequence of a gene may constitute a patentable invention, even if the structure of that element is identical to that of a natural element.

Accordingly, the Board allowed claims relating to DNAs encoding the human protein preprorelaxin and to the human preprorelaxin *per se*, emphasizing that these

are described in the patent in suit as having been obtained by technical processes. They, thus, answer the definition of patentable elements of the human body given in Rule 23(e)(2)

EPC. Accordingly, they do not fall within the category of inventions that may not be patented for being discoveries (Art. 52(2)(a)).

Similar considerations led to the decision **T 666/05 (Mutation/UNIVERSITY OF UTAH)**, where the Board held that a claim relating to a nucleic acid probe comprising partial DNA sequences of the human BRCA1 gene, described in the patent in suit as having been obtained by technical processes, relates to an isolated element of the human body as defined in Rule 29(2) EPC, thus defining patentable subject matter.

In decision **T 80/05 (Method of diagnosis/UNIVERSITY OF UTAH)**, the Board held that the findings of decision **T 272/95** relating to products are *a fortiori* also applicable to method claims.

In decision **T 338/00 (Multimeric receptors/SALK INSTITUTE)**, the Board held that in relation to the evaluation of the question whether or not claimed subject matter represented a discovery, the requirements of being susceptible of industrial application had to be evaluated in the context of the claimed subject-matter. The Board stated that

in the present case the Board felt it necessary to examine whether for the claimed heterodimeric receptor or dimer and for the claimed method to modulate transcription activation of a gene the way in which they are capable of being exploited in industry can be derived from the description (...). These questions are directly linked to the question whether the disclosed interaction of receptors to form heterodimers is a mere “discovery”, i.e. the result of purely intellectual activity with no practical or technical character. The Board agrees with the Appellant in that the present application not only discloses the presence of cooperative interactions to form heterodimeric receptors between the retinoic acid receptor RXR and other members of the steroid/thyroid hormone receptor hormone superfamily, but also provides further evidence on the use of these heterodimers for modulating suitable transcription expression systems.

The Board concluded that the activities and products disclosed in the application are not aimed at an abstract or intellectual character but at a direct technical result that may be clearly applied in an industrial activity (modulation of the expression of a gene/product of interest in a particular expression system, screening of products with specific pharmacological activity etc.), so that the invention could not be considered as a discovery.

In decision **T 2050/07 (DNA mixture Analysis/PERLIN)** the Board questioned whether a claimed method including method steps directed to solving specific coupled linear equations based on data obtained by analyzing an amplified DNA sample was a mathematical method which as such should not be regarded as a patentable invention. The Board held:

It is established case law that claimed subject-matter is not excluded from patentability as a non-invention under Article 52(2) EPC for the sole reason that it contains features which might be considered to be non-technical. In the present case, claim 1 as well as dependent claims 2 to 21 are directed to a method of analyzing a DNA sample. This method comprises inter alia a step of amplifying the DNA sample, wherein the amplification product produces a signal comprising signal peaks (see step (a)), a step of detecting signal peak amounts and a step of quantifying the amounts using quantifying means that include a computing device [...] (see

step (b)). Already for the reason that both steps (a) and (b) are obviously performed using dedicated laboratory equipment and devices the claimed methods cannot be considered as being devoid of technical character.

The Board thus considered a claim comprising a method step being directed to a mathematical method as being in accordance with the requirements of Art. 52(2) EPC since it did contain additional method steps considered by the Board as being of technical nature.

C.I.2. Exceptions to patentability

The EPC mentions several exceptions to patentability in Art. 53 EPC, each exception being relevant in the field of life science inventions as will be discussed in the following.

C.I.2.a. Inventions contrary to “ordre public” or morality

Exceptions to patentability based on “ordre public” or morality are addressed in Art. 53(a) EPC. According to this provision, a patent shall not be granted if the commercial exploitation of an invention would contravene the “ordre public” or morality requirement. However, such exploitation shall not be deemed to be so contrary merely because it is prohibited by law or regulation in some or all of the Contracting States.

In addition to the exploitation of an invention, Art. 53(a) EPC 1973 also referred to the publication of an invention. With the coming into force of Art. 27(2) of the TRIPS Agreement and Directive 98/44/EC of 6 July 1998, the publication of an invention was no longer considered as a possible obstacle with regard to “ordre public” or morality. Consequently, the term “publication or” was deleted and the term “commercial” was added in connection with the exploitation. Art. 6(1) of the Directive exclusively refers to inventions being unpatentable if the commercial exploitation would be contrary to “ordre public” or morality. Art. 6(2) of the Directive specifies four subject matters which, in particular, are considered unpatentable, namely

- (a) processes for cloning human beings;
- (b) processes for modifying the germ line/genetic identity of human beings;
- (c) uses of human embryos for industrial or commercial purposes;
- (d) processes for modifying the genetic identity of animals which are likely to cause them suffering without any substantial medical benefit to man or animal, and also animals resulting from such processes.

The subject of Art. 6(2) of the Directive was identically introduced into the EPC 1973 as Rule 23d EPC, which is now Rule 28 EPC.

Since it is the generally accepted principle in the interpretation of a law that an exception to a general provision is to be construed in a narrow manner, this approach equally applies to exceptions to patentability based on “ordre public”

or morality. Indeed, document IV/2071/61-E, page 5, point 2, first paragraph of the historical documentation of the EPC Working Party states that “the concept of patentability in the European patent law must be as wide as possible”. The Boards of Appeal have adopted a narrow interpretation regarding Art. 53(a) EPC in numerous decisions. Therefore, the basic approach in this regard is:

Can this subject matter be protected?

rather than

Can this subject matter be excluded from protection?

In order to answer this question, it is necessary to have a closer look at the concepts of “ordre public” and morality.

There are at least two decisions from the Boards of Appeal defining the concepts of “ordre public” and morality.

In decision **T 356/93 (Plant cells/PLANT GENETIC SYSTEMS)**, the concept of “ordre public” was interpreted as covering

the protection of public security and the physical integrity of individuals as part of society. This concept encompasses also the protection of the environment. Accordingly, under Article 53(a) EPC, inventions the exploitation of which is likely to breach public peace or social order (for example, through acts of terrorism) or to seriously prejudice the environment are to be excluded from patentability as being contrary to “ordre public”.

Later decision **T 866/01 (Euthanasia compositions/MICHIGAN STATE UNIVERSITY)** refers to certain general principles of “ordre public” by stating:

In general “ordre public” is formed by the ethically based constitution or other rules, usually backed up by penal provisions that reflect the basic values prevailing in society and trade. These protected values can in particular include public safety, the integrity of the individual and nowadays, certainly also the protection of environment [...].

According to **T 356/93 (Plant cells/PLANT GENETIC SYSTEMS)**, the concept of morality is

related to the belief that some behaviour is right and acceptable whereas other behaviour is wrong, this belief being founded on the totality of the accepted norms which are deeply rooted in a particular culture. For the purposes of the EPC, the culture in question is the culture inherent in European society and civilisation. Accordingly, under Article 53(a) EPC, inventions the exploitation of which is not in conformity with the conventionally accepted standards of conduct pertaining to this culture are to be excluded from patentability as being contrary to morality.

Decision **T 866/01 (Euthanasia compositions/MICHIGAN STATE UNIVERSITY)** refers to certain general principles of morality by stating:

Morality is an old legal concept. It was adopted in western legal systems from Roman law as “boni mores”. Morality is one of the fundamentals of our legal system and at the same time forms the basis for the inclusion of extra-legal principles of ethics in the law. The legal approach based on morality for the EPC can be found in the concepts of the European cultural and legal systems. Morality constitutes actual ethically-based norms of behaviour that have be-

come socially binding through being generally accepted. The exploitation of an invention only infringes morality if it is regarded as reprehensible by society in general or at least by the trade concerned (see Singer/Stauder/Schatz, Art. 53, Rdnr. 16–18; and see also T 356/93, (loc. cit.), point 6 of the Reasons).

The decisions which are discussed in the following are based on these concepts of “ordre public” and morality.

Recent years have seen very controversial discussions with respect to the morality of protecting biotechnological inventions relating, in particular, to transgenic animals and plants, human genes, gene therapy, human embryos and stem cells. Before addressing these subjects, one decision in the field of small molecules will be discussed.

T 866/01 (Euthanasia compositions/MICHIGAN STATE UNIV.) deals with a composition comprising a cardiotoxic compound in a cardiotoxic amount and another compound in a lethally anesthetic amount. According to the patent, the composition is used for the humane killing of lower animals. The Board stated that the avowed use indicated in the patent is decisive for judging whether Art. 53(a) EPC is infringed. The mere possibility of abuse of the invention would not be sufficient to deny patent protection pursuant to Art. 53(a) EPC if the invention can also be exploited in a way which does not and would not infringe “ordre public” and “morality”.

With respect to transgenic animals, the early decision **T 19/90 (Oncomouse/HARVARD)** develops a test for judging whether Art. 53(a) EPC is infringed in the case of animals. The Board of Appeal held that, on the one hand, the suffering of the animal and possible danger to the environment and, on the other hand, the usefulness of the invention to mankind have to be carefully evaluated. Patentability would not be excluded for reasons of immorality if the advantages outweigh the disadvantages. In the following opposition procedure of the patent in question, the Board of Appeal issued decision **T 315/03 (Transgenic animals/HARVARD)**, which discusses in great detail the differences between the **T 19/90** test and the test of Rule 28(d) EPC, which rule had, in the meantime, been introduced into the EPC 1973 as Rule 23d(d) EPC. The Board stated that the **T 19/90** test balances suffering of animals against usefulness to mankind, but not against substantial medical benefit to man or animal as found in the Rule 28(d) EPC test and, accordingly, the **T 19/90** test would be broader. Further, whereas the Rule 28(d) EPC test only requires a likelihood of animal suffering and a likelihood of substantial medical benefit, the **T 19/90** test requires a “careful weighing up” of the matters to be balanced. The Board emphasized that the Rule 28(d) EPC test requires three matters to be established: likely animal suffering, likely substantial medical benefit, and the necessary correspondence between the two in terms of the animals in question. Further, if a case falls within an exception set out in Rule 28(d) EPC, then it must *ipso facto* be denied a patent under Art. 53(a) EPC. However, cases not falling within the limited exclusions of Rule 28(d) EPC must then be considered under the broader concept of Art. 53(a) EPC. In the Board’s opinion in **T 315/03**

(Transgenic animals/HARVARD), there are, thus, in effect two quite different Art. 53(a) EPC objections:

On the one hand, a “Rule 23d-type” Article 53(a) EPC objection which requires only that the invention is assessed as to whether or not it falls in one of the four limited categories set out in the Rule and, on the other hand, a “real” Article 53(a) EPC objection which requires an assessment as to whether or not exploitation of the invention in question would be contrary to morality or “ordre public”. When making the latter assessment, the case law offers some guidance.

The Board considered that the only starting point for a “real” Art. 53(a) EPC assessment is the test suggested in **T 19/90** for the assessment of cases concerning the genetic manipulation of animals.

Due to the reasons outlined above regarding transgenic animals, it is clear that the protection of transgenic plants or parts thereof should be less critical with regard to moral considerations if the achieved results, e.g. higher yield, resistance to diseases and parasites, etc. are of benefit for man. In **T 356/93 (Plant cells/PLANT GENETIC SYSTEMS)** it was emphasized that one must establish whether or not the claimed subject-matter relates to a misuse or to a destructive use of plant biotechnology. Further, an objection under Art. 53(a) EPC on the grounds that the exploitation of the invention would seriously prejudice the environment would presuppose that the threat to the environment be sufficiently substantiated at the time the decision is made by the EPO. This ruling was adopted in **T 475/01 (Phosphinothricin – Resistenzgen/BAYER)**.

With respect to human genes, **T 272/95 (Relaxin/HOWARD FLOREY INSTITUTE)** points to Rule 23(e)(2) EPC 1973 (now Rule 29(2) EPC 2000) and concludes that human genes are generally not considered as an exception to patentability under Art. 53(a) EPC.

In the later decision **T 1213/05 (Breast and ovarian cancer/UNIVERSITY OF UTAH)**, the Board observed that the EPC contains no provision establishing a requirement for Applicants to submit evidence of a previous informed consent or a benefit-sharing agreement and, in this respect, referred to recital (26) of the Directive 98/44/EC stating that the person from whose body the material is taken must have had all opportunity of expressing free and informed consent thereto, in accordance with national law. The decision further emphasizes that Art. 53(a) EPC refers to the “exploitation of the invention” and not to the “exploitation of the patent”. Objections based on socioeconomic and ethical consequences of patenting diagnostic methods involving the use of human genetic material are directed to the exploitation of the patent and, thus, do not fall within Art. 53(a) EPC (see also **T 80/05 (Method of diagnosis/UNIVERSITY OF UTAH)** and **T 666/05 (Mutation/UNIVERSITY OF UTAH)**).

With respect to human embryonic stem cells, in **T 1374/04 (Stem cells/WARF)**, the following questions were referred to the Enlarged Board of Appeal in 2006.

1. Does Rule 23d(c) EPC 1973 [now corresponding to Rule 28(c) EPC] apply to an application filed before the entry into force of the rule?
2. If the answer to question 1 is yes, does Rule 23d(c) EPC 1973 [now corresponding to Rule 28(c) EPC] forbid the patenting of claims directed to products (here: human embryonic stem cell cultures) which – as described in the application – at the filing date could be prepared exclusively by a method which necessarily involved the destruction of the human embryos from which the said products are derived, if said method is not part of the claims?
3. If the answer to question 1 or 2 is no, does Article 53(a) EPC forbid patenting such claims?
4. In the context of questions 2 and 3, is it of relevance that after the filing date the same products could be obtained without having to recur to a method necessarily involving the destruction of human embryos (here: e.g. derivation from available human embryonic stem cell lines)?

The Enlarged Board of Appeal, in decision **G 2/06 (Use of embryos/WARF)**, answered questions 1 and 2 with yes. No answer was thus required for question 3. Regarding question 4, it was stated that in the context of the answer to question 2, it is irrelevant that after the filing date, the same products could be obtained without having to resort to a method necessarily involving the destruction of human embryos.

In answering question 2, the Enlarged Board of Appeal in particular referred to the provision of Art. 6(2)(c) of Directive 98/44/EC corresponding to Rule 28(c) EPC (formerly Rule 23d(c) EPC 1973) excluding “uses of human embryos for industrial or commercial purposes” and pointed out that neither the EU Legislator nor the EPC Legislator has defined the term “embryo”, which definition was however rendered by the ECJ in a later decision (**C 34/10, Brüstle case**) which defined an “embryo” starting already at the stage of a fertilized egg. Since Rule 28(c) EPC refers to “invention” in the context of its exploitation, one must look at the technical teaching of the application as a whole, not just the explicit wording of the claims. The terms “for industrial or commercial purposes” in Rule 28(c) EPC had been used in order to distinguish between the uses of human embryos for industrial or commercial purposes (which were excluded from patentability), and inventions for therapeutic or diagnostic purposes applied to the human embryo and useful to it (which were not). In real life, it might prove very difficult to decide when a method performed on an embryo might be useful to it. Whether or not a diagnostic method might be useful to the embryo may well depend on the result of the diagnostic method.

In line with decision **G 2/06**, the Board in **T 522/04 (Stem cells/CALIFORNIA)** ruled that methods involving the destruction of human embryos are to be regarded as non-patentable in view of Art. 53(a) EPC in combination with Rule 28(c) EPC. The same applies to an apparatus comprising cells within the channels of a matrix, said cells including embryonic stem cells of human origin, as decided in **T 329/06 (Perfused microtissue/MIT)**.

In **T1836/10 (Obtaining embryonic stem cells/WÜRFEL)** the Board held in an *obiter dictum* that a claim in which human embryos are used as starting material for isolating stem cells would be in conflict with Rule 28c EPC even if the embryo is not destroyed by the claimed process. For this reason, a direct use of an embryo for obtaining stem cells is not allowable, regardless of the fate of the embryo.

In a recent case, **T 2221/10 (Culturing stem cells/TECHNION)**, the Appeal Board found that an invention which makes use of stem cell lines which were initially obtained under destruction of human embryos is excluded under Art. 53(a) and Rule 28(c) EPC.

In CJEU Case **C-364/13** the Advocate General recently issued his opinion stating that activated oocytes which are induced to undergo initial embryogenesis (parthenotes) should not be regarded an embryo since such parthenotes could not develop into a human being. It remains to be seen if the CJEU will follow this opinion in its final decision.

C.I.2.b. Plant and animal varieties

According to Art. 53(b) EPC, plant and animal varieties are excluded from patentability.

C.I.2.b.a. Plant Varieties

The definition of the term “plant variety” has previously been the subject of a number of decisions of the EPO Boards of Appeal, in particular, **T 49/83 (Propagating material/CIBA-GEIGY)**, **T 320/87 (Hybrid plants/LUBRIZOL)** and **T 356/93 (Plant cells/PLANT GENETIC SYSTEMS)**. The EPC now provides a formal legal definition of the term “plant variety” in Rule 26(4) EPC, which reads as follows:

“Plant variety” means any plant grouping within a single botanical taxon of the lowest known rank, which grouping, irrespective of whether the conditions of the grant of a plant variety right are fully met, can be:

- (a) defined by the expression of the characteristics that result from a given genotype or a combination of genotypes,
- (b) distinguished from any one other plant grouping by the expression of at least one of said characteristics, and
- (c) considered as a unit with regard to its stability for being propagated unchanged.

This rule makes clear the Legislator’s intention that in order to be considered a plant variety, the plant in question must be both genetically homogenous as well as stable in its propagation.

Rule 26(4) EPC is substantially identical to Art. 1(vi) of the UPOV Convention of 1991 (see Annex 8) as well as to Art. 5(2) of the EC Regulation 2100/94 on Community Plant Variety Rights (CPVR; see Annex 8), which establishes protection for plant Breeder rights relating to plant varieties. Unifying the definition for “plant variety” in the UPOV Convention, CPVR and the EPC has

the effect that where protection for a “plant variety” is possible outside the EPC, it is excluded from patentability under the EPC. Conversely, where protection is possible for a non-varietal plant under the EPC, protection under e.g. CPVR is impossible because this regulation applies only for plant varieties. As an EPO Board of Appeal succinctly noted in decision **T 1854/07 (Oil from seeds/ CONSEJO SUPERIOR)**:

The extent of the exclusion for patents is the obverse of the availability of plant variety rights.

Enlarged Board of Appeal decision **G 1/98 (Transgenic plant/NO-VARTIS II)** provided further clarification regarding the exclusion of plant varieties under Art. 53(b) EPC. This decision stated that a claim encompassing plant varieties is not excluded from patentability under Art. 53(b) EPC as long it does not individually claim these varieties. This has the effect that it is fundamentally possible to obtain patent protection in the EPO for a genus of plants which may include individual plant varieties, as long as the subject matter of the claim is not directed to a single plant variety.

G 1/98 also held that when examining a claim to a process for the production of a plant variety, Art. 64(2) EPC is not to be taken into consideration. Art. 64(2) EPC stipulates that if the subject matter of the European patent is a process, the protection conferred by the patent extends to the products directly obtained by such process (but not to identical products obtained by some other process than that claimed). So a claim directed to a process of producing a specific plant also covers the resulting plant in as far as it was produced by the claimed method. The holding of **G 1/98** means that even if this specific plant is a “plant variety” in the sense of Rule 26(4) EPC, the process claim will not be excluded from patentability under Art. 53(b) EPC. **G 1/98** therefore suggests that process claims should be treated differently than product claims in regard to the exclusion of “plant varieties” under Art. 53(b) EPC.

Finally, the Enlarged Board stated in decision **G 1/98** that the exclusion of plant varieties in Art. 53(b) EPC applies to plant varieties (when claimed as products) regardless of the way in which these varieties are produced. Decision **G 1/98** therefore makes clear that the question of whether or not a plant is considered to be an excluded plant variety depends only on whether or not it meets the criteria set out in the definition of Rule 26(4) EPC.

C.I.2.b.b. *Animal Varieties*

Art. 53(b) EPC in its English wording excludes animal varieties (German wording: “Tierrassen” (animal breeds); French wording: “races animales” (animal breeds)) from patentability. The EPC mentions animal varieties in the context of patentable biotechnological inventions. Rule 27(b) and (c) EPC stipulates that

Biotechnological inventions shall also be patentable if they concern:
[...]

- (b) plants or animals if the technical feasibility is not confined to a particular plant or animal variety;
- (c) a microbiological or other technical process, or a product obtained by means of such a process other than a plant or animal variety.

Unlike the term “plant variety” which is explicitly defined in Rule 26(4) EPC, the term “animal variety” is not formally defined in either the EPC or case law of the EPO Boards of Appeal. However, decision **T 315/03 (Transgenic animals/HARVARD)** held in its headnote 7.2 that

a definition [of the term “animal variety”] by reference to taxonomical rank would be both consistent with the position in relation to plant varieties and in the interest of legal certainty. With such a definition, an assessment could be made as to whether the claimed subject-matter is excluded from patentability under Article 53(b) EPC as interpreted by Rule 27(b) EPC – i.e. whether, in a case concerning animals, the technical feasibility of the invention is not confined to a particular animal variety.

Unfortunately, the Board was not more specific as to the level of “taxonomical rank” which is sufficient to meet the threshold of “animal variety”. In doubt, this will likely be the taxonomical rank which specifies a particular animal species meeting the requirements of Rule 26(4) EPC for plants, i.e. any animal grouping within a single animal taxon which can be (a) defined by the expression of the characteristics that results from a given genotype or combination of genotypes; (b) distinguished from any other animal grouping by the expression of at least one of said characteristics; and (c) considered as a unit with regard to its suitability for being propagated unchanged.

The reader will note that the above corresponds to the definition of Rule 26(4) EPC, simply applied to animals rather than plants. However, given multiple Boards’ statements that the EPO’s stances for the exclusion provision of Art. 53(b) EPC regarding plants should also apply for animals, such an extension seems justified.

C.I.2.c. Essentially biological processes for the production of plants or animals

In addition to plant and animal varieties, Art. 53(b) EPC also excludes from patentability “essentially biological processes for the production of plants or animals”. From the wording of this exclusion alone, it is clear that essentially biological processes are excluded from patentability, regardless of whether the plants or animals produced by these processes are “varieties”. This exclusion provision is to be interpreted in a narrow manner, especially in view of the fact that it does not apply to microbiological processes or the products thereof (as stipulated in Art. 53(b) EPC, second half sentence).

The term “essentially biological” is formally defined in Rule 26(5) EPC, which states that

[a] process for the production of plants or animals is essentially biological if it consists entirely of natural phenomena such as crossing or selection.

A difficulty with this provision is interpreting the terms “crossing” and “selection”, specifically when considering whether these verbs are intended to be interpreted in a transitive or an intransitive sense. The Legislator intended to give these verbs in Rule 26(5) EPC a transitive meaning, i.e. that plants or animals are crossed or are selected by human intervention. However, these verbs also carry an intransitive meaning equivalent to what happens in nature, where plants self-cross, for example, by pollination, and self-select, for example, by differential survival of plants having advantageous characteristics for thriving in their environment. The definition in Rule 26(5) EPC thus appears insufficient.

Questions regarding the definition of the term “essentially biological” were referred to the Enlarged Board of Appeal in the two decisions **T 83/05 (Broccoli/PLANT BIOSCIENCE)** and **T 1242/06 (Tomatoes/STATE OF ISRAEL)**. The Enlarged Board of Appeal consolidated their response to these two referrals in respective decisions **G 2/07 (Broccoli/PLANT BIOSCIENCE)** and **G 1/08 (Tomatoes/STATE OF ISRAEL)**, the headnotes of which are identical and read as follows:

1. A non-microbiological process for the production of plants which contains or consists of the steps of sexually crossing the whole genomes of plants and of subsequently selecting plants is in principle excluded from patentability as being “essentially biological” within the meaning of Article 53(b) EPC.
2. Such a process does not escape the exclusion of Article 53(b) EPC merely because it contains, as a further step, or as part of any of the steps of crossing and selecting, a step of a technical nature which serves to enable or assist the performance of the steps of sexually crossing the whole genomes of plants or of subsequently selecting plants.
3. If, however, such a process contains within the steps of sexually crossing and selection an additional step of a technical nature, which step in itself introduces a trait into the genome or modifies a trait in the genome of the plant produced, so that the introduction or modification of that trait is not the result of the mixing of the genes of the plants chosen for sexual crossing, then the process is not excluded from patentability under Article 53(b) EPC.
4. In the context of examining whether such a process is excluded from patentability as being “essentially biological” within the meaning of Article 53(b) EPC, it is not relevant whether a step of a technical nature is a new or a known measure, whether it is trivial or a fundamental alteration of a known process, whether it does or could occur in nature or whether the essence of the invention lies in it.

By the wording of its opinion, the Enlarged Board of Appeal made clear that the exclusion of “essentially biological processes” under Rule 26(5) EPC is intended to apply to the transitive meaning of “crossing” and “selection” by which plants (or animals) are crossed and are selected, as the objects of human activity. In their further holdings, the Board drew a clearer dividing line between processes which are “essentially biological” and those which are not by requiring that the “essentially biological” process is a) non-microbiological and b) consists of the steps of sexually crossing the whole genomes of plants and of subsequently selecting plants.

The EPO Guidelines for examination provide some helpful examples of situations in which the holdings of **G 2/07 (Broccoli/PLANT BIOSCIENCE)**

and **G 1/08 (Tomatoes/STATE OF ISRAEL)** might apply. Some of these examples relate to animals, suggesting that the holding of **G 2/07 (Broccoli/PLANT BIOSCIENCE)** and **G 1/08 (Tomatoes/STATE OF ISRAEL)** with regard to the term “essentially biological process” should not be restricted to plants, but should also apply to animals. According to the Guidelines, a method of crossing, inter-breeding or selectively breeding animals such as horses, involving merely selecting for breeding and bringing together those animals (or their gametes) having certain characteristics would be “essentially biological” and therefore unpatentable. This method would remain essentially biological and unpatentable even if it would contain an additional feature of a technical nature, for example, the use of a genetic molecular marker to select either parent or progeny. However, a process involving inserting a gene or trait into a plant by genetic engineering does not rely on recombination of whole genomes and the natural mixing of plant genes, and would therefore be patentable. Further, a process of treating a plant or animal to improve its properties or yield or to promote or to suppress its growth, for instance, a method of pruning a tree, would not be an essentially biological process for the production of plants or animals since it is not based on the sexual crossing of whole genomes and subsequent selection of plants or animals. The same would apply to a method of treating a plant characterized by the application of a growth-stimulating substance or radiation. As a final example, the EPO Guidelines note that the treatment of soil by technical means to suppress or promote growth of plants would also not be excluded from patentability.

From the above holdings of the Enlarged Board of Appeal in decisions **G 2/07** and **G 1/08**, taken together with the examples provided in the EPO Guidelines, it is clear that the EPO views the sexual crossing of whole genomes of plants (or animals) and the subsequent selection of the resulting organisms as the crucial criteria in determining whether or not a process is “essentially biological” and therefore excluded from patentability under Art. 53(b) EPC.

The exclusion provision of Art. 53(b) EPC does not, however, apply to microbiological processes or the products thereof. Decision **T 19/90 (Oncomouse/HARVARD)** points out that the allowability of microbiological processes or the products thereof is actually “an exception to the exception to patentability” provided for by Art. 53(b) EPC. Consequently, patents are obtainable for animals produced by a microbiological process. The term “microbiological process” – as the exception to an exception – should be broadly construed.

According to **T 356/93 (Plant cells/PLANT GENETIC SYSTEMS)** the above principle evaluated for the patentability of animals should apply correspondingly for plant varieties. Specifically, the Board was satisfied that

the proper course of action, in view of the recent important developments in the field of microbiology, is to interpret Article 53(b), second half-sentence, EPC according to objective teleological criteria and that this way of interpreting is consistent with the legislative intent underlying this provision. Among these criteria, the principle of equal treatment of what is of the same kind or similar is of great importance. (point 32)

The Board further stated that according to the current practice of the EPO, the term “microorganism” includes

not only bacteria and yeasts, but also fungi, algae, protozoa and human, animal and plant cells, ie all generally unicellular organisms with dimensions beneath the limits of vision which can be propagated and manipulated in a laboratory. Plasmids and viruses are also considered to fall under this definition (see Guidelines for Examination, C-IV, 3.5). (point 34)

Accordingly, the term “microbiological” was interpreted as

qualifying technical activities in which direct use is made of micro-organisms as defined above. These include not only traditional fermentation and biotransformation processes, but also the manipulation of micro-organisms by genetic engineering or fusion techniques, the production or modification of products in recombinant systems, etc., ie, briefly, all activities in which an integrated use is made of biochemical and microbiological techniques, including genetic and chemical engineering techniques, in order to exploit the capacities of microbes and cultured cells [...]. (point 35)

In the Board’s judgment the concept of “microbiological processes” refers to

processes in which micro-organisms as defined above [...], or their parts, are used to make or to modify products or in which new micro-organisms are developed for specific uses. Consequently, the concept of “the products thereof” under Article 53(b), second half-sentence, EPC, encompasses products which are made or modified by micro-organisms as well as new micro-organisms as such. (point 36)

The Board further concluded that

“technical processes including a microbiological step” may not simply be equated with “microbiological processes”. Nor can the resulting final products of such technical processes (e.g. plant varieties) be defined as “products of microbiological processes” within the meaning of Article 53(b), second half-sentence EPC [...]. (point 39)

G 2/07 and **G 1/08** include a definition (of sorts) for the term “microbiological process”, defined as the converse “non-microbiological”. A non-microbiological process is defined as containing or consisting of the steps of sexually crossing the whole genomes of plants and of subsequently selecting plants. This “non-microbiological process” is defined in the context of clarifying the term “essentially biological” within the meaning of Art. 53(b) EPC.

A subsequent decision **T 1199/08 (Selected sperm/XY)** confirmed that the process referred to in **G 2/07** was a “non-microbiological process” for the production of plants which includes the step of sexually crossing the whole genome of plants and subsequently selecting plants, i.e. a traditional method of breeding new plant varieties.

From these converse definitions, it can be concluded that a microbiological process in the sense of Art. 53(b) EPC is a process, the nature of which departs from traditional breeding processes by the inclusion of further technical steps, e.g. altering of plant genomes by recombinant techniques.

New questions were recently raised regarding products of essentially biological processes. Art. 53(b) EPC does not exclude products of essentially biological processes from patentability. Two decisions have referred relevant questions re-

lating to this provision of the EPC to the Enlarged Board of Appeal for review. **T 1242/06 (Tomatoes II/STATE OF ISRAEL)** and **T 83/05 (Broccoli II/PLANT BIOSCIENCE)** have each considered, and asked the Enlarged Board of Appeal to clarify, whether the exclusion of essentially biological processes for the production of plants in Art. 53(b) EPC can have a negative effect on the allowability of a product claim directed to plants or plant materials such as plant parts when the product is claimed in product-by-process format (see section C.I.3.e.a for an explanation of product-by-process format). Specifically: Is a claim directed to plants or plant material other than a plant variety allowable if its process features define an (otherwise excluded) essentially biological process for the production of plants? By the bare wording of Art. 53(b) EPC, only three things are excluded from patentability: plant varieties, animal varieties and essentially biological processes for the production of plants or animals. The Board's questions to the Enlarged Board of Appeal in **T 1242/06** and **T 83/05** essentially ask whether this list should be expanded to contain a fourth exclusion: products of essentially biological processes for the production of plants or animals when the claims to these products are defined in terms of the methods of production. These questions are currently pending before the Enlarged Board of Appeal as **G 2/12 (Tomatoes/STATE OF ISRAEL)** (referred by **T 1242/06**) and **G 2/13 (Broccoli II/PLANT BIOSCIENCE)** (referred by **T 83/05**). As this book goes to press, the Enlarged Board of Appeal has not yet issued its opinion in response to these questions.

C.I.2.d. Methods for treatment of the human or animal body by surgery or therapy and diagnostic methods practised on the human or animal body

Biotechnological processes and products resulting from them are often applied in methods for treatment of the human or animal body by surgery or therapy and diagnostic methods practiced on the human or animal body. Such methods fall under the exceptions to patentability in accordance with Art. 53(c) EPC (formerly Art. 52(4) EPC 1973).

One intention underlying this exclusion from patentability is to ensure that no one who wants to use the above methods as part of the medical treatment of humans or animals is prevented from doing so by patents. As an exclusion clause the prohibition must, however, be narrowly construed.

The following decisions of the EPO address this provision.

In decision **T 19/86 (Pigs II/DUPHAR)** a Board of Appeal held that treatment by therapy includes both prophylactic and curative treatments of disease.

Similarly, in case **T 81/84 (Dysmenorrhea/RORER)** a Board concluded:

Irrespective of the origin of pain, discomfort or incapacity, its relief, by the administration of an appropriate agent, is to be construed as "therapy" or "therapeutic use" in the sense of Article 52(4) EPC, [...] (headnote)

Decision **T 116/85 (Pigs I/WELLCOME)** states that a method which requires the treatment of an animal body by therapy is a method which falls within the prohibition of patentability set out in Art. 52(4) EPC 1973 (now Art. 53(c) EPC) since:

It is not possible as a matter of law to draw a distinction between such a method as carried out by a farmer and the same method as carried out by a veterinarian, and to say that the method when carried out by a farmer is an industrial activity and therefore patentable under Article 57, and when carried out by a veterinarian is a therapeutic treatment not patentable under Article 52(4). (headnote II)

In case **T 290/86 (Cleaning plaque/ICI)** a Board of Appeal held:

If the claimed invention is not directed solely to a cosmetic effect, but is also necessarily defining a treatment of the human body by therapy as well, such a claim is excluded from patentability (citation omitted). (headnote I)

In decision **T 24/91 (Cornea/THOMPSON)** a Board of Appeal decided that a method for treatment of the human body falls within the exclusion of Art. 52(4) EPC 1973 (now Art. 53(c) EPC) in those cases where,

in view of the health risks connected with such a treatment, a claimed method for treatment has to be performed by a physician or under his supervision, [...] (point 2.4)

Furthermore, a Board of Appeal observed in decision **T 820/92 (Contraceptive method/THE GENERAL HOSPITAL)** that a method involving administration of two or more substances falls under the prohibition of Art. 53(c) EPC

already if the administration of one of the substances is a treatment by therapy, and the administration of this substance is a feature of the claim. (point 5.9)

It can be seen from the above decisions that under European practice a method is considered as being excluded from patentability as soon as it has any therapeutic application, irrespective of whether or not it may additionally have a non-therapeutic application.

Although the case law established over the years appears to be fairly restrictive for Applicants in that a method is excluded from patent protection as soon as it contains one therapeutic step, the good thing is that case law allows so-called purpose-limited product claims as a claim type for claiming inventions in the medical treatment field. Case law basically acknowledges any measure forming part of a medical treatment for establishing patentability even if the only novel feature in such a claim would be e.g. the time point at which a certain drug is administered. As long as the proper claim format is maintained, basically any type of a new use of a known compound can be used for establishing patentability of a claim. This was explained in **G 2/08 (Dosage Regime/ABBOTT RESPIRATORY)**. The following cases give some indication of which measure(s) within a medical treatment may be used to delimit a claim from the prior art.

In landmark decision **G 5/83 (Second Medical Indication/EISAI)**, the Enlarged Board of Appeal allowed a claim for preparing a medicament for a new

therapeutic indication. The novel feature over the prior art was a new disease to be treated with a known substance. In that case, the Board stated that:

A European patent may be granted with claims directed to the use of a substance or composition for the manufacture of a medicament for a specified new and inventive therapeutic application.

Many further decisions followed this finding, for example **T 1127/05 (Inhibition of Angiogenesis/SCRIPPS RESEARCH INSTITUTE)** where the Board acknowledged that the use of a known organic compound for the inhibition of an $\alpha v\beta 3$ -mediated angiogenesis was a novel teaching over the disclosure that the same compound can be used for treating $\alpha v\beta 5$ -mediated angiogenesis.

Besides the treatment of a **novel disease** with a known compound, case law has also acknowledged other features forming part of a medical treatment as suitable for delimiting a claim over a prior art teaching. Such a further feature can be a different **dosage** of the claimed embodiments over the prior art. For example, in **T 230/01 (Descarboethoxyloratadine/SEPRACOR)** the Board acknowledged that there was no hint in the prior art to treat an allergic condition at dosage levels significantly lower than what was recommended in the prior art, and therefore found the claim to be novel in view of the different, i.e. lower dosage level.

A further feature for delimiting medical use claims is the **route/mode of administration**. In **T 51/93 (HCG/SERONO)**, the Appeal Board acknowledged the novelty of a subcutaneous administration of a substance via intramuscular administration as described in the prior art. In a further case, **T 290/86 (Cleaning Plaque/ICI)**, the Board explained that the mode of administration is a critical factor in a medical treatment and there is no reason for any *a priori* bar to rely on such a feature in order to distinguish the claim over the prior art. In **T 904/98 (Dermal Aspirin/GUNDERSON)**, the Board saw a distinction between the subcutaneous administration versus the sublingual administration of aspirin.

A further option to delimit a medical use claim over the prior art is to define a **different patient group**. In **T 19/86 (Pigs II/DUPHAR)**, the Board acknowledged a group of seronegative pigs as being novel over a group of seropositive pigs; the new group of animals would confer novelty to the second medical use claim. The holding of this case was confirmed by several others including **T 233/96 (Adrenaline/MEDCO RESEARCH)** where the new group of subjects was distinguished from a prior art group by its physiological or pathological status.

In some cases, a new **technical effect** can form the basis for delimiting a claim over the prior art. In **T 836/01 (Interferon-beta2/YEDA RESEARCH AND DEVELOPMENT CO. LTD.)**, the Board observed that the invention relied upon a different technical effect as compared to the prior art, which disclosed the use of interferon- $\beta 2$ for activating mature lymphoid cells which in turn exerted a cytolytic T-cell activity on cancer cells, thus teaching an

indirect effect of interferon- β 2 on cancer cells. The Board held that the technical effect underlying the invention was a **direct** effect of interferon β 2 on tumorous cell growth. Hence the Board found that the technical effect underlying the invention was not merely an explanation of how interferon- β 2 heals cancer. Rather, the newly identified direct effect led to a new clinical situation identifying a new subgroup of patients to be treated, where it was preferable to target the cancer cells themselves and not via the lymphoid cells as in the prior art. In line with such reasoning, the Appeal Board acknowledged novelty in **T 509/04 (Cerebral palsy/ALLERGAN)** based on a new technical effect, even though the technical effect may have inherently taken place in the course of carrying out what was known in the art.

Case law does however exist which does not regard a new technical effect as being sufficient to establish novelty of a claim. For instance, in **T 486/01 (IGF-1/GENENTECH INC. et al.)** the Board was of the opinion that the Applicant's finding that a medical treatment reduced the loss of glial cells following CNS injury could not establish novelty over the treatment of CNS injury using the same compounds as described in the prior art. In this case, obviously the "loss of glial cells" as the observed technical effect did not lead to any kind of new clinical situation in the sense of **T 836/01**, but at best explained why the prior art treatment might be successful.

Last but not least, even a treatment regimen (i.e. the time point of administration as the sole feature differing from the prior art) can establish novelty when the prior art discloses an otherwise identical medical treatment. The landmark decision in this respect is **T 1020/03 (IGF-1/GENENTECH, INC.)** where the Board stated:

Any use to which Article 52(4) EPC 1973 [now Art. 53(c) EPC] first sentence applies [...], allows a second medical use claim to the preparation of the composition for that second medical use, irrespective of in what detail that use was specified, subject that the use being novel and inventive. For the purposes of novelty also under Article 54(5) EPC 2000, this depends on whether the use for therapy is novel, irrespective of the detail with which the therapy is stated in the claim.

Consequently, the Board acknowledged that the administration regimen of a medicament would be a suitable feature to delimit the claim over the prior art teaching. This case law was contradictory to the finding of other cases such as in **T 317/95 (Gastrointestinal compositions/PROCTER & GAMBLE)** and **T 584/97 (Use of nicotine/ELAN CORPORATION)**. This discrepancy was observed by an Appeal Board in a later case, **T 1319/04 (Dosage regimen/KOS LIFE SCIENCES, INC.)**, and led the Board to refer this issue to the Enlarged Board of Appeal. The resulting decision **G 2/08 (Dosage regime/ABBOTT RESPIRATORY)** mentioned above, basically confirmed the findings of **T 1020/03**.

As mentioned above, Enlarged Board of Appeal decision **G5/83** established that a claim directed to an excluded "method of treating disease Y comprising administering substance X" could be admissibly reformulated as a "use of sub-

stance X in the formulation of a medicament for the treatment of disease Y” (this became known as the traditional “Swiss-type” format of medical use). Under the EPC 2000, Art. 54(5) EPC, in conjunction with Art. 53(c) EPC established the purpose-limited product format, allowing reformulation of the above excluded method of treatment claim as “substance X, for use in a method of treating disease Y”. It was the EPO’s stated intent that the older Swiss-type and newer purpose-limited product format should be equivalent. A recent case before a Board of Appeal specifically addressed this question of equivalency. In **T1780/12 (Cancer treatment/BOARD OF REGENTS, THE UNIVERSITY OF TEXAS SYSTEMS)** the Board held that the subject-matter of a second medical use claim in “Swiss-type” format is different than the subject matter of a purpose-limited product claim. The Board held that the scope of protection conferred by the Swiss-type claim – as a purpose-limited process claim – must be different from that of a purpose-limited product claim. In the Board’s view, then, no double patenting issue exists if a parent application is directed to one of the formats, while the divisional is directed to the other.

One must take particular care in drafting a patent in cases where a compound has both a medical and a non-medical effect. Whereas the medical effect allows the drafting of a purpose-limited product claim, the non-medical effect allows only a classical use claim. This issue had serious consequences for an application in **T 1635/09 (Zusammensetzung für Empfängnisverhütung)/BAYER SCHERING PHARMA AKTIENGESELLSCHAFT)** where the Applicant finally lost the case due to its failure to draft a claim which was formally admissible (purpose-limited product claim admissible only for medical applications) and novel (non-medical applications cannot derive novelty by way of a purpose-limited product claim).

Medical use claims, especially those relating to a second or further medical use, are normally based on the use of a particular substance to achieve a stated therapeutic aim. In practice, the substance used is most often the active ingredient of a therapeutic to be administered to a patient. **T 2003/08 (Dilated cardiomyopathy/EDWARDS)** is an interesting case in which an Appeal Board considered whether a second medical use claim is also available when the prepared product is not a medicament but, as in this case, a column with a coupled active agent. In that decision, the claim was directed to “Use of a specific ligand ... in the manufacture of a column having said ligand coupled ...”. The column was used to remove antibodies from a patient’s serum by *ex vivo* treatment of the blood. The Board held that second medical use claims can be used for any kind of “substance or composition” in a medical treatment. The Board held that there existed no requirement under the EPC that the “substance or composition” must be a medicament. What is decisive is that it is the “substance or composition” that exerts the medical effect and not a device (point 18).

In the Enlarged Board of Appeal case, **G 1/04 (Diagnostic method/–)** the Board decided that a diagnostic method is to be excluded from patent protection

if – and only if – the method contains all necessary steps for making the diagnosis and all steps are performed on the human body.

Diagnostic methods which are practiced outside the human body or contain at least one step performed outside the human body, e.g. on body tissues or fluids, such as blood or urine, are not excluded from patentability as diagnostic methods under Article 53(c) EPC.

A fairly new field that developed over the last few years is known under the term “Companion diagnostics” or “Personalized Medicine” and will be discussed in the following.

This field combines diagnostic measures with therapeutic measures. Patients are first analyzed by the diagnostic method in order to identify e.g. those patients who might be responders to a given drug or those patients who have a higher risk of negative side effects by the treatment. In most cases, the treatment is indeed an established treatment using known drugs for the treatment of a known disease, but the diagnostic method is intended to help identify a sub-population of patients for which the treatment is of particular help (the so-called “responders”). This approach is also intended to help to reduce costs by limiting treatment to only those patients who are likely to benefit from an often expensive therapy. Generally, the genetic marker defining the sub-population to be treated is the only novel feature, whereas features such as dosage regimen, or route of administration, etc. are already known from the prior art. A claim directed to a method of companion diagnostics will therefore contain “therapeutic” features as well as “diagnostic” features. A claim in which a known compound for the treatment of a known disease is to be drafted, and the only novel feature is that the patient to be treated is characterized by a certain genetic marker, may have the following general wording:

Compound x for use in the treatment of disease y wherein the patient has the genetic marker z.

A problem with the patentability of such a claim could occur if it can be established that the prior art (inherently) discloses treating at least one patient having the genetic marker z with compound x for the same disease y. Such an “inherent disclosure” could constitute a novelty bar as stated in the EPO Guidelines under G-VI, 6. If for example the number of patients known to be treated by the prior art method (albeit without knowledge of the existence of the genetic marker z) is very high, the EPO might well object that, based on such high patient numbers already treated, there is no reasonable doubt that the prior art had already treated patients having the genetic marker z. In such a case, the Applicant might be forced to introduce further details about the detection of the genetic marker z in the patient group by indicating in the claims active steps as to how to perform the detection of the genetic marker z. Such further limitation of the claim might however have a negative impact on the enforceability of the claim where the drug manufacturer itself does not actively perform steps of detecting the genetic marker z. One might well argue that the “inherent disclosure” of a treatment of patients with marker z is not sufficient

to deny novelty. Such an argument could find support in case law such as **G 2/88 (Friction reducing additive/MOBIL OIL III)** or **G 6/88 (Plant growth regulating agent/BAYER)**, in which the novelty of a use claim was acknowledged based on a technical effect which, although inherently achieved by the prior art method, was not realized as such in the prior art. One may analogously argue that in a claim relating to companion diagnostics, the technical effect is to treat only a narrow group of patients (those showing marker z) and not the broad, less defined group as disclosed in the prior art. To apply the known treatment to a narrower patient group should be a novel use in the sense of **G 2/08**. According to **T 1399/04 (Combination therapy HCV/SCHERING)**, a more narrow definition of a patient group which overlapped with a more generic patient group of the prior art was accepted as a feature to delimit the claim over the prior art. It appears, however, that the EPO practice has not yet been finally settled in this field.

A further difficulty in obtaining appropriate patent protection in the medical field relates to medical devices, in particular, protecting new medical uses for known devices. Although Art. 53(c) EPC acknowledges that generally **products**, and not merely **substances** or **compositions**, are patentable even if their intended use is the use in a medical treatment, it is often difficult to draft a medical device claim in a manner that satisfies novelty. Analogously to purpose-limited product claims, one may draft a device claim in the form “medical device X for use in therapy Y”. Whereas for substances and compositions, a new purpose/use can render the purpose-limited product claim novel over the prior art (see Art. 54(4) and (5) EPC), these provisions are in fact limited to **substances** or **compositions**. This in turn means that a medical device which is neither a “substance” nor a “composition” cannot benefit from this regulation in the EPC. Rather, a medical device being characterised by a certain use/purpose faces the problem that according to the established case law, the purpose does not make a device novel over a device disclosed in the prior art which exhibits the same features but for a different purpose. This is well in line with the Guidelines at section F-IV, 4.13. However, a medical device which also comprises a substance or composition might derive a benefit from Art. 54(5) EPC when this substance or composition can be used in a medical treatment. For such a product, one might draft a claim of the following type:

Compound/composition X for use in the treatment of disease Y, wherein the compound/composition is contained in a device having the following features ... and is to be administered by steps ...

Such a claim was formally accepted in case **T 559/08 (Intradermal delivery of substances/BECTON, DICKINSON AND COMPANY)**. While the claim in this case was finally rejected for lack of an inventive step, the Board did not raise any formal objections against the format of the claim.

As regards treatment by surgery, the Enlarged Board of Appeal held in decision **G 1/07 (Treatment by surgery/MEDI-PHYSICS)** that a method practiced on the human body and comprising an invasive step which might lead

to a substantial health care risk even when carried out with the required professional care and expertise is to be regarded as a surgical step which excludes such a method from patent protection. It might not always be easy to define when a certain method step might qualify as a surgical step as defined by the Enlarged Board of Appeal.

C.I.3. Requirements for grant

For any subject matter that qualifies as an invention under Art. 52 EPC, several criteria must be met to render the invention patentable.

C.I.3.a. Novelty, inventive step and industrial application

The general prerequisites for patentability, namely novelty, inventive step and industrial application, which are valid for any chemical product and therefore also for life science and biotechnological matter, will not be specifically addressed in this book. There are, however, some peculiarities to be considered. These are discussed in the following.

C.I.3.a.a. Naturally occurring products

Many products in the life sciences are naturally occurring products, e.g. proteins, nucleic acids, etc. The patentability of such products is explicitly mentioned in Rule 27 EPC. Moreover, the novelty of naturally occurring products has been addressed in several decisions of the EPO Boards of Appeal.

According to **T 301/87 (Alpha-interferons/BIOGEN)**, a DNA sequence which is contained in a known gene library is novel as long as the specific hybridizing probes necessary for its isolation and characterization are not known.

In the decision **T 272/95 (Relaxin/HOWARD FLOREY INSTITUTE)**, the Board of Appeal stated:

There are no documents on file where the existence of the H2-relaxin gene is mentioned, let alone the sequences of this gene and of the corresponding H2-relaxin protein. Novelty is acknowledged.

The Board confirmed the position taken by the Opposition Division in the first instance, which had decided

to recognize novelty for a natural substance, which has been isolated for the first time and which has no previously recognized existence.

Thus, novelty of naturally occurring products resides in the first provision and description of the isolated product.

C.I.3.a.b. Products for use in methods for treatment of the human or animal body by surgery, therapy or diagnostic methods practiced on the human or animal body

The provisions of Art. 54(4) and (5) EPC are an exception to the general principle that substances or compositions comprised in the state of the art are not novel, i.e. cannot be protected by means of a product claim. According to these provisions, such products can be protected as medicinal products (purpose-limited product protection) even if they are known in the art as non-medicinal products. The novelty of the products resides in their first (or second/further) use in the medical field. The basic EPO decision was **G 5/83 (Second Medical Indication/EISAI)**, allowing use claims for any second and further medical indication drafted in the Swiss-type claim format. With the implementation of the EPC 2000 the changes to Art. 54 EPC lead to a differing practice regarding the wording of claims directed to second and further medical uses. In the decision **G 2/08 (Dosage Regimen/ABBOTT RESPIRATORY)** the Board held:

In respect of second and further medical indications the EPC now allows use-related product claims directed to the substance itself whereas under EPC 1973 decision G 5/83 allowed claims directed to the use of a substance for the manufacture of the drug for a therapeutic indication (“Swiss-type claims”). [...] Article 54(5) EPC now permits purpose-related product protection for any further specific use of a known medicament in a method of therapy. [...] Where the subject matter of a claim is rendered novel only by a new therapeutic use of a medicament, such claim may no longer have the format of a so called Swiss-type claim as instituted by decision G 5/83.

Regarding the wording of the claims for medicinal products, see C.I.2.d. and C.I.3.e.d.

C.I.3.a.c. Processes of analogy

Many processes in the life science field are processes of analogy resulting in a new product obtained in a manner that is known *per se*. Such processes of analogy are considered as being allowable, in particular as involving an inventive step, if the process results in a new technical effect or a new product having surprising characteristics, as outlined in **T 119/82 (Gelation/EXXON)**. In this decision, the Board held:

It is well established that analogy processes are patentable insofar as they provide a novel and inventive product. This is because all the features of the analogy process can only be derived from an effect which is as yet unknown and unsuspected (problem invention).

In decision **T 2/83 (Simethicone Tablet/RIDER)**, the Board held:

The discovery of a yet unrecognised problem may, in certain circumstances, give rise to patentable subject-matter in spite of the fact that the claimed solution is retrospectively trivial and in itself obvious (“problem inventions”).

For instance, the so-called analogy processes in chemistry are only patentable as long as the problem, i.e. the need to provide certain patentable products as their effect, is not yet within the state of the art.

Similarly, in decision **T 1131/05 (Thermoplastic Elastomer/BASF SE)**, the Board held that a process claim directed to an analogy process was in accordance with the requirements of novelty and inventive step in view of the fact that a skilled person would come to the conclusion of a trivial and obvious process only with the knowledge of the problem to be solved and inadmissible hindsight.

C.I.3.b. Sufficiency of disclosure

As for any other inventions, inventions relating to life science matter must be disclosed in a manner sufficiently clear and complete to permit them to be carried out by a person skilled in the art in accordance with Art. 83 EPC. Generally, the broader the claim, the broader the disclosure in the description should be. As stated in **T 435/91 (Hexagonal Liquid Crystal Gel/UNILEVER)**, this approach is based

on the general legal principle that the protection covered by a patent should correspond to the technical contribution to the art made by the disclosure of the invention described therein, which excludes that the patent monopoly be extended to subject-matter which, after reading the patent specification, would still not be at the disposal of the skilled person.

The EPC contains no requirement for examples, and experimental data is not necessary to sufficiently disclose the claimed invention. However, there is a difference between experimental data and the embodiments of the invention. An embodiment of the invention describes, without referring to data, a way in which the claimed invention can be put into practice. This distinction was clearly brought out in decision **T 1191/03 (Virus proliferation/MEYER)**. The claim in this case related to an antisense HIV for gene-therapeutic treatment of humans, in particular for blocking propagation. The antisense virus was made of an HIV envelope in which nucleic acids containing the HIV genome in reverse orientation, as well as reverse transcriptase, were inserted. The Board reviewed the disclosure of the application to determine whether the skilled person would be able to produce such a virus. The Board noted that the description was extremely general and did not provide a single explanation of how to make the claimed virus. This included the lack of any explanation as to how to insert the reverse transcriptase into the virus as claimed. In the Board's view, this lack of explanation would have forced the skilled person to experiment independently, constituting an undue burden. The Board conceded that the EPC contains no requirement for examples. However, the Board did note Rule 42(1)(e) EPC which requires the description to describe in detail at least one way of carrying out the invention. In the Board's view, the application contained no such description. The Board noted that Art. 83 EPC in conjunction with Rule 41(1)(e) EPC are together intended to prevent the Applicant from obtaining protection for a teaching which can only be put into practice using insights other than those provided by the Applicant. This decision is a good illustration

of the importance of providing at least one way in the description of performing the claimed invention, irrespective of any examples.

In the field of chemical applications it is commonly held that a broad claim must usually be supported by several examples in the description in order to provide sufficient information to allow a skilled person to carry out the invention over the whole ambit of the claim (**T 409/91 (Fuel Oils/EXXON)**). In biotechnological cases broad claims were allowed, even if the description contained only one example (or even no example, see above) of performing the invention. This previous more liberal practice is consistent with decision **T 292/85 (Polypeptide expression/GENENTECH I)** stating that an invention is sufficiently disclosed

if at least one way is clearly indicated enabling the person skilled in the art to carry out the invention.

This liberal interpretation of Art. 83 EPC was followed by the Board in decision **T 412/93 (Erythropoietin/KIRIN-AMGEN)**. One can take from this decision that the requirements of Art. 83 EPC are fulfilled, if the application discloses any practical method of making something covered by the claim.

This question, which frequently arises concerning the need for examples in order to comply with the requirements of sufficiency of disclosure, was further addressed in decision **T 127/02 (Herpes Virus mutants stromal keratitis/HARVARD)** in which the claim related to the medical use of a herpes virus having certain structural and functional characteristics in the treatment of specified classes of diseases. The application contained no experimental data. Nevertheless, the Board held that the fact that no specific experimental data are provided does not render the teaching insufficient (point 7 of the decision). This is because there was no particular problem or special difficulty that could have prevented or hindered the skilled person from putting the teaching of the application into practice. This decision illustrates the concept that sufficiency of disclosure is not a matter of showing results, but rather enabling the skilled person to perform the invention as claimed.

In decision **T 923/92 (Human t-PA/GENENTECH)**, however, the Board applied the principle set out in the aforementioned decisions **T 409/91** and **T 435/91** for conventional chemical matter, requiring sufficient information reflecting the whole claimed area, a position which has been followed more and more in the biotechnology field as well, emphasizing that broad claims require a broad range of examples to fulfill the requirements of an enabling disclosure.

When considering sufficiency of disclosure of medical use claims, the EPO applies certain additional requirements going beyond the general requirements discussed above. Decision **T 801/06 (Cancer treatment with HSV mutant/CRUSADE)** is a good illustration of these additional requirements and relates to claims directed to the use of a mutant herpes simplex virus with specified genetic characteristics for the treatment of a metastatic tumor of specified origin. In this decision the Board referred to previous decision **T 609/02**

(**AP-1 complex/SALK INSTITUTE**), where it was held that a medical use claim is only sufficiently disclosed when, in addition to the general requirements for sufficiency of disclosure, evidence exists either in the patent and/or from common general knowledge, that the therapeutic effect underlying the claim in fact exists. In **T 801/06**, the Board therefore considered whether a mutant HSV virus with the claimed characteristics could in fact be used to treat metastatic cancer of the type claimed. Although the evidence supported only the mutant HSV's ability to treat cancer, the Board believed that this was sufficient for demonstrating the oncolytic effect underlying the claim. The Board confirmed that the claimed subject matter was sufficiently disclosed.

In **T 491/08 (Improved immunogenicity/GOVERNMENT USA)**, the Board applied similar thinking in its assessment of sufficiency of disclosure of a medical use claim, although it reached the opposite conclusion of insufficient disclosure. In this case, the claim related to the use of i.a. a recombinant NYVAC or ALVAC poxvirus vaccine to potentiate a CD8+ response to HIV-1 epitopes in a human. The Board conceded that the patent system does not require an absolute proof that a compound is approved as a drug before it may be claimed as such. But for a medical use claim, the Board stressed that it is required that the patent application provides some information to the effect that the claimed compound, administered as stated in the claims, has a direct effect on a metabolic mechanism specifically involved in the recited disease. This mechanism may be known either from the prior art or from post-published evidence, which however may only be taken into account to back up the findings in the patent application, and not in itself to establish sufficiency of disclosure (see point 6 of the decision). In this case, the Board concluded that the application did not contain sufficient information regarding the technical effect underlying the claims to support sufficiency of disclosure. The Board thus denied sufficiency of disclosure.

In the medical field the question may arise whether clinical data is required in relation to the requirement of sufficiency. In decision **T 433/05 (Fusion Peptide Inhibitors/CONJUCHEM)** the Board held that

where a therapeutic application is claimed in the form of the use of a substance or composition for the manufacture of a medicament for a defined therapeutic application, attaining the claimed therapeutic effect is a functional technical feature of the claim. As a consequence, under Article 83 EPC, the application must disclose the suitability of the product to be manufactured for the claimed therapeutic application. Taking into account the intrinsic difficulties for a compound to be officially certified as a drug, it is the practice of the Boards of Appeal that for acceptance of a sufficient disclosure of a therapeutic application in a patent/patent application, it is not always necessary that results of clinical trials are provided at the relevant date, but that it is required that the patent/patent application provides some information to the avail that the claimed compound has a direct effect on a metabolic mechanism specifically involved in the disease.

Once this evidence is available from the patent/patent application, then post-published evidence may be taken into account to support the disclosure in the patent application.

Thus the Board confirmed one important principle regarding procedures at the EPO, namely that, provided that some initial disclosure is derivable from an application as filed, supplementary information may be submitted during the procedure, even if the information had been generated only after the relevant time rank of the application, to provide evidence in support of sufficiency.

However, decision **T 609/02**, mentioned above, illustrates that experimental data generated after the relevant date of a patent may not always be employed to provide support for the question of sufficiency of disclosure. The claim in question in this case related to the use of a functionally specified steroid hormone or analogue thereof for the preparation of a medicament for the treatment of AP-1 stimulated tumor formation and other medicinal indications. Said hormone was to be identified by a claimed method. The specification however did not provide any evidence at all relating to the claimed use. No hormone was identified and no data were specified indicating that such a hormone (if it were identified) could have an impact on any of the listed specific diseases. Only a very brief outline of potential uses was provided in the application as filed. Under these circumstances the Board held:

In short, the patent specification is not concerned with giving a technical basis to what is claimed.

Taking into account post-published evidence provided by the Patentee showing examples of suitable hormones and proving their efficacy in the claimed treatments in **T 609/02**, the Board considered the question of sufficiency starting from the same considerations as employed in the above mentioned case **T 433/05** and found:

Where a therapeutic application is claimed in the form allowed by the Enlarged Board of Appeal in its decision G 5/83, i.e. in the form of the use of a substance or composition for the manufacture of a medicament for a defined therapeutic application, attaining the claimed therapeutic effect is a functional technical feature of the claim. As a consequence, under Article 83 EPC, unless this is already known to the skilled person at the priority date, the application must disclose the suitability of the product to be manufactured for the claimed therapeutic application. [...] It is required that the patent provides some information in the form of, for example, experimental tests, to the avail that the claimed compound has a direct effect on a metabolic mechanism specifically involved in the disease [...]. Once this evidence is available from the patent application, then post-published (so-called) expert evidence (if any) may be taken into account, but only to back-up the findings in the patent application in relation to the use of the ingredient as a pharmaceutical, and not to establish sufficiency of disclosure on their own.

The Board of Appeal in **T 609/02** accordingly came to a different conclusion than in **T 433/05**, namely that in the absence of technical evidence in the patent application as filed post-published evidence could not be taken into consideration for the question of sufficiency.

In **T 920/10 (Sebaceous gland disorders/GENERAL HOSPITAL CORPORATION)** the Board assessed the quality of data in an application directed to a medical use from the standpoint of the sufficiency of disclosure

(Art. 83 EPC). The Board held that there is no fixed standard as to the quality or quantity of data required to support a claimed medical effect. Clearly “absolute proof” is not required to make the claimed effect plausible. Moreover, the mere allegation by an Examining Division that the data are insufficient – without giving any reasoning why this is so – is not enough to support a sufficiency objection under Art 83 EPC (see point 8).

In **T 1150/09 (-/-)** the Board found that the claimed therapeutic effect in a second medical use claim is a functional technical feature of the claim. The application must therefore disclose the suitability of the product for the claimed therapeutic application. This can be proven by any kind of data as long as they directly and unambiguously reflect the therapeutic application (see point 4).

In the context of functionally defined inventions and with the development of high-throughput screening methods, the EPO has had to consider patent applications directed to functional definitions of compounds as such or uses of such compounds. Here, the EPO has started from the established jurisprudence of the Boards of Appeal, holding that the requirement of sufficiency of disclosure is met only if the invention as defined in the independent claims can be performed by a skilled person over the entire scope claimed without undue burden, using common general knowledge and having regard to further information given in the application. The Boards of Appeal have held that the above principle applies to any invention irrespective of the way the claims are defined, be it by way of a structural or a functional feature. For instance, the Boards have been called upon to consider sufficiency of disclosure for so-called reach-through claims. A reach-through claim is a claim directed to an as yet unidentified product and defines this product using functional characteristics formulated in terms of the desired effect (e.g. “an inhibitor of target X”). The common finding by the Boards in this relation has consistently been that this mode of definition comprises an indefinite and innumerable host of possible alternatives of diverse structures. This is only acceptable as long as all these alternatives achieve the desired result and are available to the skilled person. According to the Boards, this reflects the general principle and law whereby the protection sought must correspond to the invention’s technical contribution to the art. Typically, the Boards considered these requirements as not met for reach-through claims because the task of finding all the suitable alternatives constitutes an invitation to perform a research program and, thus, an undue burden.

In decision **T 1063/06 (Reach-through claim/BAYER SCHERING PHARMA AKTIENGESELLSCHAFT)**, the Board held that

a formulation of the claim whereby functionally defined chemical compounds are to be found by means of a new kind of research tool using a screening method set out in the description constitutes a reach-through claim, which is also directed to future inventions based on the one now being disclosed. As the Applicant is entitled to claim patent protection only for his actual contribution to the art, it is therefore both reasonable and imperative to limit the claim’s subject-matter accordingly.

A functional definition of a chemical compound (in this case a reach-through claim) covers all compounds possessing the capability (e.g. binding to a certain target) recited in the claim. In the absence of any selection rule in the application in suit, and without the possibility of having recourse to his common general knowledge, the skilled person must resort to trial and error experimentation on arbitrarily selected chemical compounds to establish whether they possess the recited activity. This represents for the skilled person an invitation to perform a research program and, thus, an undue burden. This is in line with decision **T 609/02**, discussed above, which emphasizes that if the description provides no more than a vague indication of a possible medical use for a chemical compound yet to be identified, later more detailed evidence cannot be used to remedy the fundamental insufficiency of disclosure.

In decision **T 155/08 (IMPDH-inhibitors/BAYER CROPSCIENCE)**, the Board had to consider a claim directed to the use of an inhibitor of an IMP-dehydrokinase derived from specified sources for the abatement of phytopathogenic fungi. The Board considered the definition of the fungicidal compound to be employed as being based on a functional definition so that the claim was construed as comprising the use of all chemical compounds having the required function, without restricting it to specific classes of compounds or chemical structures. The Board considered that such a definition again would require the skilled person to carry out a research program in order to test unlimited numbers of compounds. So in this case the Board applied the principles as outlined in decision **T 1063/06** discussed above, and the claim was regarded as being insufficiently disclosed.

Similarly, in decision **T 852/09 (Enhancers/AVENTIS PHARMACEUTICALS INC. et al.)**, the Board had to consider the question of sufficiency for a claim directed to the use of an enhancer which preferentially enhances a specific enzymatic reaction in the manufacture of a composition for lowering the level of LDL cholesterol in a patient. The application as filed defined the enhancer with respect to an increase in the expression of a polypeptide or increase regarding a specified enzymatic activity, i.e. providing a functional definition. In this connection, the Board held

that the enhancer of claim 1 is not defined by any specific structural features, but merely by this functional feature and the capability to lower the level of LDL cholesterol in a patient. Consequently, claim 1 concerns all chemical compounds which increase the expression of the LIPG polypeptide or which increases the enzymatic activity of the LIPG polypeptide and can lower the level of LDL cholesterol in a patient without any restrictions to compound classes or chemical structure.

The Board can concur with the Appellants that the application describes a number of assay methods which can be used to identify enhancers and inhibitors (modulators) of LIPG activity as recited in the claimed composition. [...] Furthermore, although the application does contain theoretical examples how enhancers which increase the expression of the LIPG polypeptide or which increase the enzymatic activity of the LIPG polypeptide could be identified, the application as filed does not contain any guidance for the skilled person which would allow her/him an educated guess as to, for example, a particular

chemical structural class to which the enhancers recited in claim 1 belong. In addition, the application does not teach any guidance how to effectively select such compounds which also comply with the functional feature of lowering the level of LDL cholesterol in a patient.

Accordingly, in a search for enhancers recited in claim 1, the skilled person would have to test a virtually unlimited amount of chemical compounds of various chemical structures. The Board judges therefore that the application as filed does not provide the skilled person at the relevant date of the application with any guidance enabling her/him without undue experimentation, to identify the enhancers as defined in claim 1.

Again, the Board referred to the principle of decision **T 1063/06** in judging that since the enhancers to be used are characterized in functional terms only and therefore represent an invitation for the skilled person to perform a research program, it is not possible to carry out the invention over the entire scope claimed without undue burden. Sufficiency of disclosure was therefore denied.

Decision **T 32/97 (Deleted tk-PRV vaccines/NOVAGENE)** demonstrates the concept that the disclosure of a patent need not be absolutely correct from a scientific standpoint in order to be sufficiently disclosed. The claims in this case were directed, among other things, to a pseudorabies virus which fails to produce any functional TK as a result of a deletion in the tk gene. The tk gene was indicated as corresponding essentially to the tk gene sequence of Figure 5 of the patent. In addition, Table 3 of the patent showed the results of TK expression in a tk⁻ mutant. However, even the tk⁻ mutant showed a residual expression of TK. Objections relating to sufficiency of disclosure were based on the residual TK expression despite tk deletion in Table 3, as well as a sequence error in Figure 5. However, with regard to Table 3 the Board held that the assay is a relative assay which does not require that the “zero level” for TK expression always has the same value, or is zero. As a relative assay, what is important is that the assay sets a floating zero-level for TK expression against which any tk⁻ mutant should be compared. With regard to Figure 5, the Board held that the error in a sequence was unimportant for the skilled person’s ability to generate a deletion variant, because the relevant restriction sites were known, and these could be used to excise segments of the tk gene regardless of knowledge of that gene’s specific sequence. In drafting a patent application, of course every effort should be made to make sure that the data and results are correct. However, this case is a good illustration of the fact that even incorrect or incomplete data need not necessarily preclude sufficiency of disclosure as long as the erroneous disclosure still enables the skilled person to put the invention into practice without undue burden.

Within the context of sufficiency of disclosure, inventions containing parameter definitions in the claims have been of relevance. Here similar considerations apply as outlined herein in relation with the question of clarity (see C.I.3.e.b). Considerable care must be taken with parameters in the claims. If it is not possible for the skilled person to determine a parameter reliably on the basis of his common knowledge, all the critical details for measurement of every parameter must be fully set out. It is not enough to refer merely to a standard test method

or commercially available apparatus if critical conditions must be selected arbitrarily or subjectively for the test.

The Board in decision **T 815/07 (-/THE PROCTER & GAMBLE COMPANY)** held:

In a claim which defines the subject matter of the invention by reference to a parameter, it therefore follows that the parameter defines an essential technical feature of the invention. Taking the case of an article defined by reference to a parameter specifying a particular quality or quantity, the significance of the parameter is that the particular quality or quantity when exhibited by the article contributes to the solution of the technical problem underlying the invention. An article which does not exhibit the specified quality or quantity will not solve the problem.

Further, Article 83 EPC requires that the skilled person trying to solve the problem underlying the patent should be in a position to obtain an article which does indeed solve that problem. Where, as in the present case, a claimed article is defined by reference to a parameter range to be measured by a specified method, and where the specified method is such that in relation to any particular article it produces values which sometimes fall within the claimed range and sometimes fall significantly outside it, the skilled person has no means of knowing whether the article in question will solve the problem or not. It places upon him an undue, if not insuperable burden when trying to reproduce the invention.

Similar considerations were applied in decision **T 120/08 (-/-)**, where sufficiency of disclosure of a method claim had to be considered. The claim comprised the method step requiring the simultaneous application of “vacuum 1,000 mbar”. In view of the fact that the term in question could be interpreted in different manners and under due consideration that the patent in question did not reveal any further information regarding the interpretation of this process parameter, the Board concluded that sufficiency of disclosure had to be denied.

In decision **T 593/09 (-/TOYO KOHAN CO., LTD)**, the Board had to consider the question of sufficiency for a claim containing a parameter definition where the results of any measurement of the parameter strongly depended upon a heating rate which was not specified in the application as filed. In view of these circumstances, the Board held:

In view of the fact that the LTC temperature strongly depends on the heating rate applied and in the absence of any knowledge of what heating rate to apply, the skilled person thus is not able to establish whether a given polyethylene terephthalate film has an LTC temperature as required according to the opposed patent in order to obtain the desired peel, permeation and impact resistance. Hence, because of the unclear “heating rate” parameter, the crucial LTC temperature is so ill-defined that the skilled person, when trying to carry out the invention underlying the opposed patent, is left with having to test each individual polyethylene terephthalate as to its peel, permeation and impact resistance.

This amounts to an undue burden to solve the problem addressed in the opposed patent.

Particular care has to be taken with unusual parameters, in particular parameters defining in a functional manner a technical result to be achieved. In decision **T 1914/11 (Liquid formulation of nicotine/MCNEILL)** the Board held:

When the solution to a technical problem is expressed in the form of an effect on a patient, as in present case, the Patentee has the duty not only to give sufficient technical guid-

ance for the preparation of compositions achieving the effect but also to define the said effect in the description in such a way that the skilled person can reproduce and measure it reliably for the whole scope of the claims, without undue burden or experimentation. The method of determining such technical effect on a patient must be described with due care, to avoid uncertainties and guesswork.

Overall, given the nature of the subject matter, the question of sufficiency under Art. 83 EPC is an especially important issue for a patent in life sciences.

C.I.3.b.a. Nucleotide and amino acid sequences

Rule 30(1) EPC together with the Decision of the President of the EPO of April 28, 2011 (OJ EPO 2011, 372) requires that if nucleotide or amino acid sequences are disclosed in the application, an electronic sequence listing complying with WIPO Standard ST.25 (ST.25) be submitted to the EPO. ST.25 applies to any unbranched sequences of four or more amino acids, and ten or more nucleotides (ST.25 paragraph 2 (ii)).

The sequence listing must be submitted electronically and, if additionally submitted on paper, must be accompanied by a statement that the listing on paper is identical to the electronic version. If no ST.25-compliant sequence listing is filed on the filing date the Applicant is invited to file the sequence listing within a non-extendable time limit of two months. Non-observance of this time limit can be remedied by further processing, necessitating payment of the further processing fee. In the event that the electronically submitted listing is incomplete or unreadable, the affected part shall be deemed not to have been filed. Any sequence listing that is submitted after the date of filing must not extend beyond the content of the application as filed and must be accompanied by a statement confirming this fact.

A sequence listing filed on the filing date will be published together with the application documents and the patent specification as part of the description.

The EPO recommends using the BiSSAP software, which can be downloaded from the EPO homepage, to generate ST.25-compliant sequence listings. This software can also be used to check existing sequence listings for ST.25 compliance.

If the EPO acts as International Searching Authority, Supplementary International Searching Authority, or International Preliminary Examining Authority, and no ST.25-compliant electronic sequence listing is available to the EPO, the Applicant is invited under Rule 13ter PCT to furnish the sequence listing within a non-extendable period of one month. If the EPO acts as designated or elected office (Euro-PCT application) and no ST.25-compliant electronic sequence listing is available to the EPO, the Applicant will be invited under Rule 163 (3) EPC to furnish the missing listing within a non-extendable period of two months. In this case, the regulations laid out above for Euro-direct applications apply in the same way. The most recent requirements for filing sequence listings are of October 18, 2013 and are published in the Official Journal of the EPO (see Annex 3).

C.I.3.b.b. Microorganisms

Rules 31 to 34 EPC (see Annex 4) supplement the general provisions of Art. 83 EPC.

Rule 31 EPC relates to “biological material” which is not available to the public and which cannot be described in the European patent application in such a manner as to enable the invention to be carried out by a person skilled in the art. Rule 26(3) EPC defines “biological material” as any material containing genetic information and capable of reproducing itself or being reproduced in a biological system.

According to Rule 31(1) EPC, when an invention involves the use of or concerns “biological material”, the invention shall only be regarded as being sufficiently disclosed if:

- (a) a sample of the biological material has been deposited with a recognized depositary institution not later than the date of filing of the application;
- (b) the application as filed gives such relevant information as is available to the Applicant on the characteristics of the biological material; and
- (c) the depositary institution and the accession number of the culture deposit are stated in the application.

In a further subparagraph (d), Rule 31(1) EPC specifies that when the biological material has been deposited by a person other than the Applicant, the name and address of the Depositor must be stated in the application and a document must be submitted to the EPO providing evidence that the Depositor has authorized the Applicant to refer to the deposited biological material in the application and has given his unreserved and irrevocable consent to the deposited material being made available to the public in accordance with the requirements of the EPC.

According to decision **T 223/92 (HIF-Gamma/GENENTECH)** paragraph (1) of Rule 31 EPC cannot be interpreted such

that there is an obligation to deposit material to facilitate the reproduction if the invention can be repeated on the basis of the written description, even if this should be a much more cumbersome way than by merely growing the deposited micro-organism. (point 3.2)

This opinion was confirmed by a Board in decision **T 412/93 (Erythropoietin/KIRIN-AMGEN)** stating that a deposit is not required in cases where the claimed invention can be reproduced without relying on a deposited microorganism. It was emphasized that the EPC does not require disclosure of the “best mode” for performing the invention.

The Board in decision **T 418/89 (Monoclonal antibody/ORTHO)** did not consider a deposit of a hybridoma as sufficient for the disclosure requirement,

if and when it is only possible to reproduce the invention after repeated requests to the depositary institution and by applying techniques considerably more sophisticated than those recommended by the depositary institution (citation omitted). (headnote I)

Rule 31(2) EPC stipulates three periods for filing the information referred to in paragraphs (1)(c) and (d). The controlling period is the one which expires first. In decision **G 2/93 (Hepatitis A virus/UNITED STATES OF AMERICA II)** the Enlarged Board of Appeal decided that the information referred to in Rule 31(1)(c) EPC may not be submitted later than sixteen months after the filing date (or priority date) of the application as set out in Rule 31(2)(a) EPC.

According to Rule 31(2), sentence 3 EPC, the communication of the information of Rule 31(1)(c) or (d) EPC is considered as constituting the unreserved and irrevocable consent of the Applicant to the deposited culture being made available to the public.

As emphasized in decision **T 118/87 (Amylolytic enzymes/CPC INT.)**:

The Applicant of an invention for a microbiological process and the Depositor of a micro-organism must in principle be one and the same. Exceptionally it is justified to consider the parent company and subsidiary as one entity for the purpose of Rule 28 EPC, if the parent company has full control of the deposits made by the subsidiary company. (headnote II)

The availability of the deposited microorganism is independent of the consent by the Depositor (see also decision **T 239/87 (Micro-organisms/NA-BISCO)** and decision **T 106/88 (Micro-organisms/CPC)**).

In the specification of a patent application the Applicant must describe the microorganism as precisely as possible, i.e. by indicating its morphological and biochemical characteristics and the proposed taxonomic description. The Guidelines provide a list of indications of the most important groups of micro-organisms (see e.g. EPO Guidelines at F-III,6.3).

Under Rule 31(1)(a) EPC, the deposit must be made with a recognized depositary authority on the same terms as those laid down in the Budapest Treaty.

The deposited culture shall be available upon request to any person from the date of publication of the patent application. Such availability is effected by the depositary institution by issuing a sample of the microorganism to the person making such a request. Issue of a sample shall be made only if the Requester has undertaken not to make the deposited culture or any culture derived therefrom available to a third party, and to use it for experimental purposes only. A “derived culture” is deemed to be any culture of the microorganism which still exhibits those characteristics of the deposited culture which are essential for carrying out the invention.

Instead of the release of a sample of the microorganism to any third party, the Applicant may request that a sample of the microorganism only be made available to an independent expert nominated by the Requester (so-called “expert option”, regulated in Rule 32 EPC). Under Rule 32(2) EPC, the expert may be nominated by the Requester or may be recognized as an expert by the President of the EPO.

If a microorganism in accordance with Rule 31 EPC is no longer available from the depositary institution, the microorganism can be newly deposited in accordance with Rule 34 EPC.

If Europe (EP) is designated in a PCT application, Rule 13^{bis} PCT relating to microbiological inventions has to be considered.

C.I.3.c. Priority

In life sciences, priority is often of great importance since, on the one hand, the claiming of multiple priorities is quite common and, on the other hand, it is frequently the case that relevant patent applications which were filed before the claimed priority date, but published thereafter (prior art according to Art. 54(3) EPC) or documents made available to the public within the priority year, are cited during examination or opposition proceedings. Examining the patentability requirements (novelty and inventive step) of claimed subject-matter requires prior establishment of its effective date.

Arts. 87 to 89 EPC set out the requirements for claiming a priority right.

In decision **T 81/87 (Preprorennin/COLLABORATIVE)** a Board held that

the subject-matter of the claims of the European application must be clearly identifiable in the previous application as a whole (headnote)

in order to be entitled to priority.

It was further stated that

the disclosure of all essential elements, i.e. features of the invention in the priority document must either be express, or be directly and unambiguously implied by the text as filed. Missing elements which are to be recognised as essential only later on, are thus not part of the disclosure. (headnote)

In the case of decision **T 301/87 (Alpha-interferons/BIOGEN)** a Board expressed the view that

if an entity itself is disclosed to the skilled person, this does not necessarily mean that a component part is also disclosed for the purpose of priority if this cannot be envisaged directly and unambiguously as such, and requires considerable investigation to reveal its identity. (point 6.3)

In decision **T 296/93 (HBV antigen production/BIOGEN INC)** a Board had to decide the entitlement to priority in relation to the issue of the enablement by the disclosure of the priority documents. It was concluded that the claims and the priority on which they were based related to the same invention within the meaning of Art. 87(1) EPC since

no essential elements, (i.e. features) of the claimed invention can be said to have been recognised or added only later on in the sense that they are not part of the disclosure of the priority document, [...] (point 4.6)

In decision **T 923/92 (Human t-PA/GENENTECH)** a Board did not acknowledge a claimed priority for a protein defined by its sequence because the protein sequence of the priority document and the sequence of the claimed protein were not completely identical. The Board concluded that the two respective

polypeptides were “distinct variants of human t-PA possibly with similar, but not necessarily identical characteristics”. The Board thus held that the claim in question was not entitled to priority since it did not relate to the same invention as described in the priority document.

Enlarged Board of Appeal opinion **G 3/93 (Priority interval/-)** considered:

A document published during the priority interval, the technical contents of which correspond to that of the priority document, constitutes prior art citable under Article 54(2) EPC against a European patent application claiming that priority, to the extent such priority is not validly claimed. (headnote I)

This also applies if a claim to priority is invalid due to the fact that the priority document and the subsequent European application do not concern the same invention because the European application claims subject-matter not disclosed in the priority document. (headnote II)

Later the legal standard to be applied when assessing whether a claim is entitled to a priority date was given by Enlarged Board of Appeal opinion **G 2/98 (Requirement for claiming priority of the “same invention”/-)**.

The requirement for claiming priority of “the same invention”, referred to in Article 87(1) EPC, means that priority of a previous application in respect of a claim in a European patent application in accordance with Article 88 EPC is to be acknowledged only if the skilled person can derive the subject-matter of the claim directly and unambiguously, using common general knowledge, from the previous application as a whole.

As regards the meaning of the expression “the same invention”, point (9) of the reasons explains:

[A]n extensive or broad interpretation of the concept of “the same invention” referred to in Article 87(1) EPC, making a distinction between technical features which are related to the function and effect of the invention and technical features which are not, with the possible consequence that a claimed invention is considered to remain the same even though a feature is modified or deleted, or a further feature is added (cf. point 8.3 supra), is inappropriate and prejudicial to a proper exercise of priority rights. Rather, according to that analysis, a narrow or strict interpretation of the concept of “the same invention”, equating it to the concept of “the same subject-matter” referred to in Article 87(4) EPC (cf. point (2) supra), is necessary to ensure a proper exercise of priority rights.

With respect to disclaimers, the Enlarged Board of Appeal in decision **G 1/03 (Disclaimer/PPG)** held:

As has been stated in decision G 2/98 (for its relation to G 1/93 see Reasons, points 2 and 2.1.2. above), the extent of the right of priority is determined by, and at the same time limited to, what is disclosed in the priority application. In order to avoid any inconsistencies, the disclosure as the basis for the right to priority under Article 87(1) EPC and as the basis for amendments in an application under Article 123(2) EPC has to be interpreted in the same way. This means that a disclaimer, not providing a technical contribution as outlined above, which is allowable during the prosecution of a European patent application does not change the identity of the invention within the meaning of Article 87(1) EPC. Therefore, its introduction is allowable also when drafting and filing the European patent application without affecting the right to priority from the first application, which does not contain the disclaimer.

In applying Opinion **G 2/98**, the Boards of Appeal have defined the concept of “the same invention” and “the same subject-matter” in a number of decisions, in particular in connection with inventions referring to nucleotide and amino acid sequences.

Decision **T 351/01 (Tissue Factor Protein/GENENTECH)** related to a polynucleotide characterised both in structural and functional terms. The priority document disclosed a polynucleotide having the same function but the structure differed from the claimed polynucleotide by five bases, all found in the non-coding portion of the sequence. Here, the Board concluded that the sequences are structurally different and thus cannot be seen as the same subject-matter. Priority entitlement was thus denied.

In decision **T 30/02 (Xylanase/NOVOZYMES)**, the Board decided that the presence of two additional guanine residues in the sequence of a prior art document which were missing in its priority document, results in different DNA sequences; additionally, there was no evidence on file that the specific sequences were derived from the same cloned DNA insert. Therefore, the sequences could not be considered to represent the same subject-matter and, thus, the same invention. Priority entitlement for the prior art document was therefore denied.

In decision **T 70/05 (Apoptosis/GENENTECH)**, the Board held that a prior art document defining a specific extracellular fragment of a receptor was not entitled to the claimed priority because the priority document did not disclose said specific fragment. The Board also stated that based on a disclosure of a “wrong” nucleotide or amino acid sequence in the priority document,

it would not be fair to acquire a right over a broad area from which, only later on, the “correct” sequence might be selected and disclosed in a patent application. The possible advantages conferred by such a practice would only encourage and, in the long term, lead to a mischievous use of priority rights.

The following three decisions relate to patents based on the same priority documents. The patent in decision **T 666/05 (Mutation/UNIVERSITY OF UTAH)** was directed to a diagnostic method which comprises determining in a tissue sample whether there is a specific mutation in a specific gene. In the relevant priority document, the nucleotide sequence deviated from the corresponding sequence disclosed in the patent by 15 nucleotide residues, six of which did not lead to an amino acid change in the sequence. Further, none of the 15 nucleotide changes was an insertion or deletion or results in a stop codon. The Board concluded that the above sequence differences would not have any impact on the invention claimed and the skilled person would not have had any problems to perform the claimed method on the basis of the information in the priority document. The priority could therefore be validly claimed.

Decision **T 80/05 (Method of diagnosis/UNIVERSITY OF UTAH)** also refers to a diagnostic method which comprises determining in a tissue sample whether there is a frameshift mutation in the sequence of a specific gene. In

line with **T 666/05** (supra), the Board decided that the skilled person would have been able to rely on mRNA sequence information in order to identify those frameshift mutations that could otherwise be potentially missed. Further, the Board was not convinced that the missing sequence information for introns in the priority document would produce wrong results. The right to priority could thus be acknowledged.

In its decision **T 1213/05 (Breast and ovarian cancer/UNIVERSITY OF UTAH)**, however the Board concluded that claim 1 was not entitled to priority since it was a product claim directed to a specific isolated nucleic acid, the amino sequence of which was a technical feature of the invention and was different from the amino acid sequence disclosed in the priority document.

C.I.3.d. Person skilled in the art

The person relevant for evaluating the novelty, inventive step and sufficiency of disclosure is the notional “person skilled in the art”. Generally, this person skilled in the art is a hypothetical person having a general technical background and special knowledge and expertise in the field of the invention.

In view of the rapid developments in the field of biotechnology and of the particular problems associated therewith, EPO case law has provided specific definitions for the person skilled in the field of biotechnology, in which the time when the invention was made is an important parameter to define the skills of the notional artisan.

In decision **T 60/89 (Fusion proteins/HARVARD)** a Board held that the skilled person in the field of genetic engineering in 1978 is not to be defined as a Nobel Prize laureate,

but as

a graduate scientist or a team of scientists of that skill, working in laboratories which developed from molecular genetics to genetic engineering techniques, at that time. (point 2.2.4)

This interpretation was followed in decision **T 500/91 (Alpha-interferon II/BIOGEN)** emphasizing that the skilled person would be

oriented towards practicalities [citation omitted], and the development of the art normally expected by him does not include solving technical problems by performing scientific research in areas not yet explored. (point 2.2)

In decision **T 223/92 (HIF-Gamma/GENENTECH)** a Board observed that in view of the fact that in 1981 a substantial number of genes had been made the subject of cloning and expressing methods, the notional skilled person in this technical field was not a team, but a

highly skilled technician carrying out a project where the initial instructions received are already adequate to tell the technician how to overcome any problems likely to arise. (point 5.5)

Decision **T 455/91 (Expression in yeast/GENENTECH)** deals with the attitude of a person skilled in the field of biotechnology vis-à-vis possible

changes, modifications and/or adjustments in known products or procedures. In the Board's view the notional skilled person

would adopt a conservative attitude [...] in the sense of being cautious. (point 5.1.3.3)

It was further held that he would

neither go against an established prejudice nor try to enter into "sacrosanct" or unpredictable areas nor take incalculable risks. (point 5.1.3.3)

He would, however,

regard a means conveniently adopted in a neighbouring field ... as being readily usable also in that field, if this transfer of technical knowledge involves nothing out of the ordinary. (point 5.1.3.3)

Decision **T 493/01 (Acellular vaccine/CELLTECH)** further emphasized that the definition of the skilled person as being cautious and conservative would, however, not mean

that he/she will refrain from considering information because it does not concern the main stream of research in his field of specialisation or because it "only" applies to some parts of the world. The skill and knowledge of the skilled person are not geographically limited; he/she will rather have a global point of view.

In decision **T 412/93 (Erythropoietin/KIRIN-AMGEN)**, a Board and the parties agreed that in 1983 the skilled person was

a team of three composed of one PhD researcher with several years experience in the aspect of gene technology or biochemistry under consideration, assisted by two laboratory technicians fully acquainted with the known techniques relevant to that aspect. (point 4)

With respect to Art. 56 EPC it was stated in decision **T 530/95 (XmaI/NEW ENGLAND BIOLABS)** that

the skill of the notional skilled person for the purpose of Article 56 EPC does not include solving technical problems by performing scientific research in areas not yet explored or problematic. Although it has to be accepted that at the priority date of the present application (1989) the average skill in genetic engineering had developed already to a considerable degree, in the present case account should be taken of the fact that only one year before the invention was made, i.e. in 1988, the authors of document (3), dealing with the cloning of type-II R-M systems, were not successful in achieving the claimed result, i.e. cloning of the XmaI system. Thus, further research was necessary. However, from the notional skilled person for the purpose of Article 56 EPC nothing more can be expected than the carrying out of experimental work by routine means within the framework of the normal practice of filling gaps in knowledge by application of the existing knowledge.

In decision **T 1380/05 (Protein stabilisation/NOVOZYMES)**, the Board held:

It is true that the notional "skilled person" can be understood as a team of workers in the fields of relevance to the invention (e.g. T 412/93 of 21 November 1994). Yet, this is intended to mean that the sum total of knowledge and technical experience of such a team is considered to be "as a matter of course" when assessing inventive step. On the contrary, it does not mean that the skilled person has the "creativity" of this team. This is fully confirmed in fur-

ther case law dealing with the abilities of the skilled person (T 391/91 of 22 November 1993, capable of routine experimentation; T 500/91 of 21 October 1992, conservative in attitude, T 207/94 (OJ EPO 1999,273), lacking in imagination and creativity).

With respect to Art. 83 EPC, the Board in decision **T 946/02 (Separation of Proteins/NOVOZYMES)** held that:

Even though the case law of the Boards of Appeal accepts that the skilled person may be subject to a reasonable amount of trial and error when it comes to sufficiency of disclosure, e.g. in an unexplored field or where there are many technical difficulties, the skilled person has to have at his disposal, either in the specification or on the basis of common general knowledge, adequate information leading necessarily and directly towards success through the evaluation of initial failures (cf decisions T 226/85, OJ EPO 1988, 336, point (8)).

In the pharmaceutical field, some decisions defining the skilled person and his abilities in a similar way can be found.

It was stressed in decision **T 463/06 (Transdermal patch for 17-deacetyl norgestimate/ORTHO-MCNEILL PHARMACEUTICAL)** that when judging an inventive step,

the notional skilled person in the art is expected to have the same qualifications as the skilled person referred to for the assessment of Article 83 EPC.

With respect to an opinion of an expert, the Board in decision **T 885/02 (Paroxetine methanesulfonate/SMITHKLINE BEECHAM)** held:

The opinion of an expert does not necessarily reflect the view of the skilled reader for various reasons. The declarations are necessarily made after the filing date of the patent. Those experts who are in the present case eminent scientists have their own experience which is not necessarily common general knowledge. Furthermore, apart from a few exceptions, those declarations are not supported by references to textbooks so that the Board is not in a position to easily distinguish between what is common general knowledge in the context of a particular declaration and what is not.

In decision **T 505/03 (Conjugated linoleic acid/LODERS CROK-LAAN)**, the Board concluded with regard to inventive step:

The answer to the question what a skilled person would have done in light of the state of the art depends in large measure on the technical result he had set out to achieve. In other words, the notional “person skilled in the art” is not to be assumed to seek to perform a particular act without some concrete technical reason: he must, rather, be assumed to act not out of idle curiosity but with some specific technical purpose in mind (T 939/92, *supra*; point 2.42).

C.I.3.e. Claims

According to Art. 84 EPC the claims shall

- 1) define the matter for which protection is sought;
- 2) be clear and concise and
- 3) be supported by the description.

The form and content of the claims are compiled in Rule 43 EPC, which specifically sets out that the claims shall define the matter for which protection is sought in terms of the technical features of the invention.

C.I.3.e.a. Claim categories

There are two basic categories of claims, namely product claims and process claims.

Product claims comprise, for example, chemical substances, such as DNA or proteins; chemical compositions, such as pharmaceutical compositions; and apparatus or articles, such as test kits.

Process claims comprise methods of manufacture, such as a method of preparing an antibiotic; and methods of working, such as a method of controlling weeds by applying a herbicide. According to Art. 64(2) EPC, the protection conferred by a patent directed to a process of manufacture extends to the products directly obtained by such a process (see B.I.).

A use claim is a type of process claim (see **G 5/83 (Second medical indication/EISAI)** and Guidelines Part F – IV, 3.1). The claimed use may be directed to a change of a product, e.g. the use of a DNA for producing a protein, or to a change of a condition, e.g. the use of a compound for improving the growth rate of plants.

A specific claim type in the field of pharmaceuticals is a so-called purpose-limited product claim, which reads as a product claim but its scope is limited to the indicated purpose (see Art. 54(4) and (5) EPC).

Wherever possible, a life-science product in a product claim shall be defined by its structure, preferably by its chemical formula or its composition. If such a definition cannot be provided, in exceptional cases, it is permissible to define the product by characteristics, such as physical or chemical parameters, e.g. melting point, spectral characteristics, molecular weight, etc. provided that these characteristics can be clearly and reliably determined (see Guidelines, Part F – IV, 4.11).

If there is no other way of characterizing a product than by its manufacture, a so-called product-by-process claim may be allowable. Such a product-by-process claim is interpreted as a claim to the product as such, so it is only allowable if the obtained product is novel (see **T 150/82 (Claim categories/IFF)** and **T 412/93 (Erythropoietin/KIRIN-AMGEN)**). The preferred wording of a product-by-process claim should be “Product X obtainable by process Y” or any wording equivalent thereto, rather than “Product X obtained by process Y”. Alternatively, a product-by-process claim can include a reference to a process claim such as “Product X obtainable by the process of claim ...”. A product-by-process claim may comprise product features as well as process features.

Generally, an application should recite no more than one independent claim in each category. In accordance with Rule 43(2) EPC, it is possible for one application to contain more than one independent claim in the same category (product, process, apparatus or use) only if the subject-matter of the application involves one of the following:

- (a) a plurality of interrelated products,
- (b) different uses of a product or apparatus,

- (c) alternative solutions to a particular problem, where it is inappropriate to cover these alternatives by a single claim.

C.I.3.e.b. Clarity of claims

Clarity of the claims is usually only an issue in examination proceedings since Art. 84 EPC is not an opposition ground. However, compliance with Art. 84 EPC will also be examined in opposition proceedings if amended claims are submitted. According to the prevailing case law, it is not possible to discuss clarity of the claims when the amendment was based on a combination of granted claims, but only when features of the description were introduced into the claims. Recent case law, however, opened a door for challenging claims for lack of clarity in opposition proceedings even when combining granted claims (**T 1459/05 (–/EBM-PAPST LANDSHUT)** and **T 656/07 (–/BRISTOL-MYERS SQUIBB)**).

In practice, clarity of the claims is important to provide legal certainty for third parties in evaluating whether the claims are infringed or not. The requirement of clarity is not fulfilled if doubt exists as to the subject matter covered by the claim i.e. the scope of a claim.

According to decision **T 908/04 (–/KIMBERLY-CLARK)**,

the claims must be clear in themselves when being read with the normal skills, but not including any knowledge derived from the description of the patent application (cf. decision T 988/02 of 30 October 2003, not published in OJ EPO; Reasons point 3.3.1).

It was further held in decision **T 1018/02 (Telecommunications System/BTG)**:

Although a claim must not be interpreted in a way which is illogical or does not make any sense, the description cannot be used to give a different meaning to a claim feature which in itself imparts a clear credible technical teaching to the skilled reader. This also applies if the feature has not been initially disclosed in the form appearing in the claim (catchword).

In decision **T 2256/08 (Folic acid containing pharmaceutical compositions/ORTHO-MCNEIL)**, the Board concluded:

It is sufficient that one simple alternative encompassed by the subject-matter of the claim presents a contradiction or inconsistency to render the said claim unclear.

As regards complexity of claims, the Board observed in decision **T 574/96 (Deoxytetracyclines/AMERICA CYANAMID)**:

Article 84 EPC offers no basis for objecting that the claim is too complex. In the Board's judgement, complexity as such is not equivalent to lack of clarity. Clarity under Article 84 is not at stake in a case of mere complexity of a claim provided the subject-matter for which protection is sought and the scope thereof are clear and unambiguous for a person skilled in the art, either per se or in the light of the description. Further, the Board cannot see from the description under appeal what is meant by "within a reasonable time", apart from possibly that it takes longer than average to examine the subject-matter of the claim.

In line with this decision, the Board in **T 1020/98 (Safeners/BAYER)** stated in its headnote:

Compliance with the clarity requirement of Article 84 EPC is not dependent on the time required to establish whether a given compound is covered by the product claim. The clarity requirement is not a basis for objecting to the complexity of a claim, as complexity is not tantamount to lack of clarity. The simplicity of an individual claim is not a criterion for the granting of a patent under the EPC.

Considerable care must be taken with parameters in the claims. All the critical details for measurement of every parameter must be fully set out. It is not sufficient to refer merely to a standard test method or commercially available apparatus if critical conditions must be selected arbitrarily or subjectively for the test.

The Board in decision **T 1156/01 (–/NIPPON PETROCHEMICALS)** held:

Thus, if the invention is characterized by parameters the method of and means for measurement should appear completely in the claim itself, whenever this is reasonable, or by reference to the description in accordance with Rule 29(6) EPC, if the method is so long that it would impair the conciseness of the claim. The introduction into the claim of such a definition for the determination of a parameter would only be superfluous where it could be shown that the skilled person would know from the outset which method and conditions to employ because, for instance, this methodology was the methodology commonly used in the technical field, or all the methodologies known in the relevant technical field for determining this parameter would yield the same result within the appropriate limit of measurement accuracy (cf. decision T 412/02 of 16 June 2004, not published in JO EPO; points 5.8 and 5.9 of the Reasons).

Particular care should be taken with novel or unusual parameters. In decision **T 1525/10 (Sustained release of fluvastatin/NOVARTIS AG)**, the Board observed:

If, as in the present case, the method for determining the parameter in question is specifically adapted and therefore not usual in the art, the Applicant must be expected to describe it elaborately and with due care, thus avoiding guesswork and uncertainties.

With respect to functional features in a claim, the Board held in **T 936/06 (Bacteriophage preparations/NYMOX)** that the same standards apply as for parameters:

According to the principle of legal certainty, it has been established in the jurisprudence of the Boards of appeal that, when a product for which protection is sought is defined in the claims using particular parameters, a person skilled in the art must be able to determine those parameters clearly and reliably, either using technical information provided in the application or by objective procedures which are usual in the art (see, inter alia, T 94/82, OJ EPO 1984, 75). The same applies to functional features defining a product in terms of the result to be achieved. These features must provide instructions which are sufficiently clear for the skilled person to reduce them to practice (T 68/85, OJ EPO 1987, 228; T 437/98 of 29 January 2003).

A claim containing a disclaimer must also meet the requirements of clarity of Art. 84 EPC.

In decision **G 1/03 (Disclaimer/PPG)**, the Enlarged Board of Appeal emphasized:

In any case, the requirements of conciseness and clarity of Article 84 EPC are also applicable to claims containing disclaimers. On the one hand, this means that a disclaimer is not allowable if the necessary limitation can be expressed in simpler terms in positive, originally disclosed features in accordance with Rule 29(1), 1st sentence, EPC. In addition, a plurality of disclaimers may lead to a claim drafting which puts an unreasonable burden on the public to find out what is protected and what is not protected. As in respect of other problems of clarity, a balance has to be struck between the interest of the Applicant in obtaining adequate protection and the interest of the public in determining the scope of protection with reasonable effort. If a claim containing one or more disclaimers does not meet the latter interest it cannot be allowed. On the other hand, the understanding of a claim may be considerably complicated if the terminology of the application-in-suit and of the anticipation differ and different, incompatible terms are used in the claim. Here, Article 84 EPC may require that the terminology be adapted in order to exclude what is necessary to restore novelty.

In fact, the issues of clarity and sufficiency of disclosure (addressed in section C.I.3.b) are sometimes interlinked. This interlinkage was illustrated in decision **T 923/92 (Human t-PA/GENENTECH)**. There, the granted claims related to a process involving preparing cDNA from mRNA extracted from a specific melanoma cell line, and isolating from it a DNA sequence having a specified restriction pattern for the putative mature tissue plasminogen activator sequence encoding a certain polypeptide sequence, and *having human tissue plasminogen activator function*. In the course of the proceedings, the Board considered whether the feature “having human tissue plasminogen activator function” was clear and sufficiently disclosed. The Opponent had alleged that the extent of the patent monopoly in respect of human t-PA derivatives was too large, partly because of the “vague and unclear definition” of the parameter “has human t-PA function”. The Board noted that the claim recited no specific sequences, and contained only functional features and parameters such as the restriction pattern of the encoding cDNA. The claims had no reference structure of human t-PA for the purpose of defining derivatives. As mentioned above, the Board also found the term “has human t-PA function” as vague and ambiguous, for example because human t-PA is a molecule with multiple functions. As a result, the Board held that the claim was insufficiently disclosed and unclear.

C.I.3.e.c. Support of claims by description

In addition to clarity of the claims, Art. 84 also requires that the claims must be supported by the description. Again, since Art. 84 is not an opposition ground, support of claims by the description is usually only discussed in examination proceedings.

There are two aspects to be considered. According to the first aspect, the claims must contain all features which are disclosed in the specification as being essential for solving the posed object. As outlined, for example, in decisions **T 821/96 (Piperazines/WYETH & BROTHER)** and **T 2068/10 (Fixed-**

dried platelets/UNIVERSITY OF NORTH CAROLINA), the expression “support by the description” in Art. 84 EPC

has to be interpreted as meaning that a claim has to specify all essential features which are necessary for solving the technical problem with which the application is concerned. Consequently, all technical features described in the description of an application which are apparently essential to the alleged invention, and in particular such features which distinguish the invention from the closest prior art, have to be present in the claims.

The Board in decision **T 939/92 (Triazoles/AGREVO)** stated in its head-note:

- I. If a claim concerns a group of chemical compounds per se, an objection of lack of support by the description pursuant to Article 84 EPC cannot properly be raised for the sole reason that the description does not contain sufficient information in order to make it credible that an alleged technical effect (which is not, however, a part of the definition of the claimed compounds) is obtained by all the compounds claimed (see Reasons No. 2.2.2).
- II. The question as to whether or not such a technical effect is achieved by all the chemical compounds covered by such a claim may properly arise under Article 56 EPC, if this technical effect turns out to be the sole reason for the alleged inventiveness of these compounds (Reasons No. 2.4 to 2.6).

According to a second aspect, the claims must be supported in their breadth by the description so that the claimed invention can be performed in its entire scope.

It is emphasized in **T 409/91 (Fuel Oils/EXXON)** that:

Although the requirements of Articles 83 and 84 are directed to different parts of the patent application, since Article 83 relates to the disclosure of the invention, while Article 84 deals with the definition of the invention by the claims, the underlying purpose of the requirement of support by the description, insofar as its substantive aspect is concerned, and of the requirement of sufficient disclosure is the same, namely to ensure that the patent monopoly should be justified by the actual technical contribution to the art. (point 3.4)

Consistent with this, the Board stated in decision **T 1486/08 (Filter material/PROCTER)**:

The Board observes that it is the established case law of the Boards of appeal that the scope of the claims must not be broader than is justified by the extent of the description and also the contribution to the art (T 0409/91, OJ EPO 9/1994, 653, Reasons 3.2, penultimate sentence and Reasons 3.3, second sentence).

Decision **T 127/02 (Herpes virus mutants stromal keratitis/HARVARD)** was a case in which the Board considered that the support aspect of Art. 84 EPC was the main question in assessing whether the requirements of Art. 84 EPC were fulfilled. The claim related to the medical use of a herpes virus having certain structural and functional characteristics for the treatment of different classes of diseases. The Board held that formal support, meaning simply the same words in the description as in the claims, is not sufficient for fulfilling the requirements of Art. 84 EPC. Rather, what is needed is technical support in the description in the sense that the description has to reflect the Applicant's effective contribution to the art (point 3 of the decision). The Board held that the

description made it technically plausible that the herpes simplex virus mutants could be used in the treatment of the cited diseases. This decision illustrates the importance, when drafting the description, to make sure to include technical support for as much of the claim scope as possible.

C.I.3.e.d. Claims for medicinal products

Numerous products obtained by synthesis or by biotechnological processes, e.g. antibiotics, growth factors, etc., are used in the medical field.

According to Art. 53(c) EPC, products for use in methods for treatment of the human or animal body by surgery or therapy and diagnostic methods practiced on the human or animal body are patentable. In the following discussion such products are designated as medicinal products. A similar definition for medicinal products is explicitly stated in Art. 1(a) MSPC (see B.II.2 and Annex 7).

Compared to non-medicinal products one important exception exists for medicinal products.

In the case of an invention relating to a known product which was not previously disclosed for use in any of the aforementioned methods (surgery, therapy or diagnostic methods), it is nevertheless possible to obtain protection for such a product which is limited to the medical field (“purpose-limited product protection”). This is an exception from the general principle that product claims are only allowable for absolutely novel products (see also C.I.3.a.b.)

Taking into account this important exception, there are three types of claims conceivable for medicinal products:

(i) New products having medical effects:

A claim directed to the product can be obtained resulting in absolute product protection, i.e. covering all possible processes for the preparation of said product and all possible uses of said product, including the use in the medical field.

Such a claim can read:

Substance X (or composition X).

(ii) Known products, the medical effects of which are found for the first time:

A product claim restricted to the medical use can be obtained resulting in purpose-limited product protection (purpose-limited product claim).

Such a claim can read:

Substance X (or composition X) for use as a medicinal product.

This claim extends to the whole field of medicine and not only to the treatment of a specific illness.

(iii) Known products, some medical effects of which were already known, where new medical effects are found for the first time:

Under the EPC 1973, a use claim directed to the second or further medical use could be obtained (so-called Swiss-type claim). According to decision **G 5/83 (Second medical indication/EISAI)** the EPO required that the claim comprise a step of manufacturing the medicinal product.

Such a claim could read:

Use of substance X (or composition X) for the manufacture of a medicinal product for the treatment of disease Y.

Under the EPC 2000, it is no longer possible to obtain such Swiss-type claims for applications with relevant dates after January 28, 2011. Namely, in decision **G 2/08 (Dosage regime/ABBOTT RESPIRATORY)**, the Enlarged Board of Appeal held that

when the subject-matter of a claim is rendered novel only by a new therapeutic use of a medicament, such claim may no longer have the format of a so-called Swiss-type claim as instituted by decision G 5/83

and set the above time limit for future applications to comply with this decision. New Art. 54(5) EPC of the EPC 2000 expressly acknowledges the patentability of any substance or composition for any specific use in a medical method provided that such use is not comprised in the state of the art.

A claim directed to a second or further medical use can now read:

Substance X (or composition X) for use in the treatment of disease Y

or

Substance X (or composition X) for use in a method of treatment disease Y.

C.I.3.e.e. Unity of invention

As regards unity of the invention in accordance with Art. 82 EPC, Rule 44 EPC stipulates that unity is fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression “special technical features” means those features which define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art. It is further stated in Rule 44 EPC that the determination whether a group of inventions is so linked as to form a single general inventive concept is made without regard to whether the inventions are claimed in separate claims or as alternatives within a single claim.

Rule 64 EPC relates to the proceedings following the finding that an application does not comply with the requirement of unity of invention. In this case, the EPO will issue a partial search report on those parts of the application which relate to the invention, or the group of inventions within the meaning of Art. 82 EPC, first mentioned in the claims. Moreover, it will inform the Applicant that for the European search report to cover the other inventions, a further search fee

must be paid in respect of each invention involved. The European search report will be drawn up for the parts of the application relating to inventions in respect of which search fees have been paid. Any fee shall be refunded, if during the examination the Applicant requests a refund and the Examining Division finds that the communication under Rule 64, paragraph 1 EPC was not justified.

In **G 2/92 (Non-payment of further search fees/-)**, the Enlarged Board of Appeal decided that an Applicant who fails to pay the further search fees for a non-unitary application cannot pursue that application for the subject-matter in respect of which no search fees have been paid. Such an Applicant must file a divisional application in respect of this subject matter if he wishes to seek protection for it.

Lack of unity of the invention can either arise before considering the prior art, i.e. *a priori*, or after considering the prior art, i.e. *a posteriori*. If a lack of unity objection is based on an *a posteriori* judgement, it is usually caused by an objection to a lack of novelty or lack of inventive step.

The following combinations of independent claims of different categories in the same application usually do not give rise to unity objections:

- (i) one independent product claim, one independent claim to a process of manufacture of said product and one independent claim to the use of said product;
- (ii) one independent product claim, one independent claim to a process of manufacture of said product and one independent claim to an apparatus or means specifically designed for carrying out said process;
- (iii) one independent claim to a process and one independent claim to an apparatus or means specifically designed for carrying out said process.

It is possible for one application to contain more than one independent claim in the same category, as long as all independent claims are linked by an interrelated product. So generally, claims directed to a nucleic acid, a protein encoded thereby, a host cell expressing same etc. are admissible in one application.

As regards intermediates and final products, it was held in **T 470/91 (Unity/ICI)**:

It is the established jurisprudence of the Technical Boards of Appeal that in principle there is unity of invention where several groups of novel intermediates and a group of novel end products are involved, provided the groups of intermediates oriented towards the end products are sufficiently technically closely related thereto by the contribution of an essential structural element to the end products and if the regulatory provisions of Article 82 EPC are safeguarded (cf. T 110/82 (Benzylesters) OJ EPO 1983, 274 and T 35/87 (Hydroxy-pyrazoles/BASF), OJ EPO 1988, 134).

It was further stated in this decision:

This is not prejudiced by the fact that the two sets of intermediates are not structurally related to each other since the orientation of the intermediates towards the end products permits the individual technical problems addressed by the intermediates to be combined into a unitary overall problem to whose solution of which both sets of purpose-made intermediates contribute.

In **W 13/89 (-)** relating to claims for a first and second medical indication, the Board noted:

There is a *prima facie* unity of invention between a claim to the use of a mixture or its separate components for the manufacture of a medicament for a specific indication (second medical indication) and a claim to the mixture only as a pharmaceutical composition (first medical indication).

The Enlarged Board of Appeal in **G 1/91 (Unity/SIEMENS)** emphasized that it is irrelevant in opposition proceedings that a European patent in its granted version or after amendment does not meet the unity requirement.

C.I.3.f. Description

Rule 42 EPC provides information regarding the content of the description of a European patent application. According to this rule, the description shall specify the technical field to which the invention relates, shall indicate the background art which can be regarded as useful to understand the invention, and shall disclose the invention including statements of advantageous effects of the invention and describing in detail at least one way of carrying out the invention claimed, using examples where appropriate. In particular for parameter-defined inventions, a detailed and precise description of the measurement methods for determining the relevant parameters is important, as already outlined above regarding the question of sufficiency of disclosure and clarity of claims (see C.I.3.b and C.I.3.e.b).

At the same time, the description provides a reservoir of technical information which determines *inter alia* the options of an Applicant concerning the filing of divisional applications, and the provision of additional data during examination or opposition proceedings in order to provide supporting evidence for questions such as sufficiency of disclosure as well as inventive step. The disclosure in the description of a European patent application furthermore determines the ability of Applicants to rely on effects associated with the claimed invention in order to distinguish the invention from the prior art as cited. In this regard it is the practice of the EPO that relying on experimental data not submitted with the application as filed, but at a later stage of the proceedings, is only considered admissible if the data relate to effects implied by or at least related to the technical problem initially suggested in the originally filed application.

C.I.3.f.a. Selection inventions

Selection inventions deal with the selection of individual elements, such as specific compounds, sub-ranges or sub-sets not explicitly disclosed in the prior art, but falling within a larger known range or set. In the life science field, inventions often concern the identification of specific chemical substances or groups of substances in relation to a known genus of a family of substances, under which the later inventions fall but which have not been disclosed as such in

the prior art. Another kind of invention in the life science field is concerned with inventions defined by parameter ranges (compositional ratios, process parameters, dosages etc.) where, in a similar manner, the prior art already discloses wider parameter ranges.

While these types of inventions differ with respect to their characterizing features (specific compound or group of compounds versus parameter range), the EPO has applied a consistent approach in assessing such inventions. Both types are considered as chemical selection inventions.

Decision **T 12/81 (Diastereomers/-)** is the landmark decision with regard to novelty in the field of chemistry regarding compound inventions. It is referred to time and time again in the case law of the Boards of Appeal and in communications from examining divisions. The Board stated in this decision

that the concept of substance selection presupposes the choosing of a single compound or a specific subgroup from a group of substances. Thus, the felicitous choice of the claimed threo-compound from among the multiplicity of substances covered by Formula 1 in the cited document would, of course, be a genuine selection if the cited document did not supply any further information. The compound or subgroup chosen, of course, must also be new, but that is not the case here, as shown under 7 and 8 above (where the method of the prior art was shown to lead to the claimed compound). A substance selection can come about in various ways, e.g. if an unmentioned compound or group of compounds having a formula covered by the state of the art is found, in the absence of any information as to the starting substance or substances.

The simple fact that a claimed compound represents one of the many possible compounds encompassed in the disclosure of the prior art thus cannot itself justify the novelty of a selection invention. If the prior art discloses a path to the claimed compound, this compound, though a selection out of many, will lack novelty. The converse constitutes the core view of the novelty of selection inventions established in this decision and still generally applied in the EPO: A specifically claimed compound falling within a broad structural formula of the prior art will be novel in the absence of specific information in the prior art relating to the claimed compound.

Decision **T 12/90 (-/-)**, the case before the Board concerned a claim directed to a chemical substance defined by a generic formula. In the Board's view, the prior art highlighted certain preferred substituent combinations falling within the claimed range, which precluded a selection invention:

A selection from a known collective, which justifies novelty, [...] requires it adds a new element to what is already known and, thus, contains a new teaching for technical activity. Simply copying what is already known does not lead to a new technical teaching and does not enrich technology.

Regarding the question of what constitutes an individualization, the Board further stated:

The concept of individualization only fits the notion of a structural definition of a single compound, but not that of a collective; according to the case law of the Board, a collective defined by general formula does not disclose individual entities it encompasses.

The consistent jurisprudence of the EPO has accordingly held that claiming a chemical compound representing one species from within a broader pre-published genus constitutes a chemical selection invention. As long as the prior art does not contain an individualized disclosure of the compound and does not disclose a particular method entailing specific starting materials which would inevitably lead to the claimed compound, such a chemical selection will be novel over the prior art.

A selection inventive defined by a parameter range within a broader range identified in the prior art has been considered as another form of selection invention relevant in the life science field. The case law of the Boards of Appeal, starting early with the decisions **T 198/84 (Thiochlorformiate/-)** and **T 279/89 (-/-)** has established a specific set of criteria for evaluating the novelty of a selection within a wider range known from the state of the art. According thereto, a selection can be acknowledged as being novel if:

- 1) the selected sub-range is narrow, when compared with the prior art disclosure;
- 2) the selected sub-range is sufficiently far removed from the known range illustrated by means of examples (in the prior art)
- 3) the selected area does not provide an arbitrary specimen from the prior art, i.e. not a mere embodiment of the prior description, but another invention (it must be a purposive selection).

The meaning of “narrow” and “sufficiently far removed” is a case-by-case evaluation, and likewise the third criterion has been decided upon by the Boards of Appeal of the EPO in an individual case-related manner. That said, the principles as laid out in the above cited decisions **T 12/81** and **T12/90** are applied in the evaluation of selection inventions relating to parameter sub-ranges. Here, the Boards have stressed that identifying that a sub-range singled out of a larger range was associated with a newly discovered effect occurring therein was not sufficient for establishing novelty, but that the selected sub-range itself had to be new *per se*.

C.I.3.f.b. Divisional applications

Art. 76 EPC in conjunction with Rule 36 EPC gives Applicants the option to file a divisional application relating to any pending earlier patent application. Art. 76(1) EPC defines that such a divisional application may only be directed to subject-matter disclosed in the parent application.

Regarding the filing of divisional applications the two most important questions are the time-limit for filing a divisional as outlined in Rule 36 EPC (“as long as the parent application is pending”) and the possible claimed subject-matter for a divisional defined by Art. 76(1) EPC (“may not extend beyond the content of the parent application”).

While it is common understanding and practice that the date of the publication of the notification of grant for a European patent application terminates the pendency of an application, so that any divisional will have to be filed at the latest one day prior to this date, questions have arisen concerning the situation of applications refused by Examining Divisions. Specifically, is it necessary to file any divisional application prior to the announcement of refusal (which could occur during a hearing so that, practically, any divisional would have to be filed prior to the hearing), or could a divisional still be validly filed within the appeal term for filing the formal notice of appeal even if no such notice of appeal was in fact filed. Effectively, the question asks whether a European patent application is still considered as pending even after refusal, as long as the option exists to appeal this refusal.

Decision **G 1/09 (Pending application/SONY)** dealt with this question of how the term “pending” in Rule 36 EPC had to be interpreted in relation with applications which had been refused by Examining Divisions of the EPO. In this decision, the Board had to decide on the following question:

Is an application which has been refused by a decision of the Examining Division thereafter still pending within the meaning of Rule 36 EPC until the expiry of the time limit for filing a notice of appeal, when no appeal has been filed?

The Board answered this question in the affirmative by emphasizing that:

In the case where no appeal is filed, a European patent application which has been refused by a decision of an Examining Division is thereafter pending within the meaning of Rule 36 EPC until the expiry of the time limit for filing a notice of appeal.

Accordingly, a divisional application may still be filed even after a refusal by the Examining Division, even if no appeal against this decision is filed, provided that the divisional is filed prior to the expiry of the time limit for filing a notice of appeal.

Two further decisions by the Enlarged Board of Appeal of the EPO, namely **G 1/05 (Divisional/ASTROPOWER INC.)** and **G 1/06 (Sequences of divisionals/SEIKO)**, consolidated as **G 1/05**, dealt with questions concerning the interpretation of Art. 76 EPC. The first decision dealt with the important issue of whether non-compliance with the requirements of Art. 76(1) EPC is to be considered as an objection which can be overcome by amendment even after expiry of the time limit provided by Rule 36 EPC.

Specifically, in decision **G 1/05**, the Board had to consider the following question:

Can a divisional application which does not meet the requirements of Article 76(1) EPC because, at its actual filing date, it extends beyond the content of the earlier application, be amended later in order to make it a valid divisional application?

The Board answered this question in the affirmative by emphasizing:

So far as Article 76(1) EPC is concerned, a divisional application which at its actual date of filing contains subject-matter extending beyond the content of the earlier application as

filed can be amended later in order that its subject-matter no longer so extends, even at a time when the earlier application is no longer pending. Furthermore, the same limitations apply to these amendments as to amendments to any other (non-divisional) applications.

Accordingly the Board provided Applicants with the option to change the content of a divisional application in order to comply with the requirements of Art. 76(1) EPC even after filing the divisional and expiry of the time-limit set by Rule 36 EPC, i.e. even after pendency of the parent application has ceased.

Finally, as also outlined in decision **G 1/05**, the Board had to deal with the following question:

In the case of a sequence of applications consisting of a root (originating) application followed by divisional applications, each divided from its predecessor, is it a necessary and sufficient condition for a divisional application of that sequence to comply with Article 76(1) EPC [...] that anything disclosed in that divisional application be directly, unambiguously and separately derivable from what is disclosed in each of the preceding applications as filed?

This question arose from decisions where Boards of Appeal of the EPO questioned the possibility for Applicants to claim specific subject-matter in a divisional application itself derived from an earlier divisional application, in which the subsequently claimed subject-matter itself had not been claimed. The Board answered this question by emphasizing:

In the situation of a sequence of divisional applications each having been divided out from its predecessor, according to the filing date of the first disclosure of the subject-matter concerned in the root application is only justified if the said subject-matter was disclosed in each of the preceding (earlier) applications as filed and if it was still present [...] in each earlier predecessor application at the time the – further – divisional application was filed so that it was thereby existing at all times throughout after its disclosure in the root application as filed up to and including the date of filing the divisional application under consideration.

Content which has been omitted on filing a member higher up the sequence cannot be re-introduced into that member or in divisional applications lower down the sequence from it.

Accordingly, once subject-matter is contained (but not necessarily claimed) in all of the divisionals within the sequence, it is possible to specifically claim such subject-matter in a subsequent divisional application, when divided out of the preceding divisional.

With respect to such sequences of divisional applications, the EPO introduced into its Rules Relating to Fees as of April 1, 2014, supplementary tiered fees for divisional applications filed in respect of any earlier application which is in itself a divisional application, with increasing amounts for the second, the third, the fourth and the fifth or any subsequent generation of divisionals. The introduction of this fee is based on the provision of Rule 38(4) EPC, which provides that the Rules Relating to Fees may provide for an additional fee as part of the filing fee in the case of a divisional application filed in respect of any earlier application which is in itself a divisional application.

C.I.3.f.c. Quality and filing of data

According to the long-standing jurisprudence of the Boards of Appeal, comparative tests may be submitted during proceedings before the EPO.

There are however important criteria, developed and confirmed by the Boards of Appeal, regarding the way such experimental data is generated and provided.

In decision **T 984/03 (Adhesive composition/BMG)** the Board had to decide whether the experimental data submitted by the Applicant in order to provide evidence for the presence of inventive step represented a fair comparative test in view of the closest prior art. The decision outlines that

according to the established jurisprudence of the Boards of Appeal it is necessary, in order to assess inventive step, to establish the closest state of the art, to determine in the light thereof the technical problem which the invention addresses and successfully solves, and to examine the obviousness of the claimed solution to this problem in view of the state of the art.

In order to show that the problem identified was successfully solved the Applicant submitted experimental data during the proceedings comparing an embodiment according to the teaching of the closest state of the art with examples according to the claimed invention. When evaluating this experimental data the Board emphasized that

the comparative test (submitted in the proceedings) is pertinent since it truly reflects the impact of the essential technical feature distinguishing the claimed composition from the closest prior art [...]. Thus the comparison provided by that test is fair and to be taken into consideration when assessing inventive step.

Accordingly, any experimental data submitted in order to provide supporting evidence for the presence of an inventive step vis-à-vis the closest state of the art must truly reflect the relevance of the feature rendering the claimed invention novel and inventive over the prior art.

Some decisions have considered the extent to which any reproduction of the prior art teaching must be in exact conformity with the actual embodiments disclosed in the prior art. In decision **T 1872/08 (Ink set/SEIKO EPSON)** the Board summarized the established practice of the EPO regarding the submission of experimental data, outlining:

In the case where comparative tests are chosen to demonstrate an inventive step with an improved effect over a claimed area, the comparison with the closest state of the art must be such that the effect is convincingly shown to have its origin in the distinguishing feature of the invention. For this purpose it may be necessary to modify the elements of comparison so that they differ only by such distinguishing feature [...] (T 197/86).

To the extent such a modification may be conducted the Board noted that

a modification of the elements of comparison may be achieved by modifying an example of the closest prior art, an example of the patent in suit or both. Hence, an improved effect may be demonstrated by comparative tests which do not exactly reproduce an example of the prior art as long as “the effect is convincingly shown to have its origin in the distinguishing feature of the invention”.

In any case, for experimental data to be taken into consideration, it is the obligation of the party providing such data to submit information regarding the conditions under which the tests were completed. In decision **T 246/01 (Hair**

dying composition/KPSS) the Board did not take into consideration experimental data, although timely filed in the proceedings, noting that the lack of information regarding the conditions under which the data were generated prevented any detailed analysis thereof. Accordingly, not only the results of experiments necessarily form part of any submission providing such data, but also the methodology used and all relevant experimental set-ups and conditions have to be essential and integral parts of such submissions in order to ensure consideration by the EPO.

Under certain circumstance the EPO however will not take experimental data into account at all, a situation associated with the lack of proper disclosure of a technical problem to be solved by the claimed teaching in the application as filed. The EPO bases this approach on the understanding that the definition of an invention being a contribution to the art, i.e. as solving a technical problem and not merely putting forward one, requires that it is at least made plausible by the disclosure in the application as filed that its teaching indeed solves the problem it purports to solve. In cases lacking such an original disclosure, post-published evidence, even if it may be considered in the proper circumstances, cannot serve as the sole basis to establish that the application in question in fact solves the problem it purports to solve.

In decision **T 1329/04 (Factor-9/JOHN HOPKINS)** the Board had to decide upon the question of whether or not to consider post-published evidence submitted into the proceedings in relation with the question of inventive step. For the Board, this question was intrinsically linked to the issue of whether the application as originally filed contained any factual disclosure that a technical problem had in fact been solved with the claimed subject-matter. Concerning the factual disclosure in the application in question, the Board held:

[T]he situation could most probably be looked at differently if it had been demonstrated in the application as filed that GDF-9 played a role similar to that of the transforming factor- β (as was the case for all of the factors which initially served to define the superfamily). Yet, **there is no evidence at all in this respect**. In fact the application only discloses that expression of GDF-9 is localised in ovarian tissues, which per se is useful but insufficient information in relation to any function the molecule might have.

Accordingly, when faced with the submission of post-published data the Board decided not to consider the data at all. The Board considered the original disclosure of the application in question defective, since it only provided speculation regarding a potential technical problem to be solved. The Board held:

The Applicant filed post-published evidence establishing that GDF-9 was indeed a growth differentiation factor. This cannot be regarded as supportive of an evidence which would have been given in the application as filed since there was not any. The said post-published documents are indeed the first disclosures going beyond speculation. For this reason, the post-published evidence may not be considered at all. Indeed, to do otherwise would imply that the recognition of a claimed subject-matter as a solution to a particular problem could vary as time went by.

Here, for example, had the issue been examined before the publication date of the earliest relevant post-published document, GDF-9 would not have been seen as a plausible solution to the problem of finding a new member of the TGF- β superfamily and inventive step would have had to be denied whereas, when examined thereafter, GDF-9 would have to be acknowledged as one such member. This approach would be in contradiction with the principle that inventive step, as all other criteria for patentability, must be ascertained as from the effective date of the patent.

On the basis of this reasoning the post-published data was not taken into consideration and the appeal against the decision of the Examining Division to refuse the application in question was dismissed. This decision shows, as more and more Examining Divisions appear to follow the outlined principle, that it is important in life science applications to provide evidence, by means of experimental data or plausible explanations, that the claimed subject-matter does in fact solve a problem outlined in the application.

C.II. Protection under the EU Regulations

C.II.1. SPCs

A supplementary protection certificate (SPC) provides additional protection of up to 5 years after expiry of a patent upon which it is based (basic patent). It can be extended by another 6 months if it relates to a medicinal product for which data from clinical trials conducted in accordance with an approved Paediatric Investigation Plan (PIP) have been submitted. This additional protection is intended to compensate the Patentee for loss of patent term due to time taken to obtain a marketing authorization.

SPCs only apply to patents covering human or veterinary medicines or plant protection products, e.g. insecticides and herbicides. Although the number of granted SPCs is rather small compared to the number of patents in the field of life science, SPCs are of great economic interest for the pharmaceutical industry.

SPCs are available in all member states of the EU by application to the national patent office of each state in which an SPC is desired.

This chapter summarizes some important decisions of the Court of Justice of the European Union (CJEU). Decisions of the national courts in the member states of the European Union are not considered because the practice of the national patent offices diverges in various aspects. The regulations governing SPCs should however be interpreted consistently in all EU member states.

With respect to the first marketing authorization, the CJEU held in **Case C 207/03 (Novartis)** and in **case C 252/03 (Millenium Pharmaceuticals)** that a marketing authorization issued by the Swiss authorities and, thus, automatically effective in Liechtenstein, constitutes a first authorization to place the product on the market in the community. However, in reaction to these deci-

sions, the contract between Switzerland and Liechtenstein was amended in 2005 so that there is no longer an automatic effect of a Swiss marketing authorization in Liechtenstein. Swiss marketing authorizations now only become valid in Liechtenstein twelve months after issuance.

Regarding the term “product” in Article 1(b) of the SPC Regulation (see Annex 7), the CJEU stated in Case **C 392/97 (Farmitalia)**:

[W]here a product in the form referred to in the marketing authorization is protected by a basic patent in force, the SPC is capable of covering the product, as a medicinal product, in any of the forms enjoying the protection of the basic patent.

This decision relates in particular to the case where an active ingredient in the form of a salt is referred to in the marketing authorization. The SPC is capable of covering the active ingredient as such and also its various derived forms such as salts and esters, i.e. the SPC can be broader than the actual product of the marketing authorization.

The term “active ingredient” in Article 1(b) of the SPC Regulation is however interpreted in a strict sense by the CJEU.

In Case **C 431/04 (Polifeprosan)**, it was emphasized:

Article 1(b) of Regulation No. 1768/92 must be interpreted so as not to include in the concept of ‘combination of active ingredients of a medicinal product’ a combination of two substances, only one of which has therapeutic effects of its own for a specific indication, the other rendering possible a pharmaceutical form of the medicinal product which is necessary for the therapeutic efficacy of the first substance for that indication.

With respect to the question in what circumstances an SPC directed to a combination product may be allowed, it was held in Case **C 322/10 (Medeva)**:

An SPC for a composition comprising two active ingredients which corresponds to a composition recited in the claims of the basic patent, may be granted, if the medicinal product for which a marketing authorization has been obtained, comprises not only said two active ingredients, but also additional active ingredients.

Following Case **C 322/10 (Medeva)**, the CJEU confirmed in Case **C 630/10 (University of Queensland)** and in Case **C 422/10 (Georgetown University)** that an SPC cannot be granted for active ingredients which are “not specified in the wording of the claims of the basic patent”. These decisions *inter alia* raised the question whether Article 3a of the SPC Regulation must be interpreted as meaning that, in order for an active ingredient to be regarded as “protected by a basic patent in force” within the meaning of that provision, the active ingredient must be identified in the claims of the patent by a structural formula, or whether the active ingredient may also be considered to be protected where it is covered by a functional formula in the patent claims. Further, it was uncertain whether the criteria are different when the product is a single active ingredient, as opposed to a combination of active ingredients. In this respect, it was held in Case **C 493/12 (Eli Lilly and Company, Ltd. v. Human Genome Sciences, Inc.)**:

Article 3(a) of Regulation (EC) No. 469/2009 of the European Parliament and of the Council of 6 May 2009 concerning the supplementary protection certificate for medicinal products must be interpreted as meaning that, in order for an active ingredient to be regarded as ‘protected by a basic patent in force’ within the meaning of that provision, it is not necessary for the active ingredient to be identified in the claims of the patent by a structural formula. Where the active ingredient is covered by a functional formula in the claims of a patent issued by the European Patent Office, Article 3(a) of that regulation does not, in principle, preclude the grant of a supplementary protection certificate for that active ingredient, on condition that it is possible to reach the conclusion on the basis of those claims, interpreted *inter alia* in the light of the description of the invention, as required by Article 69 of the Convention on the Grant of European Patents and the Protocol on the interpretation of that provision, that the claims relate, implicitly but necessarily and specifically, to the active ingredient in question, which is a matter to be determined by the referring court.

It was further held in the above two cases **C 630/10** and **C 422/10** that

an SPC can be granted for an active ingredient, which is specified in the claims of the basic patent, even if the market authorization does not only contain said active ingredient, but also additional active ingredients.

Case **C 518/10 (Yeda Research and Development Co. Ltd.)** relates to the question whether an SPC may be granted for an active agent which is only recited in the claims of the basic patent in combination with another active agent. The Court of Justice decided that an SPC for an isolated active agent of a composition must be refused, i.e. the scope of an SPC cannot be broader than the scope of the underlying patent.

With respect to the “basic patent” of Article 1(c) of the SPC Regulation, the CJEU decided in Case **C 181/95 (Biogen Inc./Smith Kline Beecham Biologicals S.A.)**:

Where a medicinal product is covered by several basic patents, Regulation No. 1768/92 [...] does not preclude the grant of an SPC to each Holder of a basic patent.

For an individual Patent Holder, only one SPC can be granted for a particular product but the Patent Holder can decide which of his several patents shall form the basis of the SPC. He may even file several SPC requests based on the same marketing authorization, but the Patent Office will finally grant only one SPC.

With respect to the question whether in circumstances where different active ingredients are covered by the same basic patent, more than one SPC can be granted, the CJEU issued two decisions.

In Case **C 484/12 (Georgetown University)**, the CJEU held that in circumstances

where, on the basis of a basic patent and a marketing authorization for a medicinal product consisting of a combination of several active ingredients, the patent Holder has already obtained a supplementary protection certificate for that combination of active ingredients, protected by that patent within the meaning of Article 3(a) of Regulation (EC) No. 469/2009 of the European Parliament and of the Council of 6 May 2009 concerning the supplementary protection certificate for medicinal products, Article 3(c) of that regulation must be inter-

preted as not precluding the proprietor from also obtaining a supplementary protection certificate for one of those active ingredients which, individually, is also protected as such by that patent.

In Case **C 443/12 (Actavis Group PTC EHF, Actavis UK, Ltd. v. Sanoofi)**, the CJEU, however, clarified that in circumstances

where, on the basis of a patent protecting an innovative active ingredient and a marketing authorization for a medicinal product containing that ingredient as the single active ingredient, the Holder of that patent has already obtained a supplementary protection certificate for that active ingredient entitling him to oppose the use of that active ingredient, either alone or in combination with other active ingredients, Article 3(c) of Regulation (EC) No. 469/2009 of the European Parliament and of the Council of 6 May 2009 concerning the supplementary protection certificate for medicinal products must be interpreted as precluding that patent Holder from obtaining – on the basis of the same patent but a subsequent marketing authorization for a different medicinal product containing that active ingredient in conjunction with another active ingredient which is not protected as such by the patent – a second supplementary protection certificate relating to that combination of active ingredients.

With respect to the “first authorization” in Article 3(d) of the SPC Regulation, the CJEU held in Case **C 31/03 (Pharmacia Italia SpA)** that a veterinary marketing authorization for an active ingredient anticipates the grant of an SPC based upon the first human marketing authorization for the same active ingredient.

In Case **C 202/05 (Yissum Research and Development Company)**, the CJEU decided that

in a case where a basic patent protects a second medical use of an active ingredient, that use does not form an integral part of the definition of the product.

It follows from said decision that in cases where a marketing authorization for a product has already been obtained, an SPC cannot be granted on the basis of a further special medical use of said product. This restrictive approach was not followed by the CJEU in a more recent case.

In Case **C 130/11 (Neurim Pharmaceuticals)**, the CJEU took a more liberal approach on what constitutes the first marketing authorization by stating that

the mere existence of an earlier marketing authorization obtained for a veterinary medicinal product does not preclude the grant of an SPC for a different application of the same product for which a marketing authorization has been granted, provided that the application is within the limits of the protection conferred by the basic patent relied upon.

The CJEU held further in this case that

the placement on the market of a new medicinal product commercially exploiting the new therapeutic application of the same active ingredient, as protected by the new patent, may enable its proprietor to obtain an SPC.

This means that the same Proprietor is allowed to obtain multiple SPCs for the same active ingredient, but for different therapeutic applications. It is however unclear to what extent said therapeutic application must differ from each other.

As regards the calculation of the duration of an SPC, the CJEU in Case **C 125/10 (Merck Sharp & Dohme)** handed down a decision that for an SPC for medicinal products the period between the filing of the basic patent and the date of the first market authorization may be less than 5 years, resulting in a negative duration of an SPC. Such a scenario makes sense in case where one contemplates a later filing of a request for a paediatric extension. If granted, the term of the paediatric extension begins with the lapse of the SPC.

It is, then, possible to obtain an SPC with a negative term of up to six months less one day, which would permit a later filing of a paediatric extension, when a PIP had been completed.

With respect to the scope of protection of an SPC, the CJEU held in decisions Case **C 442/11 (Novartis AG v. Actavis U.K. Ltd.)** and Case **C 574/11 (Novartis)** that the Owner of an SPC for a product consisting of an active ingredient can take action against the distribution of a medicament comprising said active ingredient in combination with other active ingredients, if the basic patent encompasses such a combination of active ingredients.

In view of the present case law of the CJEU, it is possible to obtain an SPC in the scenarios outlined in the following table:

<i>Basic Patent protects</i>	<i>MA granted for</i>	<i>SPC application for</i>	<i>SPC possible</i>
A	A + B	A	Yes
A + B	A + B + C	A + B	Yes
A + B	A + B + C + D	A + B	Yes
A + B + C	A + B + C + D	A + B + C	Yes
A	A + B	A + B	No
A + B	A + B	A	No
A + B	A + B	B	No
A + B	A + B + C	A + B + C	No

Furthermore, in order that the active ingredient is considered to be “protected” by the patent claims, the patent claims should be drafted as specific as possible. In light of the present case law of the CJEU, in particular, the recent decision **C 493/12 (Eli Lilly and Company, Ltd. v. Human Genome Sciences, Inc.)**, the following situation applies:

<i>Definition in the patent</i>	<i>SPC applied for</i>	<i>Protected by basic patent</i>
Composition comprising A and an antibiotic	A + B (B being an antibiotic)	Yes
Composition comprising A and B	A + B	Yes

Definition in the patent	SPC applied for	Protected by basic patent
Markush formula covering A	A	Probably yes
Composition comprising A and a further active ingredient	A + B (B being an antibiotic)	Probably no
Composition comprising A	A + B	No

C.II.2. Protecting plants under the CPVR

C.II.2.a. General background

The Community Plant Variety Rights system allows plant Breeders to protect their plant varieties developed, e.g. for achieving higher plant quality, disease resistance, productivity and/or ability to thrive under changing or different environmental settings. The legal framework according to which rights for new plant varieties are obtained is the Counsel Regulation (EC) No. 2100/94 of July 27, 1994 on the Community Plant Variety Rights (CPVR; see Annex 8). This regulation is modeled on the principles of the International Union for the Protection of New Varieties of Plants of 1991 (generally known by the acronym of the French name of this union, UPOV).

By the wording of Art. 6 CPVR (see Annex 8), it is clear that a prerequisite for the granting of a plant variety right is that the subject-matter of the application relates to a plant variety. The definition of a plant variety is given in Art. 5 CPVR (see Annex 8), and covers varieties of all botanical genera and species (Art. 5, paragraph 1, CPVR). Art. 5(2) CPVR corresponds to Rule 26(4) EPC. Art. 5(3) CPVR provides a further definition for the term “variety constituents”, which relates to a plant grouping consisting of entire plants or parts of plants as far as such plants are capable of producing entire plants. It is clear from the wording of Art. 5(3) CPVR that this covers plant seeds as well as actual plants.

Thus, the definition of a “plant variety” in the CPVR (Art. 5(2) CPVR) is equivalent to the corresponding definition in Art. 1(vi) UPOV, as well as to Rule 26(4) EPC. As explained above, Art. 53(b) EPC excludes plant varieties from patent protection. Identical definitions of the term “plant variety” in the EPC, CPVR and UPOV have the effect that where patent protection for a plant variety is impossible under the EPC, protection is possible under the CPVR (in the EU) and under the UPOV (internationally). The same is of course true of the converse; identical definition of subject-matter excluded under the EPC as the requirements for grant of a right under the CPRV means that only plant varieties may be protected under the CPVR, whereas patent protection remains accessible for other non-plant variety related plant matter under the EPC. Similarly to applying for a patent according to the EPC, where the Applicant may

obtain patent protection in all EPC member states by filing a single patent application, the CPVR allows the grant of a plant variety right throughout the EU by filing a single plant variety application. The Community Plant Variety Office (CPVO), located in Angers, France is responsible for receiving, processing and examining all applications for Community plant variety rights. According to the CPVO's own statistics, this office receives approximately 2800 plant variety applications every year. Of these varieties about 60% are ornamental, 20% are agricultural, and about 10% are for each of fruit and vegetable varieties.

C.II.2.b. Formal and substantive requirements for grant of a new plant variety right; legal recourse

Any application for a plant variety right must fulfill certain minimal formal requirements, set out in Art. 50 CPVR. In summary, the plant variety right application must contain at least the following elements:

- a. a request for the grant of a community plant variety right;
- b. identification of the botanical taxon;
- c. information identifying the Applicant or, where appropriate, the joint Applicants;
- d. the name of the Breeder and an assurance that, to the best of the Applicant's knowledge, no further persons have been involved in the breeding or discovery and development of the variety ...
- e. a provisional designation for the variety;
- f. a technical description of the variety;
- g. the geographic origin of the variety;
- h. the credentials of any procedural representative;
- i. details of any previous commercialization of the variety; and
- j. details of any other application made in respect of the variety.

The implementing regulation of the CPVR may lay down further details for the above requirements. Finally, the Applicant is required to propose a variety denomination which may accompany the application.

Once the plant variety application has been processed for the above formal requirements and is deemed validly filed, the CPVO examines the technical requirements for grant of a plant variety right. These are succinctly set out in Art. 6 CPVR (see Annex 8), which provides that community plant variety rights shall be granted for varieties that are distinct, uniform, stable and new.

The wording of Art. 6 CPVR indicates a presumption of entitlement to a plant variety right. Specifically, Art. 6 indicates that a plant variety right shall be granted for plant varieties which fulfill the four criteria of distinctness, uniformity, stability and novelty. If the CPVO's examination reveals that these four criteria are fulfilled, it grants a plant variety right.

The CPVR provides statutory definitions of each of the four requirements of Art. 6 CPVR, which are summarized in the following.

According to Art. 7(1) CPVR (see Annex 8), a variety shall be deemed to be distinct if it is clearly distinguishable by reference to the expression of the characteristics that results from a particular genotype or combination of the genotypes, from any other variety whose existence is a matter of common knowledge on the application date. So a plant variety is “distinct” if it is differentiable from other known varieties. Art. 7(2) CPVR provides certain (non-exhaustive) reasons as to why the existence of another variety in question may be considered a matter of common knowledge on the application date.

Art. 8 CPVR (see Annex 8) specifies that a variety shall be deemed to be uniform if, subject to the variation that may be expected from the particular features of its propagation, it is sufficiently uniform in the expression of those characteristics which are included in the examination for distinctness, as well as others used for the variety description. So a plant variety is “uniform” if its defining traits are the same from plant to plant, allowing for insubstantial changes resulting from the circumstances of its propagation.

Art. 9 CPVR (see Annex 8) specifies that a variety shall be deemed to be stable if the expression of the characteristics which are included in the examination for distinctness as well as any others used for the variety description, remain unchanged after repeated propagation or, in the case of a particular cycle of propagation, at the end of each such cycle. So a plant variety is “stable” as long as its relevant traits remain unaltered in each subsequent progeny generation.

Finally, Art. 10(1) CPVR (see Annex 8) specifies that a variety shall be deemed to be new if, at the filing date, the variety constituents or harvested material of the variety have not been sold or otherwise disposed of to others, by or with the consent of the Breeder (the Breeder being defined in Art. 11 CPVR) for the purposes of exploitation of the variety:

- a. earlier than one year before the filing date, within the territory of the community (i.e. EU);
- b. earlier than four years or, in the case of trees or vines, earlier than six years before the filing date outside the territory of the community (i.e. EU).

Art. 10(1) CPVR thus defines different statutory grace periods before which a variety in question, dependent on its type and location, may not have been sold or given to others. Art. 10 goes on to provide several specific scenarios according to which certain actions will not be deemed as constituting a disposal of the variety in question to others, i.e. will not be deemed as novelty-destroying.

C.II.2.c. Form and duration of the Community Plant Variety Right

The Holder of a plant variety right granted under the CPVR has both a positive right to perform certain specific acts himself, as well as a negative right to prohibit others from doing the same. This is in contrast to the protection of a patent, which confers a negative prohibitive right to the Patentee, but does not positively allow the Patentee to perform the claimed subject-matter.

Both the positive and negative rights conferred on the Holder of a plant variety right are set out in Art. 13 CPVR (see Annex 8). The Holder's positive right is anchored in Art. 13(1) CPVR, which specifies that a Community Plant Variety Right shall have the effect that the Holder or Holders of the Community Plant Variety Right shall be entitled to effect the acts set out in Art. 13(2) CPVR. Art. 13(2) CPVR then specifies the acts which the Holder of a Community Plant Variety Right may prohibit others from performing. These acts relate to variety constituents or harvested material of the protected variety. The acts which require the authorization of the Holder are as follows:

- a. production or reproduction (multiplication);
- b. conditioning for the purpose of propagation;
- c. offering for sale;
- d. selling or other marketing;
- e. exporting from the community;
- f. importing to the community; and
- g. stocking for any of the purposes mentioned in (a) to (f).

With regard to the duration of plant variety rights, the CPVR specifies a significantly longer right duration than provided for patented inventions. While a patent is valid for 20 years from its filing date, Art. 19(1) CPVR specifies that the term of the Community Plant Variety Right shall run until the end of the 25th calendar year following the year of grant. If the plant variety relates to varieties of vine and tree species, this term runs until the end of the 30th calendar year following grant. Coupling the duration of a Community Plant Variety Right to the date of grant rather than, for a European patent, 20 years from the filing date, effectively means that for a plant variety right, the time taken to process and examine an application does not go to the detriment of the Applicant.

Art. 19(2) CPVR further specifies that an extension of the above terms for the duration of a plant variety right by a further five years may be granted.

D. Protectable Matter in the Life Sciences

“Biotechnological matter” usually covers polymeric products such as DNA, RNA and proteins (also called biopolymers), or even more complex products such as procaryotic or eucaryotic cells. Their protection is considered in the following chapters.

Small molecules however are of course also important subject-matter for life science patents. Conventional, i.e. non-biotechnological polymers, for example in the form of delivery agents and polymeric drugs likewise form part of the protectable matter in the life sciences. If low molecular weight biotechnological products, such as nucleobases, nucleotides, oligonucleotides, amino acids and oligopeptides, are to be protected, the requirements are the same as for any other low molecular *chemical* products, except that oligonucleotides comprising an unbranched sequence of 10 or more contiguous nucleotides and oligopeptides comprising unbranched sequences of 4 or more contiguous amino acids must be presented in a sequence listing in accordance with Rule 30(1) EPC (see C.I.3.b.a).

Since the main emphasis of this book is to provide guidance for the protection of complex biotechnological matter, the following summarizes only a few important principles concerning the protection of low molecular weight products/chemical polymers.

D.I. Small Molecules and Polymers

Generally, a product is considered to be novel if it differs from known products in at least one reliable characteristic (**T 296/87 (Enantiomers/HOECHST)**). This characteristic may be a structural feature (chemical formula or composition), but may also be selected from parameters, such as physical properties for a given compound or composition. For parameter-defined inventions it is however important to consider the associated implications regarding the questions of clarity and sufficiency of disclosure for such features (see C.I.3.e.b and C.I.3.b)

A prior art document which discloses a product by means of a structure and the steps by which it is produced does not destroy the novelty of this product when claimed, if the skilled person was unable to find out from the prior art document or from common general knowledge how to obtain the required starting materials or intermediates (**T 206/83 (Herbicides/ICI)**). In order to be novelty destroying, the prior art disclosure must therefore be enabling.

If a first medical use is found for an already known product, a product claim specifying the respective use is allowable (purpose-limited product claim) (see

C.I.3.a.b and C.I.3.e.d). With the implementation of the EPC 2000 purpose-limited product claims are also now allowable for second and further medical uses as outlined in the decision **G 2/08 (Dosage Regimen/ABBOTT RESPIRATORY)**.

The inventive step of a novel product may be based on the product itself, if the product results in an enrichment of the art (**T 648/88 ((R,R,R)-alpha-tocopherol/BASF)**). In the case where a novel product is similar to a known product, the inventive step can be established by surprising or unforeseeable effects of the novel product. A comparison of the effects must be made with the structurally closest known product (**T 164/83 (Antihistamines/EISAI)**).

In order to obtain a product claim it is not necessary that the product actually has been prepared as of the filing date of the application; however, it must be preparable based on the teaching given in the application.

The disclosure of a limited number of ways of performing the invention is considered sufficient, if it allows the person skilled in the art to perform the invention over the whole range claimed (**T 409/91 (Fuel Oils/EXXON)** and **T 435/91 (Hexagonal liquid crystal gel/UNILEVER)**). The specification must provide at least one way of performing the invention. Whether such a disclosure is sufficient must, however, be decided on the basis of the available evidence and on the balance of probabilities in each individual case (**T 548/91 (Dipeptides/SCHERING)**).

A process claim is considered novel if it differs from the known processes in at least one starting product or in at least one process step. The first case relates to a process of analogy which is conducted in a manner known per se (see C.I.3.a.c). The inventive step of a process of analogy for preparing a novel product can be established based on the unexpected properties of the end product (**T 119/82 (Gelation/EXXON)**).

Use claims are allowable in cases where a novel and inventive use of an already known product is found, or in addition to product claims directed to a novel and inventive product.

In the case a further medical use of a medicinal product is found, a use claim may be drafted in accordance with **G 5/83 (Second medical indication/EISAI)** (see C.I.3.a.b and C.I.3.e.d) and/or in purpose-limited format, provided that the relevant date of the application in question is January 29, 2011 or earlier. As for applications having a later relevant date, only purpose-limited product claims are admissible, even for the second/further medical indication, in accordance with the principle laid down in decision **G 2/08 (Dosage Regimen/ABBOTT RESPIRATORY)**.

The inventive step of a use claim may be established by the surprising effects obtained by using a known compound for a specific purpose.

D.I.1. Product claims for low molecular products and polymers

Claim drafting:

Chemical products are usually defined in claims by their structure, preferably by their chemical formula or composition. If this is not possible, they can be defined by other characteristics, such as physical or chemical parameters, or by means of a product-by-process claim (see C.I.3.e.a).

Claims directed to low molecular weight products and chemical polymers may read as follows:

- a) Products defined by their structure or composition:

Substance X (or composition X)

Polymer comprising a repeating unit of formula X.

- b) Products defined by characteristics:

Substance X (or composition X) having a molecular weight of ..., a melting point of ..., characteristic peaks in the NMR spectrum at ... and an isoelectric point of ... at a pH of ... in an aqueous solution.

- c) Products defined by a process for their preparation (“product-by-process claim”):

Substance X (or composition X) obtainable by reacting compound A with compound B under the following reaction conditions ...

A product-by-process claim can also contain both product and process parameters, for example:

Substance X (or composition X) having a molecular weight of ..., a melting point of ..., and being obtainable by reacting compound A with compound B under the following reaction conditions ...

- d) Purpose-limited product claim for low molecular products:

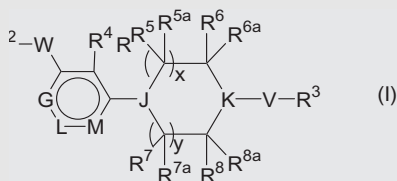
Substance X (or composition X) for use as a medicinal product.

Substance X (or composition X) for use in the treatment of disease Y.

Examples of allowed product claims are shown in the following:

EP-B1 – 1827438 – Claims 1 and 10:

1. A compound of formula (I):



wherein:

x and y are each independently 0, 1, 2 or 3;

G is $-N=$ or $-C(R^4)=$;

J and K are each independently N or C(R¹⁰);

L and M are each independently -N= or -C(R⁴)=, provided that L and M can not both be -C(R⁴)= when G is -C(R⁴)= and provided that L and M can not both be -N= when G is -N=;

V is a direct bond, -N(R¹)-, -N(R¹)C(O)-, -O-, -C(O)-, -C(O)O-, -C(S)-, -C(O)N(R¹)-, -S(O)_p- (where p is 0, 1 or 2) or -S(O)_pN(R¹)- (where p is 1 or 2);

W is a direct bond, -N(R¹)C(O)-, -C(O)N(R¹)-, -OC(O)N(R¹)-, -N(R¹)C(O)N(R¹)-, -O-, -N(R¹)-, -S(O)_t- (where t is 0, 1 or 2), -N(R¹)S(O)_p- (where p is 1 or 2), -S(O)_pN(R¹)- (where p is 1 or 2), -C(O)-, -OS(O)₂N(R¹)-, -OC(O)-, -C(O)O-, or -N(R¹)C(O)O-;

each R¹ is independently selected from the group consisting of hydrogen, C₁-C₁₂alkyl, C₂-C₁₂hydroxyalkyl, C₄-C₁₂cycloalkylalkyl and C₇-C₁₉arylalkyl;

R² is selected from the group consisting of C₁-C₁₂alkyl, C₂-C₁₂alkenyl, C₂-C₁₂hydroxyalkyl, C₂-C₁₂hydroxyalkenyl, C₂-C₁₂alkoxyalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, aryl, C₇-C₁₉arylalkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclylalkyl, C₁-C₁₂heteroaryl, and C₃-C₁₂heteroarylalkyl;

or R² is a multi-ring structure having 2 to 4 rings wherein the rings are independently selected from the group consisting of cycloalkyl, heterocyclyl, aryl and heteroaryl and where some or all of the rings may be fused to each other;

R³ is selected from the group consisting of hydrogen, C₁-C₁₂alkyl, C₂-C₁₂alkenyl, C₂-C₁₂hydroxyalkyl, C₂-C₁₂hydroxyalkenyl, C₂-C₁₂alkoxyalkenyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, aryl, C₇-C₁₉arylalkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclylalkyl, C₁-C₁₂heteroaryl and C₃-C₁₂heteroarylalkyl;

or R³ is a multi-ring structure having 2 to 4 rings wherein the rings are independently selected from the group consisting of cycloalkyl, heterocyclyl, aryl and heteroaryl and where some or all of the rings may be fused to each other;

each R⁴ is independently selected from hydrogen, fluoro, chloro, C₁-C₁₂alkyl, C₁-C₁₂alkoxy, haloalkyl, cyano, nitro or -N(R⁹)₂;

or two adjacent R⁴ groups, together with the carbons to which they are attached, may form an aryl, heteroaryl or heterocyclyl ring system;

R⁵, R^{5a}, R⁶, R^{6a}, R⁷, R^{7a}, R⁸ and R^{8a} are each independently selected from hydrogen or C₁-C₃alkyl;

or R⁵ and R^{5a} together, R⁶ and R^{6a} together, or R⁷ and R^{7a} together, or R⁸ and R^{8a} together are an oxo group, provided that when V is -C(O)-, R⁶ and R^{6a} together or R⁸ and R^{8a} together do not form an oxo group, while the remaining R⁵, R^{5a}, R⁶, R^{6a}, R⁷, R^{7a}, R⁸ and R^{8a} are each independently selected from hydrogen or C₁-C₃alkyl;

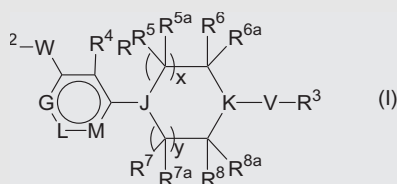
or one of R⁵, R^{5a}, R⁶ and R^{6a} together with one of R⁷, R^{7a}, R⁸ and R^{8a} forms a direct bond or an alkylene bridge, while the remaining R⁵, R^{5a}, R⁶, R^{6a}, R⁷, R^{7a}, R⁸, and R^{8a} are each independently selected from hydrogen or C₁-C₃alkyl;

each R⁹ is independently selected from hydrogen or C₁-C₆alkyl; and

R¹⁰ is independently selected from hydrogen, fluoro, chloro, C₁-C₁₂alkyl or C₁-C₁₂alkoxy;

as a stereoisomer, enantiomer or tautomer thereof, as a mixture of stereoisomers, as a pharmaceutically acceptable salt or acetate, formate and benzoate derivatives of alcohol or amine functional groups thereof.

10. Compound of formula (I):



wherein:

x and y are each independently 0, 1, 2 or 3;

G is -N= or -C(R⁴)=;

J and K are each independently N or C(R¹⁰);

L and M are each independently -N= or -C(R⁴)=, provided that L and M can not both be -C(R⁴)= when G is -C(R⁴)= and provided that L and M can not both be -N= when G is -N=;

V is a direct bond, -N(R¹)-, -N(R¹)C(O)-, -O-, -C(O)-, -C(O)O-, -C(S)-, -C(O)N(R¹)-, -S(O)p- (where p is 0, 1 or 2) or -S(O)pN(R¹)- (where p is 1 or 2);

W is a direct bond, -N(R¹)C(O)-, -C(O)N(R¹)-, -OC(O)N(R¹)-, -N(R¹)C(O)N(R¹)-, -O-, -N(R¹)-, -S(O)t- (where t is 0, 1 or 2), -N(R¹)S(O)p- (where p is 1 or 2), -S(O)pN(R¹)- (where p is 1 or 2), -C(O)-, -OS(O)₂N(R¹)-, -OC(O)-, -C(O)O-, or -N(R¹)C(O)O-;

each R¹ is independently selected from the group consisting of hydrogen, C₁-C₁₂alkyl, C₂-C₁₂hydroxyalkyl, C₄-C₁₂cycloalkylalkyl and C₇-C₁₉aralkyl;

R² is selected from the group consisting of C₁-C₁₂alkyl, C₂-C₁₂alkenyl, C₂-C₁₂hydroxyalkyl, C₂-C₁₂hydroxyalkenyl, C₂-C₁₂alkoxyalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, aryl, C₇-C₁₉aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclalkyl, C₁-C₁₂heteroaryl, and C₃-C₁₂heteroarylalkyl;

or R² is a multi-ring structure having 2 to 4 rings wherein the rings are independently selected from the group consisting of cycloalkyl, heterocyclyl, aryl and heteroaryl and where some or all of the rings may be fused to each other;

R³ is selected from the group consisting of hydrogen, C₁-C₁₂alkyl, C₂-C₁₂alkenyl, C₂-C₁₂hydroxyalkyl, C₂-C₁₂hydroxyalkenyl, C₂-C₁₂alkoxyalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, aryl, C₇-C₁₉aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclalkyl, C₁-C₁₂heteroaryl and C₃-C₁₂heteroarylalkyl;

or R³ is a multi-ring structure having 2 to 4 rings wherein the rings are independently selected from the group consisting of cycloalkyl, heterocyclyl, aryl and heteroaryl and where some or all of the rings may be fused to each other;

each R⁴ is independently selected from hydrogen, fluoro, chloro, C₁-C₁₂alkyl, C₁-C₁₂alkoxy, haloalkyl, cyano, nitro or -N(R⁹)₂;

or two adjacent R⁴ groups, together with the carbons to which they are attached, may form an aryl, heteroaryl or heterocycl ring system;

R⁵, R^{5a}, R⁶, R^{6a}, R⁷, R^{7a}, R⁸ and R^{8a} are each independently selected from hydrogen or C₁-C₃alkyl;

or R⁵ and R^{5a} together, R⁶ and R^{6a} together, or R⁷ and R^{7a} together, or R⁸ and R^{8a} together are an oxo group, provided that when V is -C(O)-, R⁶ and R^{6a} together or R⁸ and R^{8a} together do not form an oxo group, while the remaining R⁵, R^{5a}, R⁶, R^{6a}, R⁷, R^{7a}, R⁸ and R^{8a} are each independently selected from hydrogen or C₁-C₃alkyl;

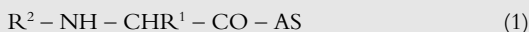
or one of R⁵, R^{5a}, R⁶ and R^{6a} together with one of R⁷, R^{7a}, R⁸ and R^{8a} forms a direct bond or an alkylene bridge, while the remaining R⁵, R^{5a}, R⁶, R^{6a}, R⁷, R^{7a}, R⁸, and R^{8a} are each independently selected from hydrogen or C₁-C₃alkyl;

each R⁹ is independently selected from hydrogen or C₁-C₆alkyl; and
 R¹⁰ is independently selected from hydrogen, fluoro, chloro, C₁-C₁₂alkyl or C₁-C₁₂alkoxy;
 as a stereoisomer, enantiomer or tautomer thereof, as a mixture of stereoisomers, as a pharmaceutically acceptable salt or acetate, formate and benzoate derivatives of alcohol or amine functional groups thereof, for the treatment of a disease or a condition mediated by stearyl-CoA desaturase (SCD) in a mammal, wherein the disease or condition is selected from of acne, Type II diabetes, impaired glucose tolerance, insulin resistance, obesity, fatty liver, non-alcoholic steatohepatitis, dyslipidemia and metabolic syndrome and any combination of these.

The first claim above (claim 1) is a product claim, whereas the second claim above (claim 10) is a purpose-limited product claim limited to the treatment of certain diseases (see underlining).

EP-B1 – 0466030 – Claim 1:

N-acyl dipeptides of the formula



wherein AS represents isoleucine, tyrosine, glutamine or cysteine, provided that R¹ signifies hydrogen and R² signifies a formyl group,

or AS represents valine, isoleucine, tyrosine, glutamine or cysteine, provided that R¹ signifies a methyl group and R² signifies a formyl group,

or AS represents isoleucine, glutamine or cysteine, provided that R¹ signifies hydrogen and R² signifies an acetyl group,

or AS represents isoleucine or cysteine, provided that R¹ signifies a methyl group and R² signifies an acetyl group,

or AS represents valine, leucine, isoleucine, tyrosine, glutamine or cysteine, provided that R¹ signifies hydrogen or a methyl group and R² signifies an acyl radical of an aliphatic monocarboxylic acid or dicarboxylic acid having 3 to 6 C atoms, except methacrylic acid and, unless R¹ is methyl and AS is isoleucine, 3-methylbutyric acid,

and the physiologically compatible carboxylates thereof.

EP-B1 – 0386563 – Claim 1:

Chemically modified antisense oligonucleotides with sequences against the TAR sequence and leader sequence nt 21–53, 74–161, 202–279 and the second and third exon of the Tat gene nt 5368–5403, 5421–5548, 5583–5617 and nt 7967–8366, 8385–9183 of the HIV I genome.

EP-B1 – 0402402 – Claim 1:

A preparation for use in therapy comprising a single stranded modified oligonucleotide of 8–50 nucleotides in length, wherein the modified oligonucleotide is one which is modified at an internucleoside phosphate, being a phosphomorpholidate, phosphopiperazine or phosphoromidate derivative, the oligonucleotide being capable of selectively hybridizing with a highly conserved region of the HTLV-III genome to induce selective hybridization arrest of HTLV-III replication and/or gene expression, the highly conserved region comprising any of:

- (i) the tRNA^{lys} primer binding site;
- (ii) regions of the HTLV-III genome vicinal in the 5' direction to the tRNA^{lys} primer binding site;

- (iii) the tRNA^{lys} primer binding site and regions of the HTLV-III genome vicinal in the 5' direction to the tRNA^{lys} primer binding site;
- (iv) the mRNA donor splice sites;
- (v) the mRNA acceptor splice sites;
- (vi) the initiator codon for the gag gene;
- (vii) the initiator codon for the env gene;
- (viii) the initiator codon for the tat gene;
- (ix) the initiator codon for the sor gene;
- (x) the initiator codon for the 3' orf gene;
- (xi) the cap nucleotide of the HTLV-III genome;
- (xii) the art gene or portions thereof;
- (xiii) the region of HTLV-III genome encoding a frameshift.

D.I.2. Process claims for low molecular products and polymers

Claim drafting:

A process claim typically defines the target compound and the educts to be reacted, and in some cases also refers to specific reaction steps and/or conditions.

Process claims for preparing a low molecular weight product may read as follows:

A process for the preparation of substance X (or composition X) comprising reacting starting compound A with starting compound B.

A process for the preparation of substance X (or composition X) comprising reacting starting compound A with starting compound B under the following reaction conditions ...

Examples of allowed process claims are shown in the following:

EP-B1 – 0326364 – Claim 47:

A process for preparing a compound according to any one of Claims 1 to 45, which process comprises the steps:

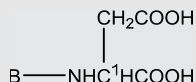
reacting together two compounds, one having a terminal carboxy group or reactive derivative thereof and the other having a terminal amino group or reactive derivative thereof, under conditions conventional for peptide synthesis, said two compounds corresponding to the fragments derivable by cleavage of any one of the peptide bonds in said compound of formula (I) or a reactive derivative of said compounds; and if necessary, de-protecting and/or salifying the resulting compound.

Claims 1 to 45 of this patent are directed to oligopeptides.

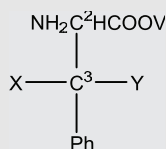
EP-B1 – 0220923 – Claim 11:

Process for producing a dipeptide as claimed in any of claims 1 to 4 said process comprising:

reacting B-substituted aspartic acid of the formula



or a salt thereof with a second amino acid having the formula



wherein B, X, Y and V are as defined in claim 1 and the C² carbon has the common natural configuration of naturally occurring amino acids; said reaction being conducted in

- d) a water-immiscible solvent in the presence of a metallo-proteinase,
- e) a water-miscible solvent in the presence of a nonmetallo-proteinase, or
- f) a water-immiscible solvent in the presence of a nonmetallo-proteinase.

Claims 1 to 4 of this patent refer to an (S)-alpha-aspartyl-(2S,3S)-beta substituted phenylalanine.

EP-B1 – 0402402 – Claim 3:

An in vitro method of inhibiting HTLV-III replication, HTLV-III gene expression or both in cells containing HTLV-III, comprising introducing into the cells a modified oligodeoxynucleotide according to claim 1 or claim 2.

Claims 1 and 2 are directed to a preparation for use in therapy comprising a single stranded modified oligonucleotide of 8–50 nucleotides in length.

EP-B1 – 0313100 – Claim 1:

A method for purifying a dipeptide ester by electrolysis in an electrolytic cell comprising an anode compartment, a cathode compartment and a central compartment partitioned by ion exchange membranes, which comprises supplying an aqueous dipeptide ester solution containing inorganic and organic cations and anions and having a pH of from 3.5 to 7.0, to the central compartment defined by anion and cation exchange membranes or by anion exchange membranes and an aqueous acid electrolyte solution to the cathode compartment and an aqueous electrolyte solution to the anode compartment, and electrically removing the inorganic and organic anions from the central compartment to the anode compartment through the anion exchange membrane and optionally electrically removing the inorganic and organic cations from the central compartment to the cathode department through the cation exchange membrane.

D.I.3. Use claims/purpose-limited product claims for low molecular products and polymers

Claim drafting:

Generally, a use claim may read as follows:

Use of substance X (or composition X) as a food additive.

A (Swiss-type) second medical use claim may read:

Use of substance X (or composition X) for the manufacture of a medicinal product for the treatment of disease Y.

A purpose-limited product claim may read as follows:

Substance X (or composition X) for use in a method of treating disease Y.

or

Substance X (or composition X) for use in treating disease Y.

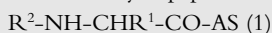
Examples of allowed use claims are shown in the following:

EP-B1 – 0386563 – Claim 7:

Use of the antisense oligonucleotides according to Claims 1 to 4 including the complementary sequences as gene probe.

EP-B1 – 0466030 – Claim 2:

Use of N-acyl dipeptides of the formula



wherein AS represents valine, leucine, isoleucine, tyrosine, tryptophan, glutamine or cysteine, R^1 signifies hydrogen or a methyl group and R^2 signifies a formyl group or acetyl group or an acyl radical of an aliphatic monocarboxylic acid or dicarboxylic acid having 3 to 6 C atoms, and the physiologically compatible carboxylates thereof, as a source of C-terminal amino acids in mixtures and solutions for the enteral or parenteral nutrition of nutrient media for cell cultures.

EP-B1 – 0326364 – Claim 48:

The use for the manufacture of a medicament for the treatment or prophylaxis of angiotensin-induced hypertension of a compound of formula (I) or a pharmaceutically acceptable salt thereof, as defined in any one of Claims 1 to 45.

Claims 1 to 45 of this patent are directed to oligopeptides.

EP-B1 – 0402402 – Claim 4:

Use of a preparation (or modified derivative thereof) according to any one of the preceding claims for the manufacture of a medicament for use in AIDS chemotherapy, e.g. in inhibiting HTLV-III replication and/or gene expression in peripheral human blood cells (e.g. human T lymphocytes) infected with HTLV-III.

Claims 1 and 2 of this patent refer to a preparation for use in therapy comprising a single stranded modified oligonucleotide of 8–50 nucleotides in length.

D.II. Nucleic acids

D.II.1. Introduction

This chapter discusses possibilities for protecting nucleic acids under the EPC.

The term “nucleic acids” (NA) as used herein includes deoxyribonucleic acids (DNA), ribonucleic acids (RNA) and NA analogs such as locked nucleic acids (LNAs) and peptidic nucleic acids (PNAs). The nucleic acids may be single or dou-

ble stranded, linear fragments or circular, vectors of any kind such as plasmids, cos-mids, virus or phage genomes. Further, they may be obtained from natural sources, recombinantly produced, chemically synthesized, or a combination thereof.

In principle, nucleic acids are chemical compounds, the patentability of which is determined according to established patent practice for inventions in the field of chemistry. However, nucleic acids may not only be obtained by classical chemical synthesis but also by isolation from biological material. Special problems therefore arise, e.g. with respect to their characterization and reproducibility. Most nucleic acids claimed in patent applications contain a coding region, i.e. a stretch of deoxyribonucleotides or ribonucleotides which is subject to transcription and/or translation processes, resulting in generation of a RNA or protein. The sequence of a given nucleic acid determines the primary sequence of the immediate expression product, such as a protein, which later may be further processed post-translationally. A protein sequence could correspond to a multitude of nucleic acid sequences coding for this sequence, only one (or a few) of which will occur in nature. The known relation between amino acid sequences and corresponding nucleic acid sequences is a peculiarity in the field of inventions concerning proteins and nucleic acids, and will therefore receive special consideration in this chapter.

D.II.2. Protecting nucleic acids under the EPC

As for any other matter in life sciences, claims relating to nucleic acids must fulfill the legal requirements of the EPC. In particular, they must not contravene the exclusion provisions laid down in Arts. 52 and 53 EPC. In addition, the claimed subject-matter has to meet the further patentability requirements, i.e. novelty, inventive step and industrial application. Furthermore, the application has to fulfill the requirements of sufficiency of disclosure, clarity and support of the claims, as discussed in C.I.3.b., C.I.3.e.b. and C.I.3.e.c.

In the following discussion, several decisions of the EPO relating to the patentability requirements and the requirements of the application as applied to nucleic acids will be briefly considered. The authors consider these decisions to be particularly informative and important and, therefore, they should be taken into account when drafting applications directed to nucleic acids.

D.II.2.a. Discoveries

According to Art. 52(2) EPC, discoveries shall not be regarded as inventions and, therefore, shall be excluded from patent protection. In their decision “**RELAXIN**”, an Opposition Division dealt with the question as to whether the finding of a DNA coding for human relaxin or one of its biological precursors is a discovery within the meaning of Art. 52(2) EPC. The Opposition Division considered the claimed DNA to be a natural substance. In the reasons given for

the decision, the Opposition Division referred to the Guidelines (C-IV,2.3 as available at that time, now G-II,5.2.), stipulating:

[T]o find a substance freely occurring in nature is mere discovery and therefore unpatentable. However, if a substance found in nature has first to be isolated from its surroundings and a process for obtaining it is developed, that process is patentable. Moreover, if this substance can be properly characterised by its structure and it is new in the absolute sense of having no previously recognized existence, then the substance per se may be patentable. (point 5.1)

The Opposition Division concluded:

The above guideline is highly appropriate in the present case. Human H2-relaxin had no previously recognised existence. The proprietor has developed a process for obtaining H2-relaxin and the DNA encoding it, has characterised these products by their chemical structure and has found a use for the protein. The products are therefore patentable under Article 52(2) EPC. (point 5.2)

The above finding was also confirmed by an Appeal Board dealing with the Relaxin case. In **T 272/95 (Relaxin/HOWARD FLOREY INSTITUTE)** the Board held that the claims do not fall under Art. 52(2) EPC, and referred to the then valid Rule 23(e) (2) (now Rule 29(2) EPC) (see point 7 of the reasons for the decision).

Thus, according to present case law as well as according to the Guidelines, nucleic acids obtained from natural sources are considered to be naturally occurring products which may be patentable. For further details relating to naturally occurring products, see C.I.3.a.a.

D.II.2.b. Morality and “ordre public”

In the following cases parties have attempted to invalidate patents relating to human or plant DNA on the basis of Art. 53(a) EPC excluding inventions, the publication or exploitation of which would be contrary to “ordre public” or morality.

The patent underlying the decision “**RELAXIN**” of an Opposition Division and the corresponding later decision by an Appeal Board in **T 272/95**, related to a DNA fragment encoding human H2-Relaxin or its biological precursors.

In their decision, the Opposition Division referred to a criterion provided by the Guidelines (Guidelines, then C-IV, 3.1, now G-II,4.1.):

A fair test to apply is to consider whether it is probable that the public in general would regard the invention as so abhorrent that the grant of patent rights would be inconceivable. If it is clear that this is the case, objections should be raised under Art. 53(a); otherwise not.

The Opposition Division held that the patent did not contravene Art. 53(a) EPC. This decision was confirmed in appeal proceedings (**T 272/95**).

Decision **T 356/93 (Plant cells/PLANT GENETIC SYSTEMS)**, which will be discussed in detail in D.VI.2, relates to a patent including claims directed to vectors for the transformation of plant cells. Applying the definitions of the concepts of “ordre public” and morality as cited in C.I.2.a, an Appeal Board

reached the conclusion that none of the claims of the patent in suit comprised subject-matter which would be contrary to Art. 53(a) EPC.

D.II.2.c. Methods of treatment

According to Art. 53(c) EPC, methods for the treatment of the human or animal body by surgery or therapy and diagnostic methods practiced on the human or animal body are excluded from patentability.

Applying a nucleic acid outside of the human body, e.g. on a sample taken from a human body as for e.g. performing a diagnostic method, is generally not in conflict with Art. 53(c) EPC, see for example **T 666/05 (Mutation/UNIVERSITY OF UTAH)** and **T 80/05 (Method of diagnosis/UNIVERSITY OF UTAH)** and Guidelines, G-II,4.2.1.

D.II.2.d. Novelty

The Applicant has several options for establishing novelty of claims directed to nucleic acids. The Applicant can object to the prior art as non-enabling, if justified; this has the consequence that the prior art is no longer relevant for assessing novelty. The Applicant can further establish novelty by demonstrating that the claimed sequence or composition differs physically from the prior art. Further, characterizing the nucleic acid by a new parameter, such as the molecular weight or the purity, can be a means to delimit a claim over the prior art. Moreover, the nucleic acid can be characterized by functional features or a certain purpose, in that for example a certain protein is encoded by the claimed nucleic acid; such a feature can also be used to delimit the claim over the prior art.

In addition, a new use of a known nucleic acid can be used to define the invention. Finally, the nucleic acid can be defined by a process of preparation which can lead to a claim sufficiently delimited over the prior art.

Examples of case law follow below, wherein one or more of the above options were used to argue novelty of the invention. Some of the case law relates to protein inventions but still should be equally applicable to nucleic acid inventions as described in this chapter.

Prior art contains non-enabling disclosure

In **T 81/87 (Preprorennin/COLLABORATIVE)** an Appeal Board confirmed that for inventions in the field of biotechnology, as for any other inventions, a prior art disclosure must be enabling without undue burden in order to destroy the novelty of a later-filed patent application. In this case, a prior art document disclosed all the steps necessary to obtain the claimed end product preprorennin by providing a general recipe for constructing and isolating precursors or intermediate substances for vectors encoding the protein preprochymosin (which is the same as preprorennin). The Board doubted both the public availability of plasmids used in the construction of the allegedly anticipating vec-

tors and the sufficiency of disclosure of the plasmids, since their exact composition was uncertain. The Board thus concluded:

Whilst it may theoretically not be absolutely impossible to proceed on the basis of the citation, a novelty-destroying document must, according to standard practice, be enabling without undue burdening to a person skilled in the art. In such circumstances, inventions might require an actual demonstration of reduction to practice and corresponding detailed instructions to the public in a document, to become available for the purposes of Article 54 EPC as part of the state of the art. (point 18)

In **T 301/87 (Alpha-interferons/BIOGEN)**, an Appeal Board had to decide whether DNA sequences contained in a certain prior art phage gene bank (“Lawn’s gene bank”) destroyed the novelty of claims relating to a nucleotide sequence, which might have been contained in such a gene bank. The Board held:

[T]he situation resembles that prevailing with natural substances, since the availability of phages is not direct, and is rather like the isolation of a component or bacterium from soil where the same exists in admixture with other useless materials. Thus, the idea that the gene bank itself would once for all anticipate an invention relating to a nucleotide sequence which may be contained therein somewhere, cannot be sustained. (point 5.8)

This principle was confirmed in **T 412/93 (Erythropoietin/KIRIN-AMGEN)** which states:

[T]he Board finds that the nucleotide sequence of the Epo gene was not part of the state of the art merely because the nucleotide sequence would have been present in the Lawn gene bank or possibly others. (point 117)

Thus, a DNA which is not isolated and characterized to an extent enabling its reproduction, does not destroy the novelty of a later claimed DNA. A similar result was found in **T 18/09 (Neutrokin/HUMAN GENOME SCIENCES)**.

The above principle of **T 81/87** was confirmed in **T 576/91 (Plasmid pTR2030/NORTH CAROLINA STATE UNIVERSITY)**. Here, an Appeal Board had to decide whether a pre-published scientific document disclosing the plasmid pTR2030 and its preparation by conjugal mating of two strains, was novelty-destroying for a claim relating to that very same plasmid. One of the two parent strains was available to the public and the other one had been obtained from a company under a research agreement.

Before answering the question relating to novelty, the Board had to consider whether the cited prior art document

can be considered intrinsically enabling merely by virtue of an unwritten ethical rule whereby the authors [...] would have been prepared to supply – upon request – samples of pTR2030 to each and every person interested in obtaining it. (point 2.2)

In the absence of any evidence to the contrary, the Board held that there is no obligation by authors of a scientific publication to release microorganisms disclosed therein. Since the microorganism containing the plasmid pTR2030 was not publicly available, the plasmid was not considered to have been available as such.

Moreover, since there was no proof that the parent strain, provided under a research agreement, was made available to the public, the Board concluded that the pre-published document did not contain an enabling disclosure for preparing the plasmid in question. Consequently, the prior art did not have a novelty-destroying effect.

In **T 179/01 (Herbicide resistant plants/MONSANTO)**, novelty of claim 1 was under dispute. Claim 1 is directed to a DNA sequence encoding an EPSPS enzyme, which is further characterized by various parameters. One of the Opponents cited a prior art document (document 2) against the novelty of claim 1, which disclosed a DNA fragment allegedly encoding a protein with EPSPS functionality, based on theoretical considerations.

The Board pointed out that in order to be relevant in the assessment of novelty, a prior art document must provide not only a clear and unambiguous, but also an enabling disclosure of the claimed subject-matter. The Board decided that since the prior art document did not experimentally prove the EPSPS activity of the disclosed DNA nor provide a teaching for obtaining said proteins, it does not provide an enabling disclosure and is therefore irrelevant for novelty.

Interestingly, the Opponent furnished post-published evidence in support of, inter alia, the EPSPS activity of the disclosed DNA (document 2); however, the Board dismissed this evidence and decided:

[A]s document (2) on its own neither points towards, nor enables any of these data, it is concluded that they do not represent the “inherent” teaching of the prior art and that, therefore, it becomes irrelevant whether or not they show that the DNA of document (2) has the inherent property of encoding a protein as is characterized in the claim. (point 15)

Accordingly the Board acknowledged novelty of claim 1.

The claimed invention is characterized by a new composition or sequence

In the appeal proceedings **T 886/91 (Hepatitis B virus/BIOGEN INC.)**, one of the Opponents argued that small differences in a claimed DNA and/or amino acid sequence vis-à-vis prior art sequences, are not sufficient to render the claimed sequence novel. The Board disagreed with this view, stating that it is well known that even a change in one amino acid can dramatically change the properties of a protein molecule. Thus, novelty was accepted.

Further, one of the Opponents argued that there were common identical stretches in the claimed sequences and the known sequences, so the claimed sequences should lack novelty. The Board held that this is

merely theoretical because none of the cited documents discloses or suggests any discrete fragments of the reported sequences as an identifiable entity which could be used for a comparison. (point 8.1.2)

With respect to DNA, the Board further clarified that identical sequence stretches in the absence of identical fragments cannot destroy novelty of a claimed DNA sequence and stated:

[D]ocument (1) [...] does not report any definite sequence data which can be said to affect the novelty of the claims at issue. In fact, although the nucleotide sequences referred to in the latter are likely to be contained in the said fragments, they are not identified and characterized in their exact primary structure and thus they are not made available in the sense of Article 54(2) EPC. (point 8.1.3)

In case **T 429/96 (Serine protease inhibitors/AMGEN)**, the Board had to decide on the novelty of a claim directed to a purified serine protease inhibitor consisting of a single unfragmented polypeptide chain, the inhibitor being characterized by an amino acid sequence. The relevant prior art disclosed a composition containing the claimed inhibitor in degraded form as a mixture of fragments. The Board found the claim directed to the undegraded polypeptide chain to be novel over the mixture of degraded protein fragments.

In **T 1121/96 (Erythropoietin/GENETICS INSTITUTE)**, novelty of claim 1 was considered. This claim is directed to a method for the production of erythropoietin in eukaryotic cells comprising as a technical feature a DNA sequence. The Opponents alleged lack of novelty of claim 1 based on a prior art document that disclosed erythropoietin production in eukaryotic cells containing a genomic DNA sequence, allegedly containing a sequence identical to the sequence recited in claim 1.

The Board, however, found claim 1 to be novel, since the cited prior art disclosed a genomic DNA sequence containing only portions of the DNA sequence of claim 1. The Board made it clear that a DNA sequence may only be anticipated by the disclosure of an identical DNA sequence as an uninterrupted nucleotide sequence. In this regard the Board regarded the disclosed DNA sequence as a single chemical compound.

In opposition appeal proceedings underlying **T 351/98 (HIV-I/CHIRON CORPORATION)**, the claimed recombinant DNA was *inter alia* characterized by encoding an antigenic protein from HIV characterized by a sequence. The prior art disclosed a region of the HTLV-3 genome which was much larger than what was claimed by the Patentee. The Board came to the conclusion that the specific DNA as claimed by the Patentee could not be derived from the disclosure of the prior art document and acknowledged novelty of the claims (points 58–62 of the decision).

In **T 58/00 (Hepatic growth factor/MITSUBISHI)** novelty of a claim directed to a cell growth factor represented by a specific amino acid sequence was found to be novel over prior art documents merely showing protein bands in an SDS gel. Additionally, the prior art disclosed proteins only deprived of the signal sequence, which however was part of the claimed protein. Novelty was acknowledged because the Opponent failed to show that the protein disclosed in the prior art corresponded to the claimed protein.

In **T 1072/00 (Borrelia burgdorferi/MIKROGEN)**, a claimed peptide was characterized by consisting of a certain amino acid sequence. The prior art disclosed sequences comprising the sequence of the shorter peptide as claimed.

The Board acknowledged novelty of the claim since the prior art did not disclose the specific claimed peptides.

Novelty conferred by a new parameter

Throughout the years the Appeal Boards have acknowledged the novelty of inventions characterized by a new parameter, such as purity of an active agent or the molecular weight of the claimed molecule.

In case **T 412/93 (Erythropoietin/KIRIN-AMGEN)**, a claim directed to a polypeptide characterized by a molecular weight was found to be novel over the naturally occurring product having a lower molecular weight.

In case **T 378/95 (Factor VIII C/CHIRON CO.)**, a claimed protein composition was defined, among other ways, by comprising a complex having a purity of at least 30% based on total protein. This feature of complex purity was sufficient for the Board to acknowledge novelty since in the Board's opinion the prior art did not disclose any preparation wherein the complex formed at least 30% of the total proteins of the composition.

In a further case, **T 767/95 (Interleukin-1/IMMUNEX CORPORATION)**, an Appeal Board had to decide on the novelty of a claim wherein the claimed protein composition was characterized by, among other things, a molecular weight as determined by SDS-PAGE. The Board acknowledged novelty of the claim because in the Board's opinion there was no evidence available that the protein preparations disclosed in the prior art exhibited the molecular weight feature as contained in the claim.

In case **T 877/90 (T-cell growth factor/HOOPER)**, the claim was directed to a growth factor preparation being serum-free and mitogen-free. The Board regarded the feature of being serum-free and mitogen-free as an essential characteristic of the claimed product and acknowledged novelty because such a product was not disclosed in the prior art.

In another case, **T 90/03 (Phytase/BASF)**, an Appeal Board again dealt with the purity of a claimed composition as a feature for establishing novelty. In that case, the Board referred to an earlier case from the small molecule field, **T 990/96 (Erythro-compounds/NOVARTIS)**, where an Appeal Board did not acknowledge purity as a feature that could establish novelty of a chemical compound. The Board in **T 90/03** *inter alia* stated:

In contrast, the present application relates to the purification of a high molecular weight enzyme obtained from a crude native biological material. Although methods for protein purification are known to the skilled person, they are far from standardized, in the sense that a protocol adapted to the specific properties of the protein has to be established for every protein. In fact, evidence to support this point may be found in document D5 itself which shows that an additional (conventional) purification step, namely a cationic chromatography, only provides a slight increase in the degree of purity and specific activity of the purified enzyme (cf. page 74, last paragraph). Decision T 990/96 is, thus, of no relevance to this case.

The appropriate jurisprudence is represented by decision T 767/95 of 5 September 2000 concerning the purification of interleukin-1 β (IL-1 β), a high molecular weight protein (17.5 kDa). In that decision a purified homogeneous preparation of IL-1 β was found to be novel

over a semi-purified mixture of proteins containing IL-1 β . A relevant consideration in that case was the provision of IL-1 β in a degree of purity that allowed the determination of its (partial) amino acid sequence, whereas »no analysis of the amino acid sequence of IL-1 that would provide definitive proof of the homogeneity of IL-1 preparations« was found in the prior art (cf. point 6 of the decision).

D.II.2.e. Inventive Step

In decision **T 609/90 (Protecting bacteria/ELI LILLY)**, the Board assessed inventive step of a recombinant cloning vector useful for protecting a bacterium from bacteriophages freely living in the environment and containing double stranded DNA with a specific restriction site, and also a process for protecting a bacterium involving use of the vector. The vector was characterized as comprising genes encoding a restriction-modification system and a gene encoding a protein, the expression of which in the bacteria was desired. A plasmid carrying the restriction-modification system used according to the claimed invention was already prior art, albeit not as part of an expression vector.

The Board first considered several alternative solutions for protecting bacteria in large-scale fermentation from adverse effects by bacteriophages, and then discussed the advantages and disadvantages of protecting bacteria using the vector according to the invention while using the alternative solutions. The Board came to the conclusion that, due to the existence of several promising alternative solutions and in view of foreseeable disadvantages of introducing a restriction-modification system into the bacterial culture, a person skilled in the art would not seriously have contemplated, if at all, protecting bacteria by using the vector according to the application. Therefore, an inventive step was acknowledged.

In **T 816/90 (CBH II/ALKO)**, the inventive step of a DNA sequence was acknowledged, although a partial amino acid sequence of the corresponding protein was known from the prior art. In particular, the Applicant claimed a DNA sequence coding for the enzyme cellobiohydrolase II from a certain microorganism, the DNA sequence being one that codes for a specific amino acid sequence recited in the claim or for a substantially identical amino acid sequence exhibiting the same enzymatic activity. The relevant prior art documents disclosed the isolation and characterization of the protein cellobiohydrolase II (CBH II) including the amino acid sequence of 20 N-terminal amino acids and the molecular cloning and characterization of the gene encoding cellobiohydrolase I (CBH I) using essentially the same techniques as used in the application in question. According to the Examining Division, the contribution to the art by the Applicant was merely the additional step of preparing an antiserum against CBH II.

The Board considered the crucial question to be whether a skilled person starting from the closest prior art, i.e. the document disclosing the isolation in homogeneous form of CBH II and the sequence of the N-terminal 20 amino acids of CBH II, in light of the teaching of the documents disclosing cloning and characterization of CBH I, would have arrived at a method for the produc-

tion of CBH II by recombinant DNA technology in a straightforward way. An inventive step was acknowledged because the Applicant had used a modified procedure for isolating mRNA, which was considered to be crucial for obtaining sufficient amounts of mRNA, and further because the application went beyond the prior art by disclosing not only cloning, but also expression.

It is interesting that the Board considered the possibility of applying alternative experimental approaches to be a “purely academic question” and explicitly stated:

As to the question whether the skilled person would have achieved the same result by a different experimental approach, e.g. through the use of an oligonucleotide probe constructed on the basis of the amino acid sequence information in document (3), the Board considers that at this stage this is a purely academic question. Firstly, what appeared to be the most probable approach (analogous use of the differential hybridisation techniques described in documents (1) and (2)), has already been considered on the whole as non-obvious [...]. Secondly, no prior art document is at present available which shows that, starting from the information in document (3), the skilled person would have easily arrived at the claimed subject-matter. (point 5.2.8)

In **T 455/91 (Expression in yeast/GENENTECH)**, the Board considered the inventive step of yeast expression vectors. Claim 1 was directed to an empty vector as follows:

A DNA vector suitable for use in expressing exogenous genes in yeast, comprising a sequence which is replicable in yeast, a 5' flanking sequence of a yeast structural gene including its promoter, a site created downstream of said 5' flanking sequence in the direction of transcription for insertion of a structural gene coding for a biocompetent polypeptide ordinarily exogenous to yeast so as to be transcribable under the control of said promoter and translatable from a start signal carried by the DNA insert, and a sequence allowing phenotypic selection of yeast transformants.

Claim 9 was directed to a corresponding vector additionally comprising a DNA sequence encoding a biocompetent polypeptide ordinarily exogenous to yeast and a translational start codon. The Board considered whether a person skilled in the art would have tried to modify the technical teaching disclosed in the closest prior art document relating to *bacterial* vectors which included an ATG (a translational start codon), but also lacked the structural gene, in order to arrive at the claimed teaching. The Board considered a person skilled in the art to

readily seek appropriate, manifest changes, modifications or adjustments which involve little trouble or work and no risk or only calculable risks, especially for the sake of obtaining a more handy or convenient product or simplifying a procedure. In particular, the skilled person working in one field (e.g. expression in yeast) would regard a means conveniently adopted in a neighbouring field (e.g. the bacterial art) as being readily usable also in that field, if this transfer of technical knowledge involves nothing out of the ordinary. (point 5.1.3.3)

In the Board's opinion, there was sufficient incentive for an expert to at least try to transform knowledge from the bacterial art to yeast (point 5.1.3.4); the only difference between the claimed vector and the prior art vector beyond the intended host, was the presence or absence of a translational start codon ATG.

Further, the prior art concerning bacterial vectors was aware of “ready-for-use vectors”, into which a DNA sequence consisting of “start signal – exogenous DNA sequence – (optionally) termination signal” could be inserted. Therefore, the Board did not acknowledge an inventive step.

T 500/91 (Alpha-interferon II/BIOGEN) relates to the same patent as **T 301/87 (Alpha-interferons/BIOGEN)**. Among the several issues discussed in **T 500/91** two are of interest:

It was held that the hypothetical skilled person, who according to **T 500/91** may be represented by a team of appropriate specialists, is not expected to solve technical problems by performing scientific research in areas not yet explored (point 2.2 of the decision).

The objection that the claimed DNA molecule represents a mere “desideratum” was rejected, since there is no provision in the EPC pursuant to which “desiderata” are excluded from patentability, provided that means to fulfil them are disclosed in a manner sufficiently clear and complete to be carried out by a person skilled in the art and that such means were not made available to the public pursuant to Art. 54(1) EPC and were not obvious to a person skilled in the art pursuant to Art. 56 EPC (point 2.3.1 of the decision).

The Board concluded:

[H]aving regard to the fact that the area of genetic engineering here under consideration was relatively new at the relevant date, having further regard to the uncertainty at that date about facts influencing the success of the attempted recombinant-DNA technique, and to the absence of a well-established general level of knowledge in this particular technical area, the present successful technical application of recombinant-DNA techniques, according to Claims 1 and 2 under consideration, involves an inventive step. (point 2.4)

In the case underlying **T 886/91 (Hepatitis B virus/BIOGEN INC.)**, the inventive step of the following claim was evaluated:

The use of a DNA sequence coding for a polypeptide displaying HBV antigenicity, said DNA sequence being selected from DNA sequences of the formulae:

- (a) [...] and fragments thereof which encode polypeptides displaying HBV antigenicity;
- (b) [...] and fragments thereof which encode polypeptides displaying HBV antigenicity; and
- (c) DNA sequences which are degenerate as a result of the genetic code to any of the foregoing DNA sequences and which encode polypeptides displaying HBV antigenicity for the production of polypeptides displaying HBV antigenicity.

The closest prior art document reported on the construction of cloning and expression vectors containing DNA fragments of HBV genome sub-type adyw, which was the same sub-type sequenced for the purpose of the patent in question. Cells transformed with the vectors are reported to produce antigenic material reacting specifically with antibodies to HBV antigens, in particular HBcAg and also HBsAg. On the basis of this prior art, the technical problem was considered to be the exact identification and characterization of DNA sequences of HBV genome sub-type adyw encoding HBcAg and HBsAg within the known discrete DNA fragments.

The Board did not acknowledge an inventive step. According to the Board's opinion it was obvious for a skilled person to try to identify and characterize DNA sequences of HBV sub-type adyw encoding HBcAg and HBsAg and there was a reasonable expectation of success in doing so. Among other things, this conclusion was based on the consideration that the attempt to complete the work of the closest prior art document would not have involved anything out of the ordinary for a skilled person in the field of molecular biology at the relevant time, since all the necessary methods and means were known in the art. The Board emphasized that the issue was expression of HBV antigen in general and not efficiency of expression.

In **T 223/92 (HIF-Gamma/GENENTECH)**, an Appeal Board considered the inventive step of claims relating to human immune interferon and a DNA isolate carrying a DNA sequence encoding human immune interferon. The DNA claim was worded as follows:

A DNA isolate comprising a DNA sequence encoding human immune interferon having the amino acid sequence depicted in Figure 5 hereof or an allele or derivative of these having the function of human immune interferon.

The situation with which the skilled person was confronted at the priority date was characterized by the Board such that

(i) little was known about the protein as such and actually contradictory data had been published making the situation particularly confusing [...], (ii) despite the fact that an improved stimulation method was known, the quantity and quality of the mRNA available from this was extremely poor making the prospects of success for the recombinant-DNA-technique route look very poor if nothing better than this known method could be found and (iii) the decisive screening method was not to be considered as a reliable way to find what could only be described as "a needle in a haystack". (point 5.11)

Considering this situation, the Board concluded:

[T]here is no sufficient certainty that the skilled person in this situation would have tried this method with any reasonable expectation of success. In other words, while someone might have chosen the route of the recombinant-DNA-technique, he would only have attempted it despite success being very uncertain, for example, because he trusted in his own luck, skill and inventive ingenuity to overcome the known and the as yet unknown problems involved, even though these problems were such that the average skilled person would expect to fail. (point 5.12)

The Board characterized the Applicant's situation of the as follows:

The goal of the Respondents can be likened to wanting to reach the peak of a mountain which is permanently covered by cloud so that the correct approach route cannot be seen. Whilst it cannot be said with certainty that the differences in the route chosen by the Respondents over known routes were decisive, the Respondents successfully reached this peak, not knowing when they started to climb whether known and as yet unknown difficulties on their chosen route might not force them to give up and try some other route. By identifying the DNA-sequence, the Respondents so to speak provided a guide rope to the peak which enabled others to be certain of getting to the same peak with much less trouble. It was for the

Appellants to show that this peak could have been reached by a route which involved no invention, and they have failed to do so. (point 5.15)

Consequently, an inventive step was acknowledged.

In **T 880/92 (Facteur IX/TRANSGENE)**, the question decided by an Appeal Board was whether the choice of a certain expression system, i.e. the pox virus expression system for expressing DNA sequences, which sequences were already known in the art, involved an inventive step. In that case, a prior art document suggested the use of other expression systems for obtaining a recombinant expression of Factor IX.

The Board acknowledged an inventive step on the basis that in view of the given suggestions for expressing Factor IX, the skilled person would in fact follow these suggestions, if there were no reasons to doubt their feasibility. The skilled person would only engage in the search for alternative solutions if it were immediately apparent that the solution provided by the prior art was not satisfactory. An inventive step was acknowledged, since the Patentee had taken a different direction towards the solution of the given technical problem.

In **T 296/93 (HBV antigen production/BIOGEN INC)**, an Appeal Board discussed the question of whether the fact that the Patentee could work under more favorable conditions than its competitors may have an impact on the evaluation of an inventive step. The Board denied any relation between working conditions and determination of an inventive step as follows:

Neither the fact that a person (or a team) (here: the Appellant) was working under more favorable conditions nor that other persons (or teams) were concurrently performing research in the same area lessens the inventive step of any subject-matter claimed in a patent specification by the said first person (or team) in relation to the said research work, if this subject-matter is not obvious to a person skilled in the art, having regard to the state of the art.

The fact that other persons (or teams) were also working on the same project might suggest that it was “obvious to try” or that it was “an interesting area to explore”, but it does not necessarily imply that there was “a reasonable expectation of success”. “A reasonable expectation of success” which should not be confused with the understandable “hope to succeed”, implies the ability of the skilled person to reasonably predict, on the basis of the existing knowledge before the starting of a research project, a successful conclusion to the said project within acceptable time limits. The more unexplored a technical field of research is, the more difficult is the making of predictions about its successful conclusion and, consequently, the lower the expectation of success. (point 7.4.4)

In the above case, the Board did not see that there was a reasonable expectation of success to solve the underlying problem. Therefore, the Board acknowledged an inventive step.

In **T 412/93 (Erythropoietin/KIRIN-AMGEN)**, an Appeal Board commented in an *obiter dictum* on the patentability of DNAs encoding a known protein as follows:

Before the Board discusses the experiments provided by the Appellants to evidence that no inventive step is involved in the provision of the DNA sequences, it would remark that in any case the fact that the DNAs code for possibly non novel subject-matter does not *ipso facto*

mean that there is no inventive step in the provision of the DNAs and consequently, of any process, plasmid or transfected cell involving or comprising said DNAs. In Decision T 500/91 [...] the Board did not reject the claims to the DNAs, plasmids and recombinant processes because interferon- α was a known protein. (point 121)

In **T 111/00 (Monokine/FARBER)**, the Applicant appealing the decision of the Examining Division claimed, *inter alia*, a DNA molecule encoding a monokine, characterized by a specific nucleotide sequence. The Appellant essentially defended an inventive step of the claimed subject matter by arguing that the closest prior art, which discloses the isolation of a cDNA encoding a mouse cytokine, only characterizes the encoded protein in a speculative manner. The Appellant further cited another document to support the view that the skilled person would not have had a reasonable expectation of success in finding another monokine homologue and that even if so, he would not have expected to find the sequence specifically claimed.

The Board phrased the objective technical problem as the provision of further cytokines induced by alpha-IFN. The Appellant's arguments regarding the speculative nature of the disclosure of the closest prior art were not found convincing and since the claimed monokine was identified in a straightforward manner using a probe based on the disclosure of the closest prior art, the Board held that an inventive step could not be derived from the mode of identification. Since the isolation was a matter of routine, the Board did not accept the approach of reasonable expectation of success. Finally, the Board made it clear that the mere fact that a specific DNA sequence is claimed is not sufficient to provide an inventive step in the absence of some unexpected properties. Therefore, the Board denied an inventive step.

In **T 142/03 (Mite allergens/INSTITUTE FOR CHILD HEALTH RESEARCH)**, the Applicant appealed the Opposition Division's decision to revoke the patent. The Applicant claimed, *inter alia*, an isolated DNA encoding Der fl protein allergen. The closest prior art is concerned with the analysis and expression of cDNA clones coding for house dust mite allergens. It discloses the cloning of the allergen Der pI and further discloses an 80% homology between Der fl and Der pI. The Applicant essentially argued that there was no reasonable expectation of success to arrive at the claimed subject-matter by probing cDNA libraries with probes of Der pI for the identification of Der fl, since the inventors faced a number of challenges, such as selecting the right hybridization conditions.

The Board held that the closest prior art directed the skilled person to the cloning method used in the application and that the skilled person had a reasonable expectation of success in using said method to clone further antigens. The Board further held that the adjustment of hybridization conditions is a routine task for the skilled person that does not require any inventive skill.

In response to an auxiliary request, amending the claim to an isolated DNA encoding Der fl protein allergen by its specific sequence, the Board found that since the skilled person had a reasonable expectation of success based on the se-

quence homology between Der fl and Der pI, introducing the specific sequence does not affect the assessment of inventive step.

Therefore, the Board rejected the main and auxiliary request for lack of an inventive step.

In the opposition appeal proceedings underlying decision **T 1190/03 (Orphan receptor/KARO BIO)**, the Patentee claimed, *inter alia*, isolated estrogen receptors (ER β) with specific amino acid sequences from rat, mouse and human. Due to lack of priority for the claimed ER β s from mouse and human, the content of intermediate documents became available for the assessment of novelty and inventive step of said murine and human ER β . These intermediate documents disclose the cloning of a rat ER β and a human ER β , respectively.

The Board concluded that it would have been obvious for the skilled person to arrive at the claimed subject matter (mouse and human ER β) based on these closest prior art documents, essentially in view of the following argument:

In the Board's view, once the sequence of a receptor from one species is known, it is normally straightforward to identify and isolate the corresponding gene from a cDNA library of another mammalian species, using probes based on the known sequence. (point 7)

The Appellant opposed this argument by stating, *inter alia*, that it could not be taken for granted that the skilled person would indeed identify the specific amino acid sequence claimed among the multitude of possible amino acid sequences that could be identified. The Board essentially disregarded this argument by pointing out that

the decisive question to be answered is whether or not the specific mouse ER β sequence according to Fig. 14A disclosed in the specification was "hidden" in the sense that it could only be arrived at by selecting, among a great number of parameters, very specific and exotic tools/techniques (tissue, library, probes, biological activity test, etc) or in the sense that there were unforeseeable difficulties requiring an inventive effort to be solved. (point 10)

The Board considered the claimed subject matter not to be "hidden" as indicated above. In principle, the Board applied the same reasoning to address an inventive step of the human ER β . Therefore, the Board denied an inventive step for the claimed mouse and human ER β .

In **T 1329/04 (Factor-9/JOHN HOPKINS)**, the appeal lay from the decision of the Examining Division against an inventive step of the claimed subject matter of a polynucleotide encoding a polypeptide having GDF-9 activity, further characterized by a specific sequence. The Appellant essentially defended an inventive step with arguments directed to the unexpected structural properties of the isolated cDNA and further supported the claimed biological activity of the protein encoded by said cDNA with post-published documents only.

The Board considered the objective technical problem to be the isolation of further members of the TGF-beta superfamily. The Board came to the conclusion that the application did not provide enough evidence to make it plausible that a solution to said problem was found and denied an inventive step. The Board's reasoning essentially comprised two arguments:

This finding and that in point 7 lead to the conclusion that, contrary to GDF-1 in document (3) [closest prior art], GDF-9 cannot be clearly and unambiguously identified as a member of the TGF-Beta superfamily by only using a “structural approach”, (point 8)

and

Of course, the situation could most probably be looked at differently if it had been demonstrated in the application as filed that GDF-9 played a role similar to that of the transforming factor-Beta [TGF-Beta] (as was the case for all of the factors which initially served to define the superfamily). Yet, there is no evidence at all in this respect. (point 9)

The Board did not consider the post-published documents provided by the Appellant in support of the biological activity, since the application as originally filed completely lacked any evidence in this regard and the post-published documents could not serve as the sole support. The Board further stated:

This approach would be in contradiction with the principle that inventive step, as all other criteria for patentability, must be ascertained as from the effective date of the patent. The definition of an invention as being a contribution to the art, i.e. as solving a technical problem and not merely putting forward one, requires that it is at least made plausible by the disclosure in the application that its teaching solves indeed the problem it purports to solve. Therefore, even if supplementary post-published evidence may in the proper circumstances also be taken into consideration, it may not serve as the sole basis to establish that the application solves indeed the problem it purports to solve. (point 12)

A major problem in this case was that the claimed GDF-9 was structurally fairly different from other members of the protein family. This raised doubts with the Board whether GDF-9 was a member of the TGF-beta family at all.

In **T 1165/06 (IL-17 related polypeptide/SCHERING)**, the Applicant appealed the decision of the Examining Division to refuse the application, *inter alia*, due to a lack of inventive step. The claims were to sequences for the polynucleotide and polypeptide of the IL-17-related protein. The closest prior art disclosed multiple IL-17 family members and conserved domains among them. The technical problem was thus phrased as the isolation of a further polypeptide of the IL-17 family.

In assessing obviousness of this technical problem, the Board turned to the concept of reasonable expectation of success. Given the lack of homology between the provided IL-17 family member IL-17 of the invention and the domains described in the closest prior art, the Board found that there was no reasonable expectation of success and, therefore, acknowledged an inventive step for the claimed subject-matter. The Board stated:

This fact [lack of homology] neither was known nor could have been foreseen by the skilled person at the filing date, and only was revealed after the identification of the IL-174 sequence by the inventors. Thus, a screening strategy designed on the basis of the domain information provided in D4 would, most probably, have failed to “fish out” the IL-174 sequence. Under these circumstances, a reasonable expectation of success as required by the case law of the Boards of Appeal of the EPO to deny an inventive step cannot be assumed. (point 22)

In **T 414/07 (Diseases of the breast/ABBOTT)**, the invention at issue related to polynucleotide and polypeptide sequences as markers for breast can-

cer. The closest prior art disclosed, *inter alia*, a single protein overexpressed in human breast cancer which, according to the disclosure, could be useful as a marker for breast cancer. The only additional prior art document disclosed the isolation of cDNA clones in a context totally unrelated to cancer, let alone breast cancer (even though sequence homology existed to one of the claimed sequences of the invention at issue). In view of these prior art documents the Board decided:

[T]he only possible conclusion is that the skilled person would simply not have arrived at the said polypeptides without the exercise of inventive skill, (point 16)

and furthermore that

the polynucleotides of claim 1 also involve an inventive step. (point 17)

In **T 1450/07 (TGF α -HII/HUMAN GENOME SCIENCES)**, the Examining Division had refused the patent application due to a lack of an inventive step. The underlying invention related to a human TGF α homolog. Other human TGF α homologs were already known from the prior art. The closest prior art, however, disclosed that the human genome did not contain any additional sequences homologous to the TGF α gene. The Board, therefore, held that the isolation of the claimed homolog was unexpected and that the claimed subject-matter should be accorded an inventive step.

In **T 18/09 (Neutrokin/HUMAN GENOME SCIENCES)**, the Board acknowledged an inventive step for a claim to an isolated nucleic acid molecule encoding a Neutrokin- α polypeptide in light of a prior art disclosure of EST sequences in EST databases. The Board argued as follows against using such prior art as closest prior art:

The EST clone of document D2, which is uncharacterized and not annotated, cannot be singled out from all the other EST clones present in the public EST database without an objective compelling reason for making such a selection. Although being physically present in the available collection of clones, a particular EST clone is not made available as such, i.e. as a particular, individualized product, but only as an integral part of the whole EST database in toto. In the absence of any specific information (such as the identification of its putative encoded polypeptide), the mere disclosure of a nucleic acid sequence in itself does not go beyond that disclosure and, in the Board's opinion, does not allow for its use or selection as closest prior art. (point 40)

The Board further noted that a large-scale pipeline screening approach of an EST database with available software would also not have been obvious, largely due to the following reason:

In view of the large number and particular nature of possible criteria that may be used to carry out the selection of those EST sequences as well as the programs, parameters and values that should have to be selected accordingly, the Board comes to the conclusion that no particular prior art, i.e. no particular group of EST sequences, has been clearly and unambiguously identified as a starting point for an automated pipeline screening nor has a document been clearly identified as representing that closest prior art. Moreover, there is no evidence on file demonstrating with certainty that each and every one of the suggested selections, or at least most of them, would have contained at least one EST sequence encoding (part of) the

Neutrokin- α sequence of the patent-in-suit, such as those shown in documents D2, D22 or D24, and that with an automated pipeline screening the skilled person would have been in a position to recognize that sequence immediately and successfully retrieve it.

D.II.2.f. Industrial application

In the past few years, the Boards of Appeal have created a new obstacle for inventions in the field of life sciences in that they put more emphasis on the relevance of Art. 57 EPC in the field of both DNA and protein inventions. An early case where an Appeal Board paved the way to objections under Art. 57 EPC was in **T 1329/04 (Factor 9/JOHN HOPKINS)**, even though this case was formally decided under Art. 56 EPC. However, in this case, the Board introduced the “plausibility concept or test” which requires that it must be plausible from the originally filed application that an alleged function of a DNA or a protein indeed exists. The basic idea is that on the relevant date the invention must be complete, and an application must contain sufficient information to make plausible that the claimed effect exists and/or the alleged solution of the underlying problem be plausible from what is stated in the application. In the application underlying **T 1329/04**, a particular problem related to the question whether the alleged function of the protein encoded by the claimed DNA qualified it as a member of the TGF- β superfamily. In particular, this was because the protein as encoded by the claimed DNA showed a different domain structure than most other known members of the TGF- β superfamily. In line with the thinking of **T 1329/04**, further decisions issued where this plausibility/credibility test of **T 1329/04** was then also applied with respect to the examination of Art. 57 EPC.

For instance, in **T 898/05 (Hematopoietic receptor/ZYMOGENET-ICS)**, the Appeal Board had to decide on the patentability of a DNA coding for a ligand-binding receptor polypeptide, the underlying patent application not containing any “wet chemistry” data concerning the alleged function of the encoded protein. Rather, the assumed function was based on computer-assisted methods. The Appeal Board nicely summarized the previous case law with respect to the application of Art. 57 EPC and came to the following result:

As seen above with reference to the case law of the Boards of Appeal, the disclosure of the function of a newly discovered protein is of utmost importance when examining the issue of “industrial applicability” as the function is the gateway to understanding the concrete benefits which may derive from exploiting the invention industrially. As shown by **T 870/04 (supra)**, the mere characterization of the structure of a protein may not be enough to comply with Art. 57 EPC if no profitable use of the protein is disclosed. On the other hand, **T 338/00** and **T 604/04 (supra)** show that a positive answer can be given in spite of the absence of actual experimental data, if a profitable use can readily be identified on the basis of the description taken into account common general knowledge (point 20 of the Reasons).

In **T 898/05**, the Board confirmed industrial applicability. The Board further stated that the fact that a function is based on computer-assisted methods, rather than on the basis of traditional wet-lab techniques, does not mean that

this function should automatically be disregarded or excluded from a careful and critical examination (catchword 2).

D.II.2.g. Sufficiency of disclosure

One of the main aspects distinguishing biotechnological inventions from classical chemical products is the possibility of supplementing a written disclosure by depositing a microorganism or DNA according to Rules 31–33 EPC in order to comply with Art. 83 EPC. The problems associated with the formal requirements of deposits have already been discussed in C.I.3.b.b. Regarding the definition of a person skilled in the art, who is determinative for evaluating the sufficiency of disclosure, see C.I.3.d.

The following discussion summarizes a number of decisions dealing with the issue of sufficiency of disclosure for nucleic acid related inventions.

T 292/85 (Polypeptide expression/GENENTECH I) is a landmark decision and relates to an Applicant's appeal against a decision to reject the application for failure to comply, *inter alia*, with Art. 83 EPC. Claim 1 of the application in question was as follows:

A recombinant plasmid suited for transformation of a bacterial host comprising a homologous regulon and heterologous DNA, the heterologous DNA encoding a functional heterologous polypeptide or intermediate therefor, said homologous regulon being arranged with said heterologous DNA so as to control transcription and translation of said heterologous DNA encoding said functional heterologous polypeptide or intermediate therefor, whereby on translation of the transcription product of the heterologous DNA in a suitable bacterium, the resulting expression product is said functional polypeptide or intermediate therefor in recoverable form.

This decision summarized the grounds for refusal by the Examining Division under Art. 83 EPC as follows:

The Examining Division insisted that all embodiments in the claims must have been capable of being carried out by the skilled person at the priority date and in a repeatable manner without practising inventive skill. No claims should rely on constituents which represent further inventions. In addition to the impossibility of providing such embodiments at the present, the later patentability of such constituent variants might be adversely affected. Claims should, in effect, at least be limited to what is available at the priority date, i.e. known bacteria, plasmids and DNA relating to known polypeptides. A process for the preparation of a human hormone could not be identically repeated since the source of the DNA in humans varied with the individual. In general, no component should be defined in functional terms in this field of technology. (point II)

The Board reversed the Examining Division's decision, commenting in great detail on the sufficiency of disclosure in view of future components, inoperable components and non-availability of starting materials for obtaining each and every variant of the expected result.

With respect to *components of the future*, the Board observed that there is neither a requirement in the EPC, nor is it an established principle in any one of the EPC contracting states, that all embodiments within the claims should be

operable (point 3.1.2 of the decision). It was acknowledged that the functional features of the claims would cover an unlimited number of possibilities including future variants. The Board held that in compliance with **T 68/85 (Synergistic herbicides/CIBA-GEIGY)** functional features are admissible if

such features cannot otherwise be defined more precisely without restricting the scope of the invention and their reduction to practice was not an undue burden. (point 3.1.2)

The Board discussed examples from fields of technology other than biotechnology and continued:

The above examples show that the need for a fair protection governs both the considerations of the scope of claims and of the requirements for sufficient disclosure. Unless variants of components are also embraced in the claims, which are, now or later on, equally suitable to achieve the same effect in a manner which could not have been envisaged without the invention, the protection provided by the patent would be ineffectual. Thus it is the view of the Board that an invention is sufficiently disclosed if at least one way is clearly indicated enabling the skilled person to carry out the invention. Consequently, any non-availability of some particular variants of a functionally defined component feature of the invention is immaterial to sufficiency as long as there are suitable variants known to the skilled person through the disclosure or common general knowledge, which provide the same effect for the invention. The disclosure need not include specific instructions as to how all possible component variants within the functional definition should be obtained. (point 3.1.5)

In view of the above, it is also irrelevant that some of the variants of bacterial strains or regulons might only exist in private collections or can only be found in locations or derived from sources which are inaccessible or were only transiently available to the public. As long as there are means available for performing the invention, such exceptional circumstances cannot counteract the possibility that the invention can be carried out. (point 3.1.7)

With respect to *inoperable components* the Board stipulated:

[T]he unsuitability of some unspecified particular variants of a functionally defined component feature of the invention is immaterial as long as there are suitable variants known to the skilled person through the disclosure or common general knowledge which provide the same effect for the invention. (point 3.2.1)

The Board emphasized that the

situation with respect to possible ineffectual bacterial variants embraced together with effective ones, must, however, be carefully distinguished from failures to obtain certain kinds of effects at all. (point 3.3.1)

Concerning the *availability of starting materials* for obtaining each and every variant of the expected result, the Board held that the non-availability of some starting materials or genetic precursors does not render generally applicable biological processes insufficiently disclosed, provided that the process as such is reproducible (point 3.3.3 of the decision).

In the case underlying **T 281/86 (PreprothauMATIN/UNILEVER)**, the application was rejected because plasmid pUR100 containing almost the complete preprothauMATIN cDNA that was used in the construction of further claimed plasmids, was not identically reproducible. This plasmid was neither deposited nor was its sequence provided. However, the specification disclosed a

process resulting in pUR100 as well as DNA sequences coding for preprothau-matin, prethaumatin and prothaumatin. Upon the Applicant's appeal, the Board decided as follows:

Whilst it is accepted that it is unlikely that the plasmid obtained on the basis of following the specific disclosure would be identical with pUR 100 originally prepared, there is no doubt that such products should be equally suitable for further processing and ought to lead just as well to the three thaumatin precursors and the suggested variant proteins through ex-pression.

It is always the case in chemistry that the outcome of experiments show some fluctuations in yield, quality etc. This is irrelevant for sufficiency unless the invention requires certain characteristics in this respect. It should therefore be even less relevant if only the conditions and the means used to carry out a process show inevitable variations as long as the ultimate result is the same. The variants within the designation pUR 100 are means of such character. (point 5)

It is therefore the view of the Board that there is no requirement under Article 83 EPC to the effect that a specifically described example of a process must be exactly repeatable. Variations in the constitution of an agent used in a process are immaterial to the sufficiency of the disclosure provided the claimed process reliably leads to the desired product. As long as the description of the process is sufficiently clear and complete, i.e. the claimed process can be put into practice without undue burden by the skilled person taking common general knowledge also into consideration, there is no deficiency in this respect. (point 6)

In **T 283/86 (-/THE REGENTS OF THE UNIVERSITY OF CAL-IFORNIA)**, the Examining Division had raised objections under Art. 83 EPC to the following claims:

Claim 1:

A DNA transfer vector comprising a deoxynucleotide sequence coding for bovine pre-growth hormone, said deoxynucleotide sequence comprising a plus strand having the se-quence:

(5'---3'),

wherein A is ...

Claim 4:

The DNA transfer vector of claim 1, wherein said transfer vector is the plasmid pBR348, or a plasmid differing therefrom only in the length of the poly(A) and/or poly(C) portions thereof.

The reasons for the refusal of the application were, *inter alia*, that (i) due to the allelic variation phenomenon the plasmid of claim 4 might not be reproduc-ible, since a different donor for the starting material (pituitaries) is to be used; and (ii) the exact length of the poly G/C strands flanking the cDNA transcript was not disclosed. With respect to (i), in the absence of evidence to the contrary, the Board concluded the unique character of the hormone to be *prima facie* es-tablished. The Board did not see any room for objections under Art. 83 EPC based on unsupported and possibly speculative knowledge. With respect to (ii), the Board acknowledged that at least one way for preparing the plasmid was dis-closed in the examples. Thus, in compliance with **T 292/85 (Polypeptide ex-pression/GENENTECH I)**, discussed above, Art. 83 EPC was considered to

be fulfilled. Furthermore, although the example might not be identically reproducible, there was no evidence indicating that a plasmid having the features of pBR348 or variants thereof, could not reliably be reproduced. Thus, sufficiency of disclosure was acknowledged.

From **T 181/87 (Hepatitis B virus/UNIVERSITY OF CALIFORNIA)**, with respect to sufficiency of disclosure, the Board distinguished between inventions (claims) relating on the one hand to specific plasmids and on the other to inventions which are broader than the specific embodiment of a certain plasmid. The Examining Division had refused the application under Art. 83 EPC on the grounds that plasmid pEco-63, which was the subject-matter of claim 6, and other plasmids contained in the examples could not be reproduced, since the starting material, i.e. certain Dane particles, was not sufficiently disclosed. According to the Examining Division, the use of a different starting material would lead to different plasmidic chemical compounds and, thus, there was no certainty that the procedure in question repeatedly produces the individual plasmids disclosed in the application.

The Board held:

If a plasmid is the invention, demonstrated by the fact that it is claimed, reproducibility of this definite plasmid has to be demonstrated in the European patent application.

If, however, the invention as claimed is broader than one certain example, describing the preparation of a definite plasmid, the requirements of Article 83 EPC are not such, that this example has to be reproducible identically, as long as there is evidence that the disclosure of the preparation of the specific plasmid leads reliably to plasmids which may differ from the definite mentioned plasmid but nevertheless fall under the broad term of the claim. This view has already been expressed by the Board in earlier decisions [...]. (point 7.2)

In this case, pEco-63 had been deposited. Further, the plasmid as well as the remaining plasmids, the production of which was disclosed in the examples, were considered to be reproducible. The Board again emphasized:

It has further to be mentioned here that even if the plasmids described in the examples would not have been reproducible identically this would not necessarily, as discussed earlier result in a conflict with the requirement of Article 83 EPC as far as working according to the examples would lead to products falling under claims being broader than the specific embodiments of the examples is concerned. (point 7.9)

In the case underlying **T 301/87 (Alpha-interferons/BIOGEN)**, the Opponents contested the sufficiency of disclosure of the subject-matter covered by parts (b) and (c) of the following claim:

A recombinant DNA molecule for use in cloning a DNA sequence in bacteria, yeasts or animals cells, said recombinant DNA molecule comprising a DNA sequence selected from:

- (a) ...
- (b) DNA sequences which hybridise to any of the foregoing DNA inserts and which code for a polypeptide of the IFN- α type, and
- (c) DNA sequences which are degenerate as a result of the genetic code to the DNA sequences and inserts defined in (a) and (b) and which code for a polypeptide of the IFN- α type.

The Board considered the materials comprised by the above claim as an unknown but probably finite number of human and animal interferons of the α -type. These materials would differ somewhat in constitution from each other but would still represent some structural similarity in view of similar affinity in hybridisation tests. Furthermore, as a class, the members provide end products with the same biological activity. (point 4.4)

The Board continued:

As long as this is achieved by the invention there is no necessity to provide instructions in advance as to how each and every member of the class would have to be prepared. In view of the nature of the technique there is not even a guarantee that the same product is obtained from the same source after an identical repetition of the complicated and lengthy experiments. At this broad level, any one member of the class is an adequate representant of the invention. (point 4.4)

It is therefore the view of the Board that variations in the construction within a class of genetic precursors, such as recombinant DNA molecules claimed by a combination of structural limitations and functional tests, are immaterial to the sufficiency of the disclosure provided the skilled person could reliably obtain some members of the class without necessarily knowing in advance which member would thereby be made available. (point 4.5)

In the examination proceedings underlying decision **T 347/87 (Cloning-vehicle/GENENTECH)**, the Examining Division had required the identical reproducibility of a plasmid comprising the structural gene encoding human growth hormone. The Board did not share this view and confirmed previous case law as follows:

[T]he disclosure was sufficient in respect of the preparation of human hormones, although each person, as a source, could only provide an individual variant of the DNA precursor of the hormone, without of course any guarantee that each and every variant of expected result of the invention, e.g. the product, could be obtained or that such source would remain available to the public, provided the process as such always worked [...]. (point 4)

In **T 158/91 (Human growth hormone/GENENTECH)**, an Appeal Board had to evaluate whether a prior art document contained an enabling disclosure. The Board held:

Certainly, the question of sufficient disclosure, be it of a prior art document or a patent application in question, has to be examined in each case on its own merits. An examination as to the sufficiency of a disclosure depends on the correlation of the facts of the case to certain general parameters.

These parameters are for example:

- (a) the character of the technical field and the average amount of effort necessary to put into practice a certain written disclosure in that technical field;
- (b) the time when the disclosure was presented to the public and the corresponding common general knowledge;
- (c) the amount of reliable technical details disclosed in a document. (point 2.3)

These rules appear to be generally applicable.

In the patent underlying **T 223/92 (HIF-Gamma/GENENTECH)**, claim 9 as granted read as follows:

A DNA isolate comprising a DNA sequence encoding human immune interferon having the amino acid sequence depicted in Figure 5 hereof or an allele or derivative of these having the function of human immune interferon.

Thus, the claim referred to the amino acid sequence of the protein provided in Figure 5. In addition, the patent provided the DNA sequence of human immune interferon.

An Opponent argued that it would be an undue burden to determine which elements in the description were essential to carry out the invention since they were only implicitly disclosed. He further considered the provision of the DNA sequence coding for human immune interferon in itself, insufficient. Thus, reproduction of the teaching on the basis of the disclosure of the opposed patent was alleged to constitute an undue burden.

The Board acknowledged that at the time of filing the priority document, i.e. 1981, cloning and expressing the human immune interferon gene would have been a difficult, complex and time-consuming task. Nevertheless, the Board considered the invention to be sufficiently disclosed since the disclosure of the DNA sequence permitted one skilled in the art to select other routes than those described in the patent for cloning and expressing the gene. The Board considered the reproduction of cloning and expression of human immune interferon as possibly being time-consuming and cumbersome, but without undue burden of experimentation and without requiring inventive skill. Most importantly, the Board clarified that there is no legal requirement to deposit a microorganism if the invention can be reproduced on the basis of the written description.

T 412/93 (Erythropoietin/KIRIN-AMGEN) was a complex decision, in which the allowability of more than ten requests was examined. The following summarizes the information in the decision relevant to certain aspects of Art. 83 EPC.

With respect to the main request, the Board examined the question whether the cDNA of erythropoietin had been made available by the patent. Table VI of the patent discloses a DNA sequence, which, however, does not provide any information as to a possible start or stop codon. In contrast to the opinion of the Proprietor, the Board considered the cDNA not to be implicitly disclosed (point 21 of the decision). Rather, the Board found that identification of cDNA in the sequence of Table VI would have been “mere guess work” (point 28 of the decision).

This evaluation is in line with earlier case law **T 301/87** (discussed above) where it was decided in respect of the entitlement to priority, that the deposit of a strain containing a total sequence in a recombinant form does not implicitly establish priority for a part of the sequence (point 6.2 of the decision).

Since according to **T 412/93** the cDNA sequence was considered undisclosed by the sequence provided in Table VI, the Board investigated whether, as a means for preparing cDNA, a reliable method for obtaining mRNA was disclosed. The evidence for this question was contradictory. The Board considered the burden of proof to be on the Proprietor (Respondent) to show that the

common general knowledge in the art would have enabled the skilled person to obtain an mRNA as of the priority date, given only the information in the patent, which was extremely scant. Since the Proprietor ultimately failed to do so, the main request including a claim relating to cDNA was rejected.

When considering the sufficiency of disclosure of Auxiliary Request 11, the Board investigated whether

any practicable method of making something falling within Claim 1 has been disclosed at all. (point 63)

Since this was the case, sufficiency of disclosure was acknowledged.

Some of the Opponents argued that repeating the invention would impose an undue burden of work. They maintained that Art. 83 EPC requires that

clones containing the Epo gene, possibly already combined with suitable expression vectors, must be made available by the Patentee to the public by deposit under Rule 28 EPC if this would allow the invention to be reproduced very much more quickly than by following only the instructions of the specification. (point 74)

The Board first pointed to the absence of any support in the relevant case law or in the reports of the Munich Diplomatic Conference on the introduction of a European patent grant procedure and its associated preparatory documents, for interpreting such a requirement in Rule 28 EPC (now Rules 31–33 EPC). They then concluded:

This need for a deposit cannot be introduced by reference to the concept of undue burden. This concept relates more to cases where the route that the reader is to follow is so poorly marked that success is not certain (citation omitted). If the route is certain but long and laborious, the Patentee is under no obligation to assist the disclosure by making actual physical samples, i.e. the "factory" available. To come to the opposite conclusion would be effectively to introduce a requirement to make the best mode immediately accessible to the public, and such a requirement is not part of the European Patent system. (point 76)

T 918/94 (Calcitonin/CELLTECH) concerns an Applicant's appeal against a decision to reject an application having the following main claim:

A vector including a structural gene encoding a polypeptide comprising the amino acid sequence of human calcitonin, wherein said polypeptide is enzymatically processable to produce human calcitonin using the C-terminal modification activity of the yeast enzyme carboxypeptidase g.

The modification allegedly effected by carboxypeptidase g is catalysis of CYS¹ – – – PRO³²-GLY⁺¹ or CYS¹ – – – PRO³² to CYS¹ – – – PRO³²-NH₂, which is the active form of human calcitonin. In the specification of the patent application, there was no protocol of the method of converting a calcitonin predecessor. Rather, the Applicant relied on a reference to two publications of a group working on carboxypeptidase g. However, later published work of this group suggested that carboxypeptidase g would not work for the purpose suggested by the Appellant. Therefore, the Board held:

In these circumstances the Board can make no assumption in the Appellant's favour that the method would work. If it had been shown that a method exists that does work, the Ap-

pellant might have been given the benefit of the doubt, at the application stage at least, on the question of whether the skilled person would have hit on this method. But where, as here, there is no experimental demonstration of success to set against very substantial indications that it does not work, this is not appropriate. (point 10)

In **T 794/94 (Plasmid/GENENTECH)**, the Patentee appealed the decision of the Opposition Division to revoke the patent. The invention related to a plasmid for the expression of heterologous proteins. The final auxiliary request was limited to a plasmid for expression of non-fusion proteins, while the prior art disclosed the same plasmid for the expression of fusion proteins. However, the description did not provide a working example for the expression of a non-fusion protein. With respect to enablement, the Board finally concluded that

either the skilled person could make what is claimed in claim 1 already on the basis of the prior art, or both the prior art and the patent in suit contain insufficient information to realize what is claimed in claim 1. (point 3.4.4)

Thus the Board made it clear that sufficiency of disclosure of the patent application and the prior art is assessed by the same standards.

In **T 838/97 (Translational inhibition/RESEARCH FOUNDATION)**, one of the Opponents lodged an appeal against the decision of the Opposition Division to maintain the patent. The invention related to an artificial nucleic acid sequence which antagonized the function of a gene when introduced into a cell. Among other things, the Appellant argued that the claimed teaching did not extend to all organisms claimed.

The Board accepted post-published documents by the respondent showing that the model could be applied across a broad range of hosts. Furthermore, the Board held that a certain amount of trial and error could be expected of the skilled person when carrying out the invention. This need not be an indicator of undue burden. Therefore, the Board saw the requirements of Article 83 EPC as fulfilled.

In **T 1055/97 (Drug delivery conjugates/ENZO)**, the appeal was against a decision of the Examining Division refusing the underlying patent application, *inter alia*, for lack of sufficiency of disclosure of claim 1 directed to a therapeutic composition comprising a polynucleotide further characterized by a complex Markush formula.

The Board held that these claims covered a virtually infinite number of therapeutic compositions and further stated that:

[S]ufficiency of disclosure is achieved if the skilled person is able to reproduce the invention over the whole range which is claimed without undue burden of experimentation, following the instructions provided in the specification of the application. (point 10)

In conclusion, the Board held that in the present case reproducing of the invention amounts to “devising a research program”, which cannot be expected from the skilled person, and that therefore claim 1 did not comply with Art. 83 EPC.

T 1074/00 (Hematopoietic growth factors/GENETICS INSTITUTE) was concerned with the appeal against the decision of the Opposition Division to maintain the patent. The invention related to DNA sequences characterized by structural and functional features of the encoded polypeptides. The Appellant (Opponent) held that the subject-matter encompassed a great number of sequences, which shed doubt on the reproducibility of the claimed subject-matter over the entire ambit of the claim and that the assays provided were not clear enough to test whether a given peptide would fall under the claim.

The Board rejected all these arguments and indicated once more (see also **T 656/94**) that the skilled person would obviously be able to prepare all the claimed peptides and that the required functional feature would limit the number of possible sequences and provide also a structural link between them. The Board furthermore considered the provided assays sufficient to provide the skilled person with a means to test for the claimed activity. Interestingly the Board also stated that:

[F]urthermore, even if the skilled person is not *stricto sensu* provided by the patent in suit with precise guidance on how to prepare an active IL-3 variant, his basic knowledge of the structure-function relationship in proteins (cf *supra* point 16), will have given him an empirical basis for estimating beforehand the impact of a given structural modification on the activity of the resulting variant; this gives him sufficient guidance for modifications leading to active variants. (point 20)

Based on these arguments, the Board saw the requirements of Art. 83 EPC as fulfilled.

T 397/02 (Endogenous gene expression/APPLIED RESEARCH SYS) concerned the appeal of the Patentee against the decision of the Opposition Division to revoke the patent. The invention was directed to a method for activating a normally transcriptionally inactive gene by inserting regulatory DNA sequences into the genome.

The Board first demonstrated that the example supporting the Appellant's enablement argument did not prove that the claimed method is successfully carried out, and therefore held that this example was not suitable to enable the claimed subject-matter. As a consequence, the Board discussed in great detail whether an example was generally necessary for enablement. This was generally answered in the negative, but depended on the individual case. After considering the specific fact pattern of the case, the Board arrived at the following conclusion:

Thus, it is concluded that if for an invention which is conceptually different from earlier approaches in the prior art, the Patentee fails to give even a single reproducible example, sufficiency of disclosure cannot be acknowledged. It would amount to undue burden for the skilled person to establish how to put the invention into practice on the basis of a sole generic teaching in the patent. (point 18)

Hence, the Board considered the requirements of Art. 83 EPC not to be fulfilled.

D.II.2.h Clarity and support of claims

Several decisions issued by Boards of Appeal contain statements as to the requirements of Art. 84 EPC, i.e. clarity of the claims and support by the description, for inventions relating to nucleic acids.

In **T 292/85 (Polypeptide expression/GENENTECH I)**, the Board of Appeal drew several parallels with the case law for the field of conventional chemical products and explicitly commented on the allowability of functional terms in biotechnological inventions as well as on the allowability of including future embodiments. The sections of the decision relevant for the purposes of Art. 84 EPC were as follows:

The suggested features in the claims are essentially functional terms in this particular context, in spite of structural connotations, and may cover an unlimited number of possibilities. It follows that the features may generically embrace the use of unknown or not yet envisaged possibilities, including specific variants which might be provided or invented in the future. This Board concurs with the decision of another Board [...] in which the possibility of using functional terminology in claims was approved if “such features cannot otherwise be defined more precisely without restricting the scope of the invention” and their reduction to practice was not an undue burden. The Board sees no valid reason why this should not be equally true for the field of biotechnology as in other fields of technology. (point 3.1.2)

The objection raised against the terms “plasmid” and “bacteria” that they are too broad since some of them rely on yet unavailable entities is untenable. The Board is of the opinion that this is quite normal practice in many technical fields where terms as “carriers”, “resilient means”, or “amplifying means”, are commonplace and embrace new components, be they inventive or not. This is not to mention that very often the generic indication of a kind of an article in the claim is followed by the non-exclusive term “comprising” and the characteristics of modifying features, leaving completely open the actual features of the rest of the article, apart from the necessity that its functioning should be as expected. (point 3.1.4)

The principles outlined above were confirmed in **T 347/87 (Cloning vehicle/GENENTECH)** in points 3.1 and 3.2 of the decision.

In the case underlying decision **T 162/86 (Plasmid pSG2/HOECHST)**, claim 1 having the following wording:

Plasmid pSG2, obtainable from *Streptomyces ghanaensis* ATCC 14 672, characterised by a molecular weight of 9.2 megadaltons, a contour length of 4.58 mm and a molecular length of about 13.8 kb,

was replaced by the following amended claim 1:

Plasmid pSG2, characterised in that it is obtainable from a culture of *Streptomyces ghanaensis* ATCC 14 672, has a contour length of 4.58 mm and a molecular length of about 13.8 kilo-bases (kb) and in that it is not fragmented by the restriction endonucleases Eco RI, Bam HI, Sal I, Hpa I and Hind III, but is cleaved by the restriction endonuclease Hind III into a fragment with a length of about 14 kb, by Cla I into two fragments with lengths of 10.15 and 3.65 kb, by Pst I into two fragments with lengths of 10.85 and 3.0 kb, by Bgl II into two fragments with lengths of 11.25 and 2.6 kb and by Bcl I into three fragments with lengths of 11.6, 1.25 and 1.0 kb.

In the reasons for the decision, the Appeal Board expressed the opinion:

For reasons of clarity, it seems imperative to include alongside the characteristics given in the rejected Claim 1 other characteristics within the limits of the original disclosure, in order to ensure unequivocal identification of the claimed plasmid. Besides details of origin (strain), contour length, molecular weight and/or molecular length, the cleavage behaviour on digestion by various enzymes must be considered essential in this connection, particularly since determining the molecular weight and/or molecular length is fraught with inaccuracy, and also since in the presence of several plasmids which may be derivatives of one and the same plasmid and which possibly had not even been recognised originally, it must at all times be clear which plasmid is protected by the claim. However, it is not absolutely necessary for this purpose to include in the claim all the cleavage results given in the original description, especially not if such details are lacking in accuracy. The present Claim 1 fulfils these criteria and therefore satisfies the conditions of Article 84 EPC. (point 2)

In the case underlying **T 181/87 (Hepatitis B virus/UNIVERSITY OF CALIFORNIA)**, the Examining Division had rejected an application including the following claim:

A DNA transfer vector comprising at least a portion of the nucleotide sequence encoding the hepatitis B surface antigen and being substantially free of the nucleotide sequence encoding the hepatitis B core antigen.

The Examining Division argued that the subject-matter of the claims represented nothing more than professional paraphrasing of a technical problem already known in the state of the art and, therefore, was not allowable with regard to the problem/solution analysis. Allegedly, there was no technical difference between the underlying technical problem and definitions given in the claims by way of solution.

The Appeal Board reversed the decision. In their opinion, the features of claim 1 represented structural and functional features, which were to be understood as “technical features of the invention”. The Board confirmed that functional features in the claims were allowable under certain conditions. The Board further held that Art. 84 EPC in connection with Rule 27(1)(d) EPC did not imply a requirement for wording of the claims in terms of problem and solution.

T 269/87 (Prochymosin/CELLTECH) was concerned with the allowability of a claim reading:

Plasmid pCT70.

The disclosure relating to the construction of the plasmid and its components was apparently considered to be adequate. However, this information was not recited in the claim. The Board decided:

Except when absolutely necessary, claims should not rely in respect of technical features on the description (Rule 29(6) EPC) [now Rule 43(6) EPC]. In order to enable the public ascertain the scope of the protection provided, the claims should be clear in themselves, whenever this is possible, and contain as much structural information as available and necessary in the circumstances. For instance, product-by-process claims, i.e. definition of a material by reference to features other than those of the entity itself, are only permissible in the absence of relevant structural information. (point 2)

The specification, in particular Figure 5, contained detailed structural information which could have been included in claim 9 to enable the public to identify and compare plasmids

vis-à-vis claimed subject-matter. The argument that claims to deposited microorganisms had been allowed in the past cannot be decisive in the present case. Whilst such depositions identify novel microorganisms by implication through their availability, they also open the possibility for comparisons for any member of the public. Depositions may therefore provide the only possibility for support and sufficient disclosure of a particular subject-matter. (point 3)

In **T 816/90 (CBH II/ALKO)**, an Appeal Board rejected claims relating to plasmids characterized by arbitrary designations since they did not have a technical meaning *per se*. In addition, the Board contested the plasmid's definition by reference to a figure as follows:

As observed in the official communication of the Board to the Appellant:

i) said plasmids are defined by use of a designation which has no technical meaning *per se*. Moreover, their structure is defined by reference to a figure. Such a definition of a plasmid cannot be accepted because it is contrary to the requirements of Article 84 EPC [...]. (point 4.1)

It should be noted that the current practice of the EPO contravenes the essence of point 4.1 of **T 816/90**, cited above, i.e. claims referring to figures are presently allowed under certain conditions as stated in the Guidelines (F-IV, 4.17).

In **T 965/98 (DNA amplification/HOFFMANN-LA ROCHE AG)**, the Examining Division found the subject-matter of very broad claim 1 unclear because the claimed oligonucleotides were defined by their capacity to bind a template, which remained unspecified.

Claim 1 was phrased as:

A first and a second single-stranded oligonucleotide allowing amplification of a specific nucleic acid sequence contained in a single- or double-stranded nucleic acid or in a mixture of such nucleic acids, wherein

- (a) one oligonucleotide of said oligonucleotides is substantially complementary to said single-stranded nucleic acid or to one strand of said double-stranded nucleic acid;
- (b) the other oligonucleotide of said oligonucleotides is substantially complementary to a complement of said single-stranded nucleic acid or to the other strand of said double-stranded nucleic acid;
- (c) said oligonucleotides additionally contain on the 5' end a sequence which is non-complementary to said nucleic acid, said sequence comprising a restriction site; and wherein
- (d) the parts of said oligonucleotides that have substantial complementarity are different and define the termini of the specific nucleic acid sequence to be amplified.

The Board, however, held that the Examining Division did not take into account that the sequence of the claimed oligonucleotides was derived from a known template sequence and further considered that the skilled person would have no difficulty in determining which oligonucleotides fell under the scope of claim 1.

In **T 1074/00 (Hematopoietic growth factors/GENETICS INSTITUTE)**, the Board also considered the feature of "hybridizing under stringent conditions" for clarity and held that in this particular case the additional functional features have to be considered (see **T 1084/00** below). The Board sum-

marized the case law and pointed out that this term is commonly used in the art and in patent practice. As a consequence the Board considered the term sufficiently clear.

In **T 1084/00 (HIV-3 variants/INNOGENETICS)**, claims 3 and 5 contained structural as well as functional features, such as “specifically hybridizes” and “stringent conditions”. The Board held that in light of the description and the prior art the meaning of these terms is clearly defined. Furthermore, the Board made the important point:

[C]laims 3 and 5 must be read as a combination of functional and structural features and it is this specific combination, and not some of these features arbitrarily removed from the others, which must be clear (Article 84 EPC) and reproducible without undue burden (Article 83 EPC). (point 9.7)

In **T 610/01 (Plant growth/LONG ASHTON RESEARCH STATION)**, the Examining Division had refused the application because, among other reasons, some claims were directed to a DNA molecule defined by a very low homology of only 50% to a given SEQ ID number. However, since the claims in question also contained functional features related to the enzymatic activity of the encoded polypeptides, and this activity was readily measurable, the Board held that the low homology did not violate Art. 84 EPC.

In **T 29/05 (PVA/BRISTOL-MEYERS)**, the Board once more considered the feature “hybridizing under stringent conditions” clear under Art. 84, here, in combination with an additional structural feature (length of polynucleotide). In this context the Board pointed out:

[T]he fact that a large number of possible nucleic acid sequences might fall within the scope of claim 1 is not a reason for raising a lack of clarity objection [...]. (point 5)

6. It follows from the foregoing considerations, and in accordance with the established case law of the Boards of Appeal which requires a balance to be struck between the interest of the Applicant in obtaining adequate protection and the interest of the public in determining the scope of protection with reasonable effort [...], that the claimed subject-matter fulfils the requirements of Article 84 EPC. (point 6)

D.II.2.i. Product claims for nucleic acids

Claims relating to nucleic acids may be directed to various forms of nucleic acids mentioned in the introduction to this chapter. Most claims are concerned with DNAs and DNA sequences and/or fragments thereof as well as vectors. The DNA may either be characterized by functional terms, part or all of the amino acid sequence of the encoded protein, part or all of the nucleic acid sequence itself, parameters, reference to a deposited microorganism or DNA, a process for its production or a combination of two or more of these possibilities.

Further, claims often include a reference to “allelic variations”, “substitutions”, “insertions” or “deletions”, or reference is made to nucleic acids which

– hybridize to a specific nucleic acid or the complementary thereof, or

- are degenerated in relation to a specific nucleic acid as a result of the genetic code while maintaining their capacity to code for a protein having a certain biological activity.

The above features are intended to include embodiments not explicitly disclosed in the application and/or sometimes not even known when filing the application (e.g. a not-yet-known allelic variant of a specific sequence disclosed in the application). Several examples of claims containing such language are provided below.

Fragments of a DNA are often characterized as being part of a defined DNA and, in most cases, also by an additional characteristic. Features characterizing a fragment of a DNA may for example be the capability to encode a polypeptide exhibiting a certain biological activity, or the capability to be recognized by a certain antibody or simply the minimum size of the DNA fragment.

Vectors are in most cases DNA vehicles of circular structure which, in addition to a desired DNA sequence, contain regulatory sequences, selective marker genes, replicons enabling autonomous replication or DNA sequences allowing homologous integration into a certain DNA. Vector claims are included in most applications involving DNA sequences in order to claim an entity in which the DNA sequence is provided in an amplifiable form or “operably linked” to regulatory sequences required for recombinant expression in a given host.

In view of the common knowledge of a person skilled in the field of biotechnology, it is generally not required that generic claims relating to vectors carrying a specific desired structural gene recite particulars of the vector, such as a specific selection marker or an origin of replication, unless this is of importance for the invention.

Nucleic acids other than those mentioned before, particularly ribonucleic acids, play a minor role in patent applications, although more recently technologies based on e.g. siRNA, miRNA and derivatives such as LNA lead to the filing of patent applications. The following comments concentrate on DNAs, DNA sequences, DNA fragments and vectors. As will be understood, the comments also apply to genes or phage DNA and other types of DNAs.

The following sections are concerned with different types of product claims characterizing a nucleic acid by functional terms, by part or all of the amino acid sequence of the encoded protein, by part or all of the nucleic acid sequence itself, by parameters, by reference to a deposited microorganism or deposited DNA, or by a process for its preparation. Further, product claims may be directed to products comprising nucleic acids as essential elements. As will become evident from the examples, nucleic acids are in most cases characterized not only by one characteristic, but rather by a combination of two or more different features. Accordingly, most of the claims could appear as examples in more than one of the following subsections.

Applications comprising nucleotide sequences of 10 or more nucleotides must include a sequence listing (Rule 30 EPC (see Annex 3)). For further de-

tails, see C.I.3.b.a. as well as the Notice from the EPO of October 18, 2013 and Guidelines A-IV,5. According to **J 8/11 (Sequence listing/DKFZ)**, a sequence listing is not required for prior art sequences.

D.II.2.i.a. Product claims characterizing a nucleic acid by functional terms

Claims of this type are very desirable, since they embrace all DNA molecules having the identical function. Typical examples of functional features are the capability of encoding a protein of a given biological activity, the capability of hybridizing to a certain DNA or, in the case of promoters, the capability of directing expression of a DNA sequence.

Claim drafting:

Product claims characterizing a nucleic acid by functional terms can for example have one of the following general wordings:

A DNA hybridizing to DNA X.

A DNA encoding a protein having the biological activity X.

Any functional term should be clearly defined in the description. For example, in the case of claims including the feature of hybridizing to another DNA specified in the claim, the specification should contain further information with respect to hybridization conditions, for example, hybridization temperature, formamide content or salt concentrations. Similarly, if the DNA is defined by the biological activity of the encoded protein, the description should contain information on how to determine the biological activity of the protein. In general, the combination of hybridization or homology language with a further function such as the activity of an encoded protein, has good chances of being accepted by the Examiner.

Examples of granted claims containing functional terms are provided below. Functional features are underlined.

EP-B1 – 0323806 – Claim 20:

A recombinant DNA comprising an insert coding for a light-chain murine variable region and/or for a heavy-chain murine variable region of chimeric monoclonal antibodies according to claim 1.

Claim 1 of the same patent was directed to a chimeric monoclonal antibody consisting of variable regions of mouse origin and human constant regions, which recognizes epitopes of human carcinoembryonic antigen (CEA) not present on non-specific cross-reacting antigen NCA55 and NCA95, on biliary glycoprotein, or on granulocytes, and derivatives thereof.

Thus, the recombinant DNA is characterized by its coding capacity for a certain protein, which in turn is characterized by its biological activity.

EP-B1 – 0237545 – Claim 30:

A DNA sequence coding for a polypeptide analog of hpG-CSF having one or more cysteine residues deleted or replaced by alanine or serine residues.

The hpG-CSF (human pluripotent granulocyte colony-stimulating factor) analog of claim 30 is not identified by a specific sequence, but rather by changes of the amino acid sequence of hpG-CSF.

EP-B1 – 0233915 – Claim 10:

An expression cassette comprising a DNA sequence having in the direction of transcription a transcriptional and translational initiation region functional in plant cells, a structural gene coding for γ -interferon, and a termination region functional in plant cells.

The above claim comprises any plant expression system capable of expressing γ -interferon in plants and comprising what may be considered the essential elements, i.e. a transcriptional and translational initiation region, a structural gene and a termination region. Since neither an amino acid sequence nor a nucleic acid sequence of γ -interferon is recited, this claim embraces expression cassettes comprising structural genes encoding any known or future protein having interferon properties.

EP-B1 – 0321488 – Claim 1:

An intron free structural gene, derived from a corresponding intron-containing structural gene from the eukaryotic microorganism *R. toruloides*, both genes encoding the same product, characterised in that the intron-free gene is capable of expressing phenylalanine ammonia lyase ('PAL') or a polypeptide which displays PAL activity within a prokaryotic or eukaryotic microorganism.

The gene according to this claim has to mainly fulfill two requirements, i.e. it has to be intron-free and must be capable of expressing a polypeptide displaying phenylalanine ammonia lyase activity within any desired host microorganism.

EP-B1 – 0182442 – Claim 1 underlying decision **T 296/93 (HBV antigen production/BIOMERIEUX INC):**

A recombinant DNA molecule characterized by a DNA sequence coding for a polypeptide or a fragment thereof displaying HBV antigen specificity, said DNA sequence being operatively linked to an expression control sequence in the recombinant DNA molecule and being expressed to produce a polypeptide displaying HBV antigen specificity when a suitable host cell transformed with said recombinant DNA molecule is cultured, the transformed host cell not producing any human serum proteins and any primate serum proteins other than the polypeptide displaying HBV antigen specificity.

EP-B1 – 0054331 – Claim 1 underlying decision **T 281/86 (Preprothumatin/UNILEVER):**

A structural gene encoding non-processed or partly processed preprothumatin not containing the introns present in naturally occurring thumatin precursor genes.

EP-B1 – 0264074 – Claim 1:

A recombinant DNA expression vector for the production in *Escherichia coli* of Met-IGF-I, said vector comprises:

- a) a promoter-encoding gene;
- b) the first cistron comprising a gene encoding a protective peptide with a molecular weight of about 500–50,000, said gene containing a translational initiation signal immediately adjacent to the codon encoding the N-terminus of said peptide and a translational termination signal positioned downstream from the codon encoding the C-terminus of said peptide;
- c) the second cistron comprising a gene encoding IGF-I, said gene containing a translational initiation signal immediately adjacent to the codon encoding the N-terminus of IGF-I and a translational termination signal downstream from the codon encoding the C-terminus of IGF-I; subject to the limitation that said vector contains two SD sequences each located upstream from the codon for the N-terminus of each peptide, and that said vector is selectable and autonomously replicable in *E. coli*.

The above claimed vector appears to deviate from the standard type of vector since its composition containing an extra cistron in front of met-IGF-I is unusual. This applies also to the following vector claim:

EP-B1 – 0227260 – Claim 1:

A vector comprising a *Bacillus*-derived enhancing DNA sequence capable of enhancing the production of a desired protease in a *Bacillus* cell, said vector being characterised in including first and second sequences, said second sequence being a *Bacillus* sequence which is not a portion of a *sacQ* sequence, said first sequence comprising a portion of a *sacQ* DNA sequence which when combined with said second sequence causes said enhancing, said first and second sequences together comprising less than the entire *sacQ* sequence.

EP-B1 – 0001929 – Claim 1 underlying decision **T 292/85 (Polypeptide expression/GENENTECH I):**

A recombinant plasmid suited for transformation of a bacterial host wherein the plasmid comprises a homologous regulon, heterologous DNA, and one or more termination codon(s), the heterologous DNA encoding a desired functional heterologous polypeptide or intermediate therefore which is not degraded by endogenous proteolytic enzymes, said DNA being positioned in proper reading frame with said homologous regulon between said regulon and the termination codon(s), whereby on translation of the transcription product of the heterologous DNA in a suitable bacterium, the resulting expression product is said desired functional polypeptide or intermediate therefore in recoverable form.

The above claim has been granted in appeal procedures with the Appeal Board explicitly acknowledging the allowability of the functional definition.

EP-B1 – 002025 – Claim 1 underlying decision **T 181/87 (Hepatitis B virus/UNIVERSITY OF CALIFORNIA):**

A DNA transfer vector comprising at least a portion of the nucleotide sequence encoding the hepatitis B surface antigen and being free of the nucleotide sequence encoding the hepatitis B core antigen.

EP-B1 – 0242236 – Claim 37 underlying decision T 356/93 (Plant cells/PLANT GENETIC SYSTEMS):

Vector for the transformation of plant cells which contains a heterologous DNA containing a promoter recognized by polymerases of cells of said plant and a foreign nucleotide sequence which codes for a polypeptide having enzymatic activity capable of causing inactivation or neutralization of a glutamine synthetase inhibitor under the control of said promoter.

The following two examples of granted claims demonstrate the use of the term "hybridizing":

EP-B1 – 0032134 – Claim 1 underlying decision T 301/87 (Alpha-interferons/BIOGEN):

A recombinant DNA molecule for use in cloning a DNA sequence in bacteria, yeasts or animals cells, said recombinant DNA molecule comprising a DNA sequence selected from:

(a) the DNA inserts of Z-pBR322(Pst)/HcIF-4c, Z-pBR322(Pst)/HcIF-2h, Z-pBR322 (Pst)/HcIF-SN35, Z-pBR322(Pst)/HcIF-SN42 and Z-pKT287 (Pst)/HcIF-2h-AH6, said DNA inserts being exemplified, but not limited to, the DNA inserts of the recombinant DNA molecules carried by the microorganisms identified by accession numbers DSM 1699–1703, respectively,

(b) DNA sequences which hybridise to any of the foregoing DNA inserts and which code for a polypeptide of the IFN- α type, and

(c) DNA sequences which are degenerate as a result of the genetic code to the DNA sequences and inserts defined in (a) and (b) and which code for a polypeptide of the IFN- α type.

EP-B1 – 0148605 – Claim 1 underlying decision T 412/93 (Erythropoietin/KIRIN-AMGEN):

A DNA sequence for use in securing expression in a procaryotic or eucaryotic host cell of a polypeptide product having at least part of the primary structural confirmation of that of erythropoietin to allow possession of the biological property of causing bone marrow cells to increase production of reticulocytes and red blood cells and to increase hemoglobin synthesis or iron uptake, said DNA sequence selected from the group consisting of:

(a) the DNA sequences set out in Tables V and VI or their complementary strands;

(b) DNA sequences which hybridize under stringent conditions to the protein coding regions of the DNA sequences defined in (a) or fragments thereof; and

(c) DNA sequences which, but for the degeneracy of the genetic code, would hybridize to the DNA sequences defined in (a) and (b).

EP-B1 – 1509251 – Claim 1:

An isolated nucleic acid comprising a nucleotide sequence encoding a rat apoptosis-specific eIF-5A polypeptide.

This claim contains the term "isolated" which is often recited in US practice. For the EPO, this term is usually not required to delimit the claim over the nucleic acid as contained in its natural environment. The term should be omitted in order to avoid difficulties in the course of enforcement where such a feature can cause problems as e.g. as in the recent case before the CJEU (**Monsanto C 428/08**; referring case Rechtbank's – Gravenhage (Netherlands) – 249983).

EP-B1 – 1660654 – Claim 1:

An expression vector, comprising (1) a selectable marker gene operably linked to a regulatory nucleic acid comprising a transcriptionally impaired promoter, and (2) one or more insertion sites for inserting a co-linked gene of interest operably linked to a regulatory sequence.

This is a typical claim using the “operably linked” language for constructs using a promoter and a gene under its control.

EP-B1 – 1500329 – Claim 14:

A nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide selected from the group consisting of:

- (a) the heavy chain of a human antibody according to claim 1;
- (b) the light chain of a human antibody according to claim 1; and
- (c) an antigen-binding portion of (a) or (b).

Claim 1 was directed to an isolated human antibody that specifically binds TNF- alpha or an antigen-binding portion thereof.

EP-B1 – 1504095 – Claim 1:

An integration vector capable of site-specific Listeria genome integration.

EP-B1 – 1532261 – Claim 1:

An expression cassette comprising the following operably linked nucleic acid sequence:

5'Pr- (TIS)D-(IBFP1)E-(CL1)G-ORF-[CL2-ORF]L-(CL3)M-(IBFP2)Q-(SSC)R(CL4) T-(Ft)W-(Tr)X-3'

wherein Pr is a promoter sequence,

TIS encodes a translation initiation sequence,

IBFP1 encodes a first inclusion body fusion partner comprising an amino acid sequence corresponding to any one of SEQ ID. NO: 1–15, or a variant thereof, wherein at least one amino acid in the inclusion body fusion partner is replaced with another amino acid that is a conservative amino acid,

CL1 encodes a first cleavable peptide linker,

ORF encodes a preselected polypeptide,

CL2 encodes a second cleavable peptide linker,

CL3 encodes a third cleavable peptide linker,

IBFP2 encodes a second inclusion body fusion partner comprising an amino acid sequence corresponding to any one of SEQ ID NO: 1–15, or a variant thereof, wherein at least one amino acid in the inclusion body fusion partner is replaced with another amino acid that is a conservative amino acid, SSC is a suppressable stop codon, CL4 encodes a fourth cleavable peptide linker,

Ft encodes a fusion tag, and Tr is a transcription terminator sequence,

wherein each of D or X is independently 0 or an integer of 1 to 4,

wherein R is 0 or an integer of 1 to 2,

wherein each of E, G, L, M, Q, T or W is independently 0 or an integer of 1 to 20,

wherein either one or both of IBFP1 or IBFP2 is present, and

wherein at least one of CL1, CL2, CL3 or CL4 is present, and

wherein expression of the expression cassette produces a protein that has an inclusion body fusion partner operably linked to a preselected polypeptide and that forms an inclusion body when expressed in a cell.

EP-B1 – 2067857 – Claim 2:

A DNA according to any one of the following [1] to [3]:

- [1] a DNA encoding the protein according to claim 1;
- [2] a DNA having the nucleotide sequence shown by SEQ ID NO: 2; and
- [3] a DNA hybridizing under stringent conditions to a DNA consisting of a nucleotide sequence complementary to the nucleotide sequence shown by SEQ ID NO: 2, and encoding a protein having dipeptide-synthesizing activity.

This claim is also a typical example for using hybridization language in combination with a testable parameter such as the dipeptide-synthesizing activity.

EP-B1 – 1556404 – Claim 2:

An isolated nucleotide sequence or fragment thereof encoding a polypeptide, wherein said polypeptide has at least 70% amino acid sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO:23, SEQ ID NO:28 and SEQ ID NO:64.

This claim also contains the problematic “isolated” language.

EP-B1 – 2298898 – Claim 1:

A purified and isolated DNA sequence having protein production increasing activity characterized in that said DNA sequence comprises a) at least one bent DNA element, wherein the bent DNA element contains at least 33% of dinucleotide TA, and/or at least 33% of dinucleotide AT on a stretch of 100 contiguous base pairs, b) at least one binding site for a DNA binding protein, and that it is a MAR nucleotide sequence consisting of the sequence SEQ ID No 27, or a sequence complementary thereof, or a sequence having at least 90% identity with said sequence SEQ ID No 27.

EP-B1 – 2292754 – Claim 1:

A purified and isolated DNA sequence having protein production increasing activity characterized in that said DNA sequence comprises a) at least one bent DNA element, wherein the bent DNA element contains at least 33% of dinucleotide TA, and/or at least 33% of dinucleotide AT on a stretch of 100 contiguous base pairs, b) at least one binding site for a DNA binding protein, and that it is a MAR nucleotide sequence consisting of the sequence SEQ ID No 26, or a sequence complementary thereof, or a sequence having at least 90% identity with said sequence SEQ ID No 26.

EP-B1 – 2231859 – Claim 1:

A vector for recombinantly expressing a polypeptide in a eukaryotic cell, comprising a eukaryotic promoter operably linked to a polynucleotide sequence comprising at least 2 copies of an mRNA translational enhancer element (TEE), wherein the TEE consists of 5'-GCGAGAGAA-3', or a full-length sequence that is at least 90% identical thereto or a fulllength sequence that is identical to SEQ ID NO: 5, and wherein the TEE is located 3' to the promoter and adapted for directional ligation of a second polynucleotide sequence encoding a polypeptide of interest.

EP-B1 – 2013349 – Claim 1:

A DNA molecule comprising an open reading frame sequence that encodes a selectable marker polypeptide that provides resistance against zeocin or against neomycin, **characterized in that** said DNA molecule in the coding strand for the selectable marker

polypeptid has a GTG startcodon or a TTG startcodon, and **in that** the open reading frame sequence that encodes the selectable marker protein has been mutated to replace at least half of its CpG dinucleotides as compared to the native open reading frame sequence that encodes the selectable marker protein.

EP-B1 – 1857122 – Claim 1:

Modified mRNA coding for at least one antigenic viral peptide or polypeptide, **characterised in that** the G/C content of the region of the modified mRNA coding for the peptide or polypeptide is increased compared to the G/C content of the coding region of the wild type mRNA coding for the peptide or polypeptide, and the encoded amino acid sequence is unchanged as compared to the wild type.

D.II.2.i.b. Product claims characterizing a nucleic acid by part or all of the amino acid sequence of the encoded protein

Claims describing the nucleic acid by part or all of the amino acid sequence of the encoded protein cover all nucleic acids coding for a certain amino acid sequence, regardless of the codons used. Due to the degeneracy of the genetic code, the claim may in effect cover thousands of different embodiments, all of which encode the very same protein. According to the present practice of the EPO, claims of this type are often denied an inventive step, if the protein encoded by the nucleic acid sequence is already state of the art, and even if the amino acid sequence is not known.

Where only partial amino acid sequences are available to the Applicant, the partial amino acid sequence information may serve to claim a DNA molecule comprising a DNA sequence containing the coding capacity for the partial amino acid sequence. Usually, claims of this type must also indicate the biological activity of the encoded protein.

Claim drafting:

A product claim characterizing the nucleic acid by part or all of the amino acid sequence of an encoded protein can have the following general wording:

A DNA encoding protein X comprising the amino acid sequence ...

Examples of granted claims referring to an amino acid sequence are provided below; the proteins defining the corresponding nucleic acid are underlined.

EP-B1 – 0073646 – Claim 1:

A DNA isolate comprising a continuous sequence encoding human serum albumin of the amino acid sequence depicted in Fig. 3 hereof and genetic variants thereof.

EP-B1 – 0091539 – Claim 1:

A DNA sequence comprising a DNA sequence coding for a polypeptide having human interleukin-2 activity, said polypeptide being selected from the following group:

- a) a polypeptide having the following amino acid sequence:
(...)
- b) a polypeptide which in respect to (a) is deficient in one or more amino acids;
- c) a polypeptide in which in respect to (a) one or more amino acids are replaced;
- d) a fusion polypeptide comprising a polypeptide according to (a), (b) or (c) in which the additively connected amino acids do not interfere with the biological interleukin-2 activity or may be easily eliminated,
- e) a polypeptide which is an allelic derivative of a polypeptide according to (a).

In addition to including DNA sequences coding for variants or allelic derivatives of the polypeptide according to (a) above, the above claim embraces DNA sequences coding for polypeptides deficient in one or more amino acids, i.e. partial peptides, and DNA coding for fusion polypeptides which, in addition to interleukin-2 related DNA sequences, comprise DNA sequences coding for a fusion part.

EP-B1 – 0323806 – Claim 22:

A recombinant DNA according to claim 20 or 21 comprising an insert coding for the polypeptide of formula I, optionally containing introns.

Claim 20 is provided above (see D.II.2.i.a). Formula I depicts the amino acid sequence of immunoglobulin light chain variable regions.

EP-B1 – 0181150 – Claim 1:

A recombinant DNA construct useful for the expression of a recombinant polypeptide in a cell containing the construct, the construct comprising control sequences which regulate transcription and translation of the recombinant polypeptide in the cell and a coding sequence regulated by the control sequences, wherein the coding sequence comprises a DNA sequence of at least about 21 bp in reading frame, characterized in that the DNA sequence encodes an antigenic HIV-I amino acid sequence of Figure 2 which sequence is immunologically non-cross reactive with HTLV-I and HTLV-II and is reactive with HIV-I.

In this example, the coding sequence forming part of the recombinant DNA construct is characterized as comprising a DNA sequence of at least about 21 bp. This DNA sequence is required to encode a partial amino acid sequence of 7 amino acids contained in the amino acid sequence shown in a figure of the patent. This language serves to embrace all variants of HIV and even fragments thereof sharing 7 amino acids with the HIV-I variant disclosed in the patent.

EP-B1 – 0077670 – Claim 9 underlying decision **T 223/92 (HIF Gamma/GENENTECH):**

A DNA isolate comprising a DNA sequence encoding human immune interferon having the amino acid sequence depicted in Figure 5 hereof or an allele or derivative thereof having the function of human immune interferon.

Claim 9 of this patent is similar to claim 1 of EP-B1 – 0073646 cited above in this section, in that both include “genetic variants” or “alleles”, respectively, with the present claim even including derivatives. However,

claim 9 of EP-B1 – 0077670 contains the additional feature of “having the function of” the respective encoded protein.

EP-B1 – 0214971 – Claim 1 underlying decision **T 816/90 (CBH II/ALKO)**:

A DNA sequence which codes for the cellulase enzyme cellobiohydrolase II from *Trichoderma reesei* which is capable, when correctly combined with an expression vector, of expressing a protein having the cellulolytic activity of the said enzyme upon transformation of a host organism by the vector, said DNA sequence coding for the following amino acid sequence:

(...)

or for a substantially identical amino acid sequence showing the same enzymatic activity.

EP-B1 – 0318216 – Claim 32:

A polynucleotide in substantially isolated form comprising a contiguous sequence of nucleotides which is capable of selectively hybridizing to the genome of hepatitis C virus (HCV) or the complement thereof, wherein HCV is characterized by:

- (i) a positive stranded RNA genome;
- (ii) said genome comprising an open reading frame (ORF) encoding a polyprotein; and
- (iii) said polyprotein comprising an amino acid sequence having at least 40% homology to the 859 amino acid sequence in Figure 14.

This claim is directed not only to DNA embodiments, but also to RNA polynucleotides. Furthermore, it should be noted that the claim comprises embodiments having a low degree of homology to the amino acid sequence actually disclosed in the patent; the homology needs only be 40%.

EP-B1 – 2199405 – Claims 9, 10 and 11:

Claim 9:

A polypeptide comprising the sequence
(W/F/R/K)(W/F/R/K)(R/K)(F/W/H/R)(Y/W/R)(S/T)(L/V/I)(R/K)(R/K)(A/Y) or (W/R)(X)(X)(F/Y/H/T)(Y/W/R)(T)(X)(R/T)(R)(X), where X represents any amino acid.

Claim 10:

The polypeptide of claim 9 consisting of or comprising the sequence WWK-FYTLRRA, WWRFYTLRKA, RLGWWKFYTLRRARQGNTKQR, RLGW-WRFYTLRKARQGNTKQR or RLGWWRFYTLRRARQGNTKQ and/or wherein the polypeptide is a GST fusion polypeptide, for example GST-RLGW-WRFYTLRRARQGNTKQR.

Claim 11:

A polynucleotide encoding a polypeptide according to claim 9 or 10.

D.II.2.i.c. Product claims characterizing a nucleic acid by part or all of the nucleic acid sequence itself

Product claims characterizing a nucleic acid by a specific sequence may not only be directed to the specific sequence, but also to a sequence containing a partial sequence. Characterization of a DNA by its specific nucleic acid se-

quence is a fallback position if the prior art includes the amino acid sequence of the protein encoded by the nucleic acid. In such a case, the sequence can be seen as a specific selection out of several sequences which, due to the degeneracy of the genetic code, can code for a certain protein.

Claim drafting:

Generally, a claim characterizing a nucleic acid by its sequence can have the following wording:

A DNA comprising the sequence ...

Alternatively, the term “having” is sometimes used which is interpreted by the EPO as “comprising”. Still the term “comprising” is preferred with regard to enforcement of the claims.

Examples of granted claims referring to a specific nucleic acid sequence are provided below; the specific sequences are underlined in the examples below.

EP-B1 – 0148605 – Claim 1* underlying decision **T 412/93 (Erythropoietin/KIRIN-AMGEN):*

A DNA sequence for use in securing expression in a procaryotic or eucaryotic host cell of a polypeptide product having at least part of the primary structural confirmation of that of erythropoietin to allow possession of the biological property of causing bone marrow cells to increase production of reticulocytes and red blood cells and to increase hemoglobin synthesis or iron uptake, said DNA sequence selected from the group consisting of:

- (a) the DNA sequence set out in Tables V and VI or their complementary strands;
- (b) DNA sequences which hybridize under stringent conditions to the protein coding regions of the DNA sequences defined in (a) or fragments thereof; and
- (c) DNA sequences which, but for the degeneracy of the genetic code, would hybridize to the DNA sequences defined in (a) and (b).

This claim is a typical example of a claim extending to hybridizing DNA sequences and DNA sequences which, but for the degeneracy of the genetic code, would hybridize to the DNA sequences previously defined. In addition, this claim also comprises complementary strands (see (a)) and fragments of the DNA sequences (see (b)).

EP-B1 – 0162067 – Claim 1:

An isolated recombinant vector containing DNA coding for human factor VIII:C, comprising a polydeoxyribonucleotide having the sequence:

5' CGC AGC TTT CAG AAG AAA ACA CGA CAC
TAT TTT ATT GCT GCA GTG GAG AGG 3'.

This claim is remarkable in that the DNA coding for human factor VIII:C is characterized by only a partial nucleotide sequence of the factor VIII:C-coding region. Thus, any vector containing DNA coding for a protein having factor VIII:C activity and comprising the above cited partial nucleotide sequence is embraced by the above claim.

EP-B1 – 0047600 – Claim 1 underlying decision **T 283/86 (–/THE REGENTS OF THE UNIVERSITY OF CALIFORNIA):**

A DNA transfer vector comprising a deoxynucleotide sequence comprising a plus strand having the sequence:

5' – (...) – 3',

wherein A is deoxyadenyl,

G is deoxyguanyl,

C is deoxycytosyl and

T is thymidyl,

or a modification thereof, said deoxynucleotide sequence coding for bovine pre-growth hormone.

EP-B1 – 1577390 – Claim 1:

Human cancer related nucleic acid consisting of

- (i) a nucleic acid sequence of SEQ ID NO: 6, or
- (ii) a nucleic acid that encodes SEQ ID NO: 7.

This claim has the term “consisting of” which, wherever possible, should be avoided. It might lead to a very narrow interpretation of the claim during litigation. The term “comprising” is preferred over “consisting”. In general, “consisting of” is interpreted as exhaustive, whereas “comprising” is interpreted as non-exhaustive. For instance, a nucleic acid which “comprises” sequence X must contain sequence X, but may also contain other sequences, while a nucleic acid which “consists of” sequence X contains this sequence and nothing more.

EP-B1 – 2048954 – Claim 1:

An isolated DNA comprising a nucleic acid promoter having a sequence consisting of SEQ ID NO:1.

SEQ ID NO 1 corresponds to a region of the human SPARC promoter.

EP-B1 – 1571221 – Claim 1:

An isolated polynucleic acid as identified by:

- (a) SEQ ID NO 73, or the complementary strand thereof;
 - (b) polynucleic acid sequences which hybridize to sequence defined in (a); or,
 - (c) polynucleic acid sequences which are degenerated as a result of the genetic code to the polynucleic acid sequence defined in (a) or (b);
- wherein the polynucleic acid of (a) to (c) encodes a polypeptide of SEQ ID NO: 74.

EP-B1 – 1556404 – Claim 1:

An isolated nucleotide sequence or fragment thereof comprising or complementary to a nucleotide sequence having at least 70% nucleotide sequence identity to a nucleotide sequence selected from the group consisting of SEQ ID NO:22, SEQ ID NO:27 and SEQ ID NO:63.

EP-B1 – 2310501 – Claim 1:

A polyadenylation signal comprising a nucleic acid comprising a sequence at least 75% identical to SEQ ID NO:8.

EP-B1 – 2298898 – Claim 1:

A purified and isolated DNA sequence having protein production increasing activity **characterized in that** said DNA sequence comprises a) at least one bent DNA element, wherein the bent DNA element contains at least 33% of dinucleotide TA, and/or at least 33% of dinucleotide AT on a stretch of 100 contiguous base pairs, b) at least one binding site for a DNA binding protein, and that it is a MAR nucleotide sequence consisting of the sequence SEQ ID No 27, or a sequence complementary thereof, or a sequence having at least 90% identity with said sequence SEQ ID No 27.

EP-B1 – 2292754 – Claim 1:

A purified and isolated DNA sequence having protein production increasing activity **characterized in that** said DNA sequence comprises a) at least one bent DNA element, wherein the bent DNA element contains at least 33% of dinucleotide TA, and/or at least 33% of dinucleotide AT on a stretch of 100 contiguous base pairs, b) at least one binding site for a DNA binding protein, and that it is a MAR nucleotide sequence consisting of the sequence SEQ ID No 26, or a sequence complementary thereof, or a sequence having at least 90% identity with said sequence SEQ ID No 26.

EP-B1 – 2231859 – Claim 1:

A vector for recombinantly expressing a polypeptide in a eukaryotic cell, comprising a eukaryotic promoter operably linked to a polynucleotide sequence comprising at least 2 copies of an mRNA translational enhancer element (TEE), wherein the TEE consists of 5'-GCCAGAGAA-3', or a full-length sequence that is at least 90% identical thereto or a full length sequence that is identical to SEQ ID NO: 5, and wherein the TEE is located 3' to the promoter and adapted for directional ligation of a second polynucleotide sequence encoding a polypeptide of interest.

D.II.2.i.d. Product claims characterizing a nucleic acid by parameters

Parameters which may be used to characterize a nucleic acid are, for example, the size of a certain restriction fragment, restriction maps established by using specified restriction endonucleases, the T_m -value of the claimed DNA, the incompatibility group in case of vectors, the % identity, homology, or similarity to a given reference sequence, etc. The specification should provide the details of any methods used to determine the respective parameter, e.g. the method used for determining the size of a certain restriction fragment, the conditions under which the T_m value is measured or the criteria applied for determining the homology.

Claim drafting:

A general type of a claim characterizing a DNA by parameters could have the following wording:

A DNA comprising the restriction sites as shown in Fig. X.

A DNA showing X% identity to sequence Y.

The following examples contain further characterizing features in addition to parameters. The parameters are underlined in the following examples.

EP-B1 – 0066701 – Claim 1 underlying decision **T 162/86 (Plasmid pSG2/HOECHST):**

The plasmid pSG2, characterized in that it is obtained from a culture of *Streptomyces ghanaensis* ATCC 14672 and has a contour length of 4.58 [μm]m and a molecular length of about 13.8 kilobases (=kb) and is not fragmented by the restriction endonucleases EcoR I, BamH I, Sal I, Hpa I and Hind II, but is cleaved by the restriction endonuclease Hind III into a fragment of length of about 14 kb, by Cla I into two fragments of lengths 10.15 and 3.65 kb and by Pst I into two fragments of lengths 10.85 and 3.0 kb, by Bgl II into two fragments of lengths 11.25 kb and 2.6 kb, and by Bcl I into three fragments of lengths 11.6 kb, 1.25 kb and 1.0 kb.

EP-B1 – 0208468 – Claim 1 underlying decision **T 576/91 (Plasmid pTR2030/NORTH CAROLINA STATE UNIVERSITY):**

The plasmid pTR2030 characterized by a molecular weight of 30.0 ± 3.0 megadaltons, having the following sensitivity to restriction endonucleases:

EnzymeSites

*Hind*III16

*Hae*III 4

*Eco*R1 8

*Xba*I5

*Hpa*I3

*Nco*II5

*Ava*II2

and carrying one or more genetic determinants for phage resistance in group N streptococci (lactococci) and exhibiting phenotypes of Tra⁺, Clu⁺, Hsp⁺ and Hrp⁺, the said plasmid being obtainable from *S.Lactis* TRSI-a(ATCC 53146) or *S.Lactis* TEK1 (ATCC 53167).

The above claim characterizes the plasmid by its molecular weight, its sensitivity to restriction endonucleases, genetic determinants for phage resistance and genetic phenotypes as well as a process for obtaining it from specific deposited microorganisms.

EP1528102 – Claim 4:

The isolated nucleic acid molecule of claim 1 or 3, wherein said molecule is hybridizable to the isolated nucleic acid molecule consisting of the DNA sequence of SEQ ID NO: 3 under high stringency hybridization conditions corresponding to a T_m greater than or equal to about 65° C.

This claim contains the problematic “isolated” language.

EP-B1 – 1556404 – Claim 2:

An isolated nucleotide sequence or fragment thereof encoding a polypeptide, wherein said polypeptide has at least 70% amino acid sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO:23, SEQ ID NO:28 and SEQ ID NO:64.

This claim also contains the problematic “isolated” language.

EP-B1 – 2298898 – Claim 1:

A purified and isolated DNA sequence having protein production increasing activity **characterized in that** said DNA sequence comprises a) at least one bent DNA element,

wherein the bent DNA element contains at least 33% of dinucleotide TA, and/or at least 33% of dinucleotide AT on a stretch of 100 contiguous base pairs, b) at least one binding site for a DNA binding protein, and that it is a MAR nucleotide sequence consisting of the sequence SEQ ID No 27, or a sequence complementary thereof, or a sequence having at least 90% identity with said sequence SEQ ID No 27.

D.II.2.i.e Product claims characterizing a nucleic acid by reference to a deposited microorganism or deposited DNA

Claims characterizing the DNA by reference to a deposit are an option if the sequence of the protein, the sequence of the DNA encoding the protein, and a reliable parameter are unknown; a reproducible process for obtaining the DNA is neither available nor disclosed; or claims containing functional terms are not possible. In these instances, depositing the DNA, which in most cases will require depositing a microorganism or virus containing the claimed DNA, provides a convenient tool for disclosing the DNA without having to spend any effort in elucidating the nucleic acid sequence. For discussion of deposits, see C.I.3.b.b, D.II.2.g. and D.V.2.f.a.

Claim drafting:

A claim belonging to this group could have the following general wording:

A DNA being deposited at ... under deposit No ...

Examples of granted claims defining a nucleic acid by deposit data (among other ways) are given in the following; the respective deposits are underlined in the claims below.

EP-B2 – 0032134 – Claim 1* underlying decision **T 500/91 (Alpha-interferon II/BIOGEN):*

A recombinant DNA molecule for use in cloning a DNA sequence in bacteria, yeast or animal cells, said recombinant DNA molecule comprising a DNA sequence selected from:

- (a) The DNA inserts of Z-pBR322(Pst)/HcIF-4c, Z-pBR322(Pst)/HcIF-2h, Z-pBR322(Pst)/HcIF-SN35, Z-pBR322(Pst)/HcIF-SN42 and Z-pKT287 (Pst)/HcIF-2h-AH6, said DNA inserts being the DNA inserts of the recombinant DNA molecules carried by the microorganisms identified by accession numbers DSM 1699–1703, respectively,
- (b) DNA sequences which hybridize to any of the foregoing DNA inserts and which code for a polypeptide of the IFN- α type, and
- (c) DNA sequences which are degenerate as a result of the genetic code to the DNA sequences and inserts defined in (a) and (b) and which code for a polypeptide of the IFN- α type.

EP-B1 – 395736 – Claim 8* underlying decision **T 340/00 (Thermostable enzyme/HOFFMANN-LA ROCHE):*

A recombinant vector comprising a DNA sequence according to any one of claims 1 to 7, except for the recombinant vectors CH35: Taq#4–2 (ATCC 40,336), pFC83

(ATCC 67,422), pFC85 (ATCC 67,421) and pLSG1 (composed of the ~ 750 bp BglII/HindIII fragment of pFC83, the ~ 2,8 kbp HindIII/Asp71 B fragment of pFC85 and the BglII/Asp71B vector fragment of BSM 13+).

EP-B1 – 081520 – Claim 2* underlying decision **T 1644/08 (Novel endoglucanases/NOVOZYMES A/S):*

The DNA construct according to claim 1, in which the DNA sequence is isolated from or produced on the basis of a DNA library of a strain belonging to the family Chaetomiaceae, preferably to the genus Thielavia, in particular a strain of Thielavia terrestris, especially Thielavia terrestris, NRRL 8126.

EP-B1 – 0939804 – Claim 2* underlying decision **T 18/09 (Neutrokinine/HUMAN GENOME SCIENCES):*

A nucleic acid molecule of claim 1, wherein the amino acid sequence of said full-length Neutrokinine- α polypeptide is the one encoded by the cDNA clone contained in ATCC Deposit No. 97768.

EP-B1 – 0472651 – Claim 4* underlying decision **T1333/04 (Endo F-Free PNGase/GENZYME CORPORATION):*

The plasmid pGB29, present in ATCC 67987.

D.II.2.i.f. Product claims characterizing a nucleic acid by a process for its preparation

As for any other products, under certain conditions DNAs may be characterized by a process for their production. For further general discussion of product-by-process claims, see C.I.3.e.a.

Claim drafting:

A product-by-process claim relating to a DNA could have the following general wording:

A DNA obtainable by a process comprising the following steps ...

Examples of granted claims directed to a nucleic acid which is characterized by the process for its production, inter alia, are shown below. The process features are underlined.

EP-B1 – 0237269 – Claim 1:

A broad host range plasmid vector which can be introduced into and stably maintained in a broad range of bacteria, which vector is derivable by mutation of a broad host range plasmid of the incompatibility group Q such that it exists in a higher copy number mutant thereof and is temperature sensitive for plasmid copy number control.

EP-B1 – 0076847 – Claim 6:

Full-length, infectious poliovirus cDNA as obtainable by a method according to any one of Claims 1 to 5 having the base sequence set forth in Table 1 and equivalents thereto containing different codons for the same amino acid sequences.

The above claim characterizes the cDNA by a method for obtaining the cDNA in combination with a specific nucleic acid sequence. The process claim referred to in this product claim is characterized by the steps of reverse transcription, forming ds cDNA sequences, inserting the DNA sequences into a vector, transforming cells, culturing transformed cells, identifying and isolating recombinant vectors, obtaining partial cDNA sequences and joining the partial cDNA sequences in order to form a recombinant vector containing a full-length infectious poliovirus ds cDNA.

EP-B1 – 093641 – Claim 1 underlying decision **T 109/91 (Composite plasmid/AJINOMOTO CO.):**

A composite plasmid which comprises (a) a DNA replication region derived from a plasmid (a) capable of propagating in a *Coryneform* glutamic acid-producing bacterium, and (B) a gene fragment derived from a plasmid (b) capable of propagating in *Escherichia coli* or *Bacillus subtilis* and having at least a region expressing drug resistance.

EP-B1 – 0321488 – Claim 1:

An intron free structural gene, derived from a corresponding intron-containing structural gene from the eukaryotic microorganism *R. toruloides*, both genes encoding the same product, characterised in that the intron-free gene is capable of expressing phenylalanine ammonia lyase ('PAL') or a polypeptide which displays PAL activity within a prokaryotic or eukaryotic microorganism.

The gene according to this claim must fulfil two main requirements, i.e. it has to be intron-free and must be capable of expressing a polypeptide displaying phenylalanine ammonia lyase activity within any desired host microorganism.

EP-B1 – 0066701 – Claim 1 underlying decision **T 162/86 (Plasmid pSG2/HOECHST):**

The plasmid pSG2, characterized in that it is obtained from a culture of *Streptomyces ghanaensis* ATCC 14672 and has a contour length of 4.58 [my]m and a molecular length of about 13.8 kilobases (=kb) and is not fragmented by the restriction endonucleases EcoR I, BamH I, Sal I, Hpa I and Hind II, but is cleaved by the restriction endonuclease Hind III into a fragment of length of about 14 kb, by Cla I into two fragments of lengths 10.15 and 3.65 kb and by Pst I into two fragments of lengths 10.85 and 3.0 kb, by Bgl II into two fragments of lengths 11.25 kb and 2.6 kb, and by Bcl I into three fragments of lengths 11.6 kb, 1.25 kb and 1.0 kb.

EP-B1 – 0208468 – Claim 1 underlying decision **T 576/91 (Plasmid pTR2030/NORTH CAROLINA STATE UNIVERSITY):**

The plasmid pTR2030 characterized by a molecular weight of 30.0 ± 3.0 megadaltons, having the following sensitivity to restriction endonucleases:

EnzymeSites
HindIII16
HaeIII 4
EcoRI 8
XbaI5
HpaI3

*NcoII*5

*AvaI*2

and carrying one or more genetic determinants for phage resistance in group N streptococci (lactococci) and exhibiting phenotypes of Tra⁺, Clu⁻, Hsp⁺ and Hrp⁺, the said plasmid being obtainable from *S.Lactis* TRSI-a(ATCC 53146) or *S.Lactis* TEK1 (ATCC 53167).

The above claim characterizes the plasmid by its molecular weight, its sensitivity to restriction endonucleases, genetic determinants for phage resistance and genetic phenotypes as well as a process for obtaining it from specific deposited microorganisms.

D.II.2.i.g. Product claims comprising nucleic acids as essential elements

Nucleic acids may be used not only for cloning and expression purposes but also as a probe for detecting specific DNA or RNA in a sample. Well known applications of nucleic acids are, e.g. the detection of virus genomes in body fluids, prenatal diagnosis of genetically inherited disorders like sickle cell anaemia or β -thalassaemia, or DNA finger print analysis for forensic purposes. Therefore, applications frequently contain claims relating to a kit comprising a specific nucleic acid.

Claim drafting:

A general wording of a claim relating to a kit may be as follows:

A kit for purpose X comprising DNA Y.

The following examples relate to granted product claims in which a nucleic acid is an essential element. The compositions/products containing a nucleic acid are underlined in the examples below.

EP-B1 – 0318216 provides three types of product claims comprising polynucleotide probes. All of these claims refer to a polynucleotide claim, which is presented first:

EP-B1 – 0318216 – Claim 32:

A polynucleotide in substantially isolated form comprising a contiguous sequence of nucleotides which is capable of selectively hybridizing to the genome of hepatitis C virus (HCV) or the complement thereof, wherein HCV is characterized by:

- (i) a positive stranded RNA genome;
- (ii) said genome comprising an open reading frame (ORF) encoding a polyprotein; and
- (iii) said polyprotein comprising an amino acid sequence having at least 40% homology to the 859 amino acid sequence in Figure 14.

The claims relating to products comprising the above polynucleotide are as follows:

EP-B1 – 0318216 – Claim 40:

A probe which comprises a polynucleotide according to any one of claims 32 to 39 further comprising a detectable label.

EP-B1 – 0318216 – Claim 41:

An assay kit comprising a polynucleotide probe according to any one of claims 32 to 40 in a suitable container.

EP-B1 – 0318216 – Claim 42:

A polymerase chain reaction (PCR) kit comprising a pair of primers capable of priming the synthesis of cDNA in a PCR reaction, wherein each of said primers is a polynucleotide according to any one of claims 32 to 37.

A further example of a product claim comprising a nucleic acid as an essential component is the following:

EP-B1 – 0162067 – Claim 6:

A screening agent for identifying deoxyribonucleotide sequences and ribonucleotide sequences which encode for at least a portion of the human gene factor VIII:C, consisting essentially of a deoxyribonucleotide having the following sequence or its inverse complement:

5' TTT CAG AAG AGA ACC CGA CAC TAT TTC
ATT GCT GCG GTG GAG CAG CTC TGG GAT
TAC GGG ATG AGC GAA TCC CCC CGG GCG
CTA AGA AAC AGG 3'.

EP-B1 – 1556081 – Claim 1:

An immunogenic composition comprising: recombinant Bacille Calmette–Guerin (BCG) having an extrachromosomal nucleic acid sequence comprising a gene encoding for a Mycobacteria tuberculosis major extracellular protein selected from the group consisting of 23.5 kDa, 32 kDa and combinations thereof, wherein said Mycobacteria tuberculosis major extracellular protein is over expressed and secreted.

EP-B1 – 438512 – Claim 9 underlying decision **T 423/01 (Längenpolymorphismen/MAX-PLANCK-GESELLSCHAFT):**

A kit for performing the method according to any one of claims 1 to 8 containing primers flanking simple or cryptically simple DNA sequences and optionally being labelled with a radioactive or fluorescent label.

EP-B1 – 1683862 – Claim 1:

A microarray for predicting prognosis of neuroblastoma, having 24 probes related to good prognosis which respectively hybridize to the gene transcripts of genes having the nucleotide sequences of SEQ ID NOs: 5, 152, 132, 145, 142, 160, 87, 16, 191, 51, 173, 163, 129, 37, 136, 171, 67, 78, 64, 130, 91, 28 and 22 and Accession No. NM_003617.1, and

30 probes related to poor prognosis which respectively hybridize to gene transcripts of genes having the nucleotide sequences of SEQ ID NOs: 183, 135, 11, 131, 105, 188, 18, 46, 7, 32, 13, 2, 3, 25, 124, 26, 175, 97, 96, 20, 172, 92, 83, 34, 179, 154, 125, 141 and 114 and Accession No. BC003629.1.

EP-B1 – 2141173 – Claim 1:

A composition comprising an oligonucleotide that hybridizes under physiological conditions to a promoter region of

a bcl-2 gene, wherein said first oligonucleotide is SEQ ID NO: 1438, and complements thereof.

D.II.2.i.h. Product claims for certain types of nucleic acids and methods of using same

The type of nucleic acid is marked by underlining.

EP-B1 – 1799825 – Claim 1:

A nucleic acid comprising:

- (i) a substrate sequence that can form a substrate for an extrinsic enzymatic activity of an RNase enzyme, and,
- (ii) an aptamer that binds to a ligand, wherein binding of the ligand to said aptamer causes a conformational change in the nucleic acid that alters the ability of said substrate sequence to form said substrate and/or alters the Km and/or kcat of said substrate for the extrinsic enzymatic activity, wherein said nucleic acid modulates gene expression in a ligand-dependent manner.

In the above claim, the aptamer is characterized by the functional feature of binding to a ligand.

EP-B1 – 04718537 – Claim 1:

An iRNA agent comprising a sense sequence and an antisense sequence, wherein the sense sequence has one or more asymmetrical 2'-O-alkyl modifications and the antisense sequence has one or more asymmetrical phosphorothioate modifications, and the antisense sequence targets a human gene sequence, wherein said asymmetrical 2'-O-alkyl modifications occur within 6 positions from the 3' end and within 6 positions from the 5' end, wherein one or more asymmetrical modifications are found on the one strand but not on the other strand.

In this claim the agent is characterized by a combination of structural and functional features.

Often iRNA is characterized by a target to which it binds. The following examples characterize the iRNA by its binding capability to a target.

EP-B1 – 1601767 – Claim 2:

An siRNA targeted against human apoptosis-specific eIF-5A1 for use in a method of treating glaucoma, wherein said siRNA targets the sequence aag ctg gac tcc tcc tac aca at.

EP-B1 – 1555317 – Claim 1:

A synthetic gene which is capable of repressing, delaying or otherwise reducing the expression of a target gene in an animal cell, wherein said synthetic gene comprises a foreign nucleic acid molecule comprising multiple copies of a nucleotide sequence (a) of greater than 20 nucleotides which is substantially identical to a nucleotide sequence of said target gene, wherein the multiple copies are presented as an interrupted palindrome sequence, and the foreign nucleic acid is operable under the control of a single promoter sequence.

EP-B1 – 1797183 – Claim 1:

A let-7 miRNA that binds to and inhibits the expression of an mRNA encoded by an oncogene containing a let-7 complementary site (LCS) selected from the group consisting of NRAS, KRAS, and HRAS, for use in a method for treating or preventing cancer by inhibiting the expression of the oncogene in a cell of a patient, wherein the let-7 miRNA is selected from the group consisting of a pri-miRNA, a pre-miRNA, and a mature miRNA.

The following examples characterize the agent by structural features or the gene encoding the agent.

EP-B1 – 1841464 – Claim 1:

An iRNA agent comprising

- (i) a sense strand, wherein said sense strand consists of the sequence of SEQ ID NO: 1545, in table 5,
- (ii) an antisense strand, wherein said antisense strand consists of the sequence of SEQ ID NO: 1546, in table 5.

EP-B1 – 1567007 – Claim 1:

An isolated miR15 or miR16 gene product for use in treating a prostate cancer in a subject in need of such treatment, such that proliferation of prostate cancer cells is inhibited.

EP-B1 – 1687435 – Claim 4:

A method to obtain significant insect mortality or significant insect control by silencing of an essential gene of a plant sap-sucking insect by application of dsRNA or siRNA to the feed of said insect, as compared to control insects fed on dsRNA or siRNA targeting a non-essential gene or a gene not expressed in the plant sap-sucking insect.

EP-B1 – 2365077 – Claim 1:

An isolated iRNA agent, comprising a sense sequence and an antisense sequence, wherein the sense and the antisense sequences form an RNA duplex, and wherein the antisense sequence comprises a nucleotide sequence sufficiently complementary to a target sequence of about 19 to 23 nucleotides of a VEGF nucleotide sequence and wherein said target sequence differs by no more than 1, 2, or 3 nucleotides from the sequence of SEQ ID NO: 344.

EP-B1 – 2361981 – Claim 1:

Isolated double stranded RNA of from 21 to 23 nucleotides that mediates RNA interference of an mRNA to which it corresponds, provided that the double stranded RNA is not ucg age ugg acg gcg acg uaa, chemically linked at the 3' end to the 5' end of the complementary RNA by a C18 linker group.

EP-B1 – 2338993 – Claim 1:

A let-7 miRNA that binds to and inhibits the expression of an mRNA encoded by an oncogene containing a let-7 complementary site (LCS) and selected from the group consisting of MYC, MYCL1, and MYCN for use in a method for treating or preventing cancer by inhibiting the expression of the oncogene in a cell of a patient, wherein the let-7 miRNA is selected from the group consisting of a pri-miRNA, a pre-miRNA, and a mature miRNA.

EP-B1 – 2336318 – Claim 1:

An antisense oligonucleotide compound 20 nucleobases in length having a sequence of nucleobases as set forth in SEQ ID NO:247 and comprising 5-methylcytidine at nucleobases 2, 3, 5, 9, 12, 15, 17, 19, and 20, wherein every internucleoside linkage is a phosphorothioate linkage, nucleobases 1–5 and 16–20 comprise a 2'-ethoxyethoxy modification, and nucleobases 6–15 are deoxynucleotides.

EP-B1 – 2260101 – Claim 1:

A compound comprising a modified oligonucleotide consisting of 12 to 30 linked nucleosides, wherein the modified oligonucleotide has a nucleobase sequence complementary to miR-21 or a precursor thereof, for use in treating, preventing, or diagnosing fibrosis in a subject.

EP-B1 – 2235180 – Claim 1:

Use of an apoptosis inducing expression modulating compound targeting a SINE repetitive element present in an untranslated region of protein coding gene transcripts as a positive control in an expression modulating assay, wherein the expression modulating compound is an RNAi modulating compound that silences the expression of the targeted genes via RNAi.

EP-B1 – 2221376 – Claim 1:

An antisense oligonucleotide 8 to 50 nucleobases in length which specifically hybridizes with at least an 8-nucleobase portion of nucleobases 81–100 of SEQ ID NO:3, and which inhibits the expression of human superoxide dismutase 1, soluble.

EP-B1 – 2121922 – Claim 1:

PNA or siRNA molecules for the biologically inactive transfection into a target cell to inhibit the gene expression therein after biological activation by bonding to mRNA and, for example, in the case of siRNA under the formation of a RISC complex, wherein for their biological deactivation outside the target cell the PNA or siRNA molecules (1) have at least one covalent bond (8, 8') that can only be broken up by the one or more cell-specific enzymes (9, 10) of said target cell, and said covalent bond has at least one peptide (2, 3) that has always one or more amino acid sequences (11) that is/are selected for the one or more enzymes typical for the target cell and is/are significant for the breakable covalent bond (8, 8').

EP-B1 – 2031057 – Claim 1:

A sense oligonucleotide having activity of suppressing production of NO which promotes decomposition of iNOS mRNA, which has a sequence complementary to iNOS mRNA antisense RNA (antisense transcript of iNOS mRNA).

D.II.2.j. Process claims for nucleic acids

Nucleic acids may be prepared by different kinds of processes, e.g. by chemical synthesis, enzymatic synthesis such as PCR, isolation from a microorganism, or a combination of any of the above.

The following discussion is concerned almost exclusively with the preparation of DNA. Claims relating to RNA are subject to the same general considerations. No reference is made to modifying nucleic acids, since the modification

of nucleosides or nucleotides is primarily a chemical problem and of minor relevance in the present context.

D.II.2.j.a. Process claims involving genetic engineering or synthesis

Processes for preparing a DNA involving genetic engineering will in most cases be directed to the construction of a certain DNA, for example by use of restriction endonucleases. This applies, for example, to processes for constructing vectors. Vectors are in most cases obtained by inserting a certain DNA sequence into a known plasmid.

Claim drafting:

A general claim relating to the construction of a vector could have the following wording; the process steps are underlined in the examples shown below.

A process for preparing a vector, comprising inserting DNA fragment X into restriction site Y of plasmid Z.

An example of a granted claim is the following:

EP-B1 – 0239425 – Claim 59:

Process for the production of a hybridization probe for the detection of RNA of HIV-2 retrovirus characterised by the insertion of a DNA sequence, particularly according to anyone of claims 46 to 53, in a cloning vector, by in vitro recombination, cloning the modified vector obtained in a competent cellular host, and recovering the DNA-recombinants obtained.

An alternative process involving genetic engineering is the generation of a cDNA by reverse transcription of a certain mRNA preparation. Preparation of cDNA in most instances will be a process of analogy, differing from known processes with respect to selection of appropriate mRNA sources, induction conditions, etc. In many cases, DNA will be produced by amplification from a given template as in PCR-based processes.

Claim drafting:

A process claim for preparing a cDNA may have the following general wording:

A process for preparing a DNA encoding protein X comprising preparation of cDNA complementary to mRNA obtained from source Y.

Examples of granted claims relating to a process for preparing cDNA are the following:

EP-B1 – 0093619 – Claim 1:

A process which comprises preparing cDNA from mRNA extracted from the Bowes melanoma cell line and isolating from it a DNA sequence having the restriction pattern shown in Fig. 4 hereof for the putative mature tissue plasminogen activator sequence and which encodes a 527 amino acid polypeptide having human tissue plasminogen activator function.

This claim provides information about the source for obtaining mRNA and provides a means for identifying the desired DNA sequence, i.e. a restriction pattern.

cDNAs may be prepared not only from mRNAs, but also from RNA viruses, as can be seen from claim 1 of the following European patent:

EP-B1 – 0076847 – Claim 1:

A method for producing full-length, infectious poliovirus cDNA comprising the steps of:

- (a) reverse transcribing poliovirus viral RNA sequences to provide poliovirus ss cDNA sequences;
- (b) forming ds cDNA sequences from said poliovirus ss cDNA sequences;
- (c) inserting said ds cDNA sequences into a DNA vector to create a recombinant vector;
- (d) transforming cells with said recombinant vector in which said recombinant vector will multiply;
- (e) culturing said transformed cells;
- (f) identifying and isolating recombinant vectors containing less than full-length, non-infectious poliovirus ds cDNA sequences;
- (g) obtaining less than full-length, non-infectious poliovirus ds cDNA sequences from the recombinant vector of step (f);
- (h) joining the less than full-length cDNA sequences obtained under (g) to form a recombinant vector containing a full-length, infectious poliovirus ds cDNA.

The following claims are examples of methods of how to prepare a nucleic acid molecule by synthesis, such as PCR.

EP-B1 – 1505151 – Claim 1:

A method for increasing concentration of a nucleic acid molecule, said method comprising:

- (a) forming a heat-stable, water-in-oil emulsion comprising encapsulated aqueous microcompartments having a density of greater than 109 microcompartments per ml;
- (b) including within a plurality of said microcompartments a nucleic acid and an aqueous solution comprising components necessary to perform nucleic acid amplification by the polymerase chain reaction, said components including a thermostable polymerase; and
- (c) conducting thermal cycling to effect amplification of said nucleic acid to produce amplified copies of said nucleic acid, thereby increasing the concentration of said nucleic acid,

wherein the thermostable polymerase has increased thermostability when compared with the corresponding wild type enzyme, increased resistance to heparin when compared with the corresponding wild type enzyme, or is capable of extending a primer having a 3' mismatch.

EP-B1 – 1544296 – Claim 1:

A method for producing a library of mutant genes comprising the following steps:

- a. Synthesizing on a DNA chip an oligonucleotide library comprising oligonucleotides complementary to one or more regions of one or more target genes and each comprising, preferably in their center, one or more mutations of the sequence of the target gene(s);

- b. Placing in solution as a mixture the oligonucleotide library synthesized on the DNA chip in a); and,
- c. Generating a library of mutant genes by using the oligonucleotide library in solution obtained in b) and one or more templates containing said target gene(s).

EP-B1 – 0988378 – Claim 1 underlying decision T 1188/06 (A method for in vitro molecular evolution of protein function/BIO-INVENT INTERNATIONAL AB):

A method of creating a polynucleotide library comprising the steps of obtaining a parent polynucleotide encoding one or more variant protein motifs;

- a) providing a plurality of pairs of oligonucleotides, each pair representing spaced apart locations on the parent polynucleotide sequence bounding an intervening variant protein motif, and using each said pair of oligonucleotides as amplification primers for PCR to amplify the intervening motif;
- b) obtaining single-stranded nucleotide sequences from the thus-isolated amplified nucleotide sequences;
- c) assembling polynucleotide sequences by incorporating nucleotide sequences derived from step b) above with nucleotide sequences encoding scaffold sequence; and
- d) inserting said polynucleotide sequences into suitable vectors.

EP-B1 – 1826215 – Claim 1:

A method for replacing a gene by targeting a DNA, termed an insert DNA, constituted by a portion of a gene which is capable of being rendered functional or more effective when it is recombined with a complementing DNA to thereby provide a complete recombinant gene in the genome of a eukaryotic cell, said method comprising:

- introducing, into eukaryotic cells that are neither human germ cells nor human embryo cells, a vector containing an insert itself comprising the insert DNA and two sequences termed “flanking” sequences on either side of the insert DNA, respectively homologous to two genomic sequences that are adjacent to the desired insertion site in a selected gene termed a recipient gene and containing the complementing DNA;
- the insert DNA comprising a portion of a gene and being heterologous with respect to the recipient gene;
- the flanking sequences being selected in order to allow, by homologous recombination, expression of insert DNA under the control of regulatory sequences of the endogenous gene where the insertion is made;
- said recombinant gene not coding for an expression product that can allow selection of transformants.

D.II.2.j.b. Process claims involving isolation from a nucleic acid source

The isolation of nucleic acids from a microorganism will in most cases be a process of analogy.

Claim drafting:

A process requiring the isolation of a nucleic acid from a microorganism may have the following general wording:

A process for preparing a nucleic acid comprising the steps of isolating DNA from source X ...

Examples of granted claims are shown below. The source materials for providing the nucleic acid in question are underlined.

EP-B1 – 0112149 – Claim 8:

A process for the production of a DNA fragment as set out in any one of claims 1 to 7, characterized in that it comprises screening a human cDNA clone bank using as a probe a fragment of human H1-relaxin DNA.

Claim 1 referred to in the above claim 8 is directed to a DNA fragment encoding human H2-preprorelaxin, the H2-preprorelaxin having the amino acid sequence set out in Figure 2 of the patent.

EP-B1 – 0923598 – Claim 1:

A process for producing a normalized genomic DNA library from an environmental sample containing a mixed population of organisms, which comprises the steps of:

- (a) isolating a genomic DNA population from the mixed population of organisms in the environmental sample;
- (b) fractionating the isolated genomic DNA population prior to normalizing, thereby increasing the chances of cloning DNA from minor species from the pool of organisms sampled, wherein the fractionating comprises a density centrifugation technique, wherein equal amounts of A260 units are removed from each peak and the nucleic acid is amplified;
- (c) preparing a normalized library of genomic DNA from the environmental sample.

D.II.2.k. Use claims/purpose-limited product claims for nucleic acids

As noted above in C.I.3.e.a, use claims are interpreted as process claims.

Use claims may for example be directed to the use of a nucleic acid for the preparation of probes or proteins, the construction of vectors or the preparation of a medicament, the latter type most recently having been replaced by purpose-limited product claims.

Claim drafting:

An example of possible general wording for a use claim is provided below:

Use of DNA X for purpose Y.

DNA X for use in a method of treating disease Y.

The following use claims have been granted by the EPO; the purposes are underlined.

EP-B1 – 0076847 – Claim 12:

Use of a full-length, infectious poliovirus cDNA according to Claim 6 for the manufacture of a vaccine.

Claim 6 referred to in this claim is provided in D.II.2.i.f.

EP-B1 – 0162067 – Claim 1 (AT):

Use of a DNA sequence coding for human factor VIII:C, comprising a polydeoxyribonucleotide having the sequence

5'GAC ATT TAT GAT GAG GAT GAA
ATT CAG AGC CCC CGC AGC TTT
CAG AAG AAA ACA CGA CAC TAT
TTT ATT GCT GCA GTG GAG AGG 3'

for producing an isolated recombinant vector containing this DNA sequence.

EP-B1 – 0162067 – Claim 6 (AT):

Use of a DNA sequence consisting essentially of a deoxyribonucleotide having the following sequence or its inverse complement

5' TTT CAG AAG AGA ACC CGA CAC TAT TTC
ATT GCT GCG GTG GAG CAG CTC TGG GAT
TAC GGG ATG AGC GAA TCC CCC CGG GCG
CTA AGA AAC AGG 3'

as a screening agent for identifying deoxyribonucleotide sequences and ribonucleotide sequences which encode for at least a portion of the human gene factor VIII:C.

EP-B1 – 2034017 – Claim 1:

A use of a polynucleotide as determinant of an immortalized cancer cell in cancer cells obtained from a test subject the polynucleotide comprising a polynucleotide having a base sequence of at least 15 bases that specifically hybridizes with a continuous base sequence of at least 15 bases within the base sequence represented by SEQ ID No. 1.

EP-B1 – 1851312 – Claim 13:

Use of a nucleic acid molecule according to claim 5, a vector according to claim 6 or a cell according to any one of claims 7 or 8 for the expression of a protein, peptide or functional nucleic acid.

EP-B1 – 1588718 – Claim 1:

Use of a vector that comprises a nucleic acid sequence encoding hepatocyte growth factor for the preparation of a medicament for enhancing tissue survival, wherein said vector is to be administered to a subject in need thereof; wherein said tissue is a flap, selected from the group consisting of a skin flap, a muscle flap, a myocutaneous flap and a cartilocutaneous flap.

EP-B1 – 2393504 – Claim 1:

The use of an L-ribozyme for producing a pharmaceutical composition.

EP-B1 – 2459721 – Claim 1:

Use of an eukaryotic expression vector comprising a nucleotide sequence encoding for the human long pentraxin PTX3 protein under the control of an effective promoter and a nucleotide sequence encoding for a selectable marker, having essentially the sequence of SEQ ID 1 for transforming a recombinant human host cell already able to express the human long pentraxin PTX3 protein, wherein said recombinant human host cell is the recombinant 293F/PTX3/2F12 clone deposited at ECACC with no. 08011001.

D.III. Proteins

D.III.1. Introduction

This chapter discusses possible ways for protecting proteins under the EPC.

The term “protein” as used herein means any polymer comprising a chain of amino acids and thus includes molecules usually referred to as polypeptides. Proteins are normally assembled from naturally occurring amino acids. Proteins may also contain amino acids modified by glycosylation, acetylation, pyruvylation or in any other way. Further, proteins may be isolated from natural sources, recombinantly produced or chemically synthesized. Although there are well-established methods for chemically synthesizing proteins, in most cases they are isolated from living material, e.g. plants, animal organs, blood, microorganisms including cell cultures, etc. Before recombinant DNA technology was available, naturally occurring proteins were mainly isolated from appropriate sources, but modern biotechnology allows unicellular or multicellular systems or even animals or plants to produce the desired protein. Today many proteins are produced by such biological “factories”.

Proteins have a wide variety of applications in life sciences: enzymes are useful for preparing products of commercial interest, peptide hormones are of commercial value as pharmaceuticals, antigenic peptides of pathogens are used for detecting antibodies associated with certain diseases or as immunizing agents, and antibodies find utility as therapeutics, diagnostics or as immune affinity reagents. This list is by no means exhaustive. Due to their importance in the pharmaceutical field throughout the years, antibodies will be dealt with in a separate chapter (see D.IV).

With increasing scientific knowledge more and more human proteins are becoming applicable for therapeutic purposes, for example, interferons, interleukins, receptor proteins, etc. The same applies to viral, protozoan or bacterial antigens, which may be used for diagnostics, but also may be suitable as vaccines. The economic importance of proteins thus cannot be overestimated.

D.III.2. Protecting proteins under the EPC

As for any other subject matter in the field of life sciences, claims relating to proteins must fulfill the legal requirements of the EPC. In particular, they must not fall within the exclusion provisions laid down in Arts. 52 and 53 EPC. In addition, the claimed subject-matter must meet the further patentability requirements of novelty, inventive step and industrial applicability. Furthermore, the application must fulfill the requirements of sufficiency of disclosure and clarity and support of the claims, as discussed in C.I.3.b, C.I.3.e.b and C.I.3.e.c.

Several decisions of the EPO relating to the above patentability requirements and the requirements of the application will be briefly discussed in connection

with proteins. The cited decisions are particularly informative and important, and should be taken into account when drafting applications directed to proteins.

D.III.2.a. Discoveries

According to Art. 52(2) EPC, discoveries are not regarded as inventions, but are excluded from patent protection. In its decision “**RELAXIN**”, an Opposition Division dealt with the question whether the finding of a DNA coding for human relaxin or one of its biological precursors is a discovery within the meaning of Art. 52(2) EPC. In the reasons for the decision, the Opposition Division referred to the Guidelines (C-IV,2.3 as available at the time, now G-II,5.2), stipulating:

[T]o find a substance freely occurring in nature is mere discovery and therefore unpatentable. However, if a substance found in nature has first to be isolated from its surroundings and a process for obtaining it is developed, that process is patentable. Moreover, if this substance can be properly characterised by its structure and it is new in the absolute sense of having no previously recognised existence, then the substance per se may be patentable. (point 5.1)

The Opposition Division concluded:

The above guideline is highly appropriate in the present case. Human H2-relaxin had no previously recognised existence. The proprietor has developed a process for obtaining H2-relaxin and the DNA encoding it, has characterized these products by their chemical structure and has found a use for the protein. The products are therefore patentable under Article 52(2) EPC. (point 5.2)

In conclusion, the subject-matter of the disputed patent does not represent a discovery and is hence not excluded from patentability under Article 52(2) EPC. (point 5.5)

The above finding was also confirmed by an Appeal Board dealing with the Relaxin case. In **T 272/95 (Relaxin/HOWARD FLOREY INSTITUTE)** the Board held that the claims do not fall under Art. 52(2) EPC by referring to the then valid Rule 23(e) (2), now Rule 29(2) EPC (see point 7 of the Reasons for the decision).

Although the decision “**RELAXIN**” is primarily concerned with DNA-related claims, it may be assumed that proteins obtained from natural sources are also considered to be naturally occurring products and, thus, are to be treated in the same manner as naturally occurring DNA.

In **T 338/00 (Multimeric Receptors/SALK INSTITUTE)**, an Appeal Board also confirmed the above finding in the **RELAXIN** case for a protein invention where a heterodimeric receptor was found to be more than a mere discovery. In particular, the Board was of the opinion that the claimed receptor could be exploited in industry and therefore was more than a mere description of an interesting research result.

For further discussion relating to naturally occurring products, see C.I.3.a.a.

D.III.2.b. Morality and “ordre public”

According to Art. 53(a) EPC, inventions the commercial exploitation of which would be contrary to “ordre public” or morality, are excluded from patent protection. To our knowledge, there is no decision discussing the allowability of a protein under Art. 53(a) EPC. However, the same criterion applies for proteins as for any other subject-matter; as stated in the Guidelines (G-II,4.1):

A fair test to apply is to consider whether it is probable that the public in general would regard the invention as so abhorrent that the grant of patent rights would be inconceivable. If it is clear that this is the case, an objection should be raised under Art. 53(a); otherwise not.

D.III.2.c. Methods of treatment

According to Art. 53(c) EPC, methods for the treatment of the human or animal body by surgery or therapy and diagnostic methods practised on the human or animal body are exceptions to patentability.

The case underlying **T 820/92 (Contraceptive method/THE GENERAL HOSPITAL)** claimed a method for preventing pregnancy in female mammals, comprising the administration of LHRH and steroid hormones. The LHRH component was the main contraceptive ingredient, and the steroids served to correct any biological functions adversely effected by the LHRH. The Appellant argued that the method as a whole is a contraceptive method which is not excluded by Art. 52(4) EPC 1973 (now Art. 53(c) EPC). The Board, however, held:

This argument is based on a misconception of the nature of the prohibition of Article 52(4) EPC. By providing that methods for treatment of the human or animal body by surgery or therapy and diagnostic methods practised on the human or animal body shall not be regarded as inventions which are susceptible of industrial application, the first sentence of Article 52(4) EPC creates an exclusion from patentability that has been consistently interpreted by the EPO Boards of appeal as meaning that such a method cannot be the subject-matter or part of the subject-matter covered by a claim. (point 5.3)

The claimed method was thus not allowable due to the therapeutic/prophylactic aspect of simultaneously administering steroids. The application of proteins outside of the human body, e.g. for performing diagnosis on a tissue sample, is generally not in conflict with Art. 53(c) EPC (Art. 52(4) EPC 1973).

D.III.2.d. Novelty

In **T 269/87 (Prochymosin/CELLTECH)**, an Appeal Board considered whether the disclosure of a DNA coding for the protein prochymosin (another name for prorennin) including the information on the sequence of the active (mature) protein chymosin, would anticipate the disclosure of a process for preparing chymosin involving cleavage of prochymosin, yielding the active, mature protein. The Board held:

The cleavage of the prochymosin protein, however, to chymosin is neither directly expressed nor unequivocally implied in the disclosure of document (1). The chapter on the ex-

pression of “methionine-prorennin” is silent on any further steps [...]. Any implied cleavage, in terms of “activation”, relates to other proteins [...]. The reference to the nucleotides responsible for the formation of the inactive “zymogen” part of rennin (chymosin) [...] which “is removed” to generate active rennins, is no disclosure of the specific cleavage step claimed in the present case, but relates to the DNA level. Document (1) is, therefore, ineffectual in destroying the novelty of claims A1 or A2 under Article 54(3) EPC, irrespective of its own priority rights. (point 15)

Therefore, in this particular case, a disclosure allowing one to deduce the structure of the mature protein, without explicitly providing it, was not considered to be novelty-destroying for the process of preparing the mature protein as such.

In **T 877/90 (T-cell growth factor/HOOPER)**, a Board of Appeal examined the novelty of a T-cell growth factor which was characterized as being serum-free and mitogen-free. The Board found that the closest prior art document discloses a T-cell growth factor which was not mitogen- and serum-free and consequently acknowledged the novelty of the claimed subject-matter.

This appears to be the first decision in the field of biotechnology in which novelty of a substance is established by a higher degree of purity compared to a known product. In order to put the results of **T 877/90** in the correct perspective, one should compare the conclusion from **T 877/90** with that of earlier decision **T 205/83 (Vinyl ester/crotonic acid copolymers/HOECHST)**. In **T 205/83**, it was held that a known product does not necessarily acquire novelty merely by virtue of the fact that it is produced in pure form (point 3.2 of the decision). Although in the decision the possibility of establishing novelty by higher purity was not definitely excluded, it was the previous practice of the EPO not to accept novelty of a protein differing from the prior art only by improved purity. As a consequence of **T 877/90**, this practice may be changing. Indeed, this practice was confirmed by **T 90/03 (Phytase/BASF)**. For the field of small molecules, the situation may be different as e.g. decided in **T 990/96 (Erythro-compounds/NOVARTIS)** where the Board did not accept the degree of purity as a feature for establishing novelty.

In **T 158/91 (Human growth hormone/GENENTECH)**, an Appeal Board confirmed established case law according to which a prepublished teaching can only defeat novelty if it enables a person skilled in the art to reproduce its teaching. The Board held:

Certainly, the question of sufficient disclosure, be it of a prior art document or a patent application in question, has to be examined in each case on its own merits. An examination as to the sufficiency of a disclosure depends on the correlation of the facts of the case to certain general parameters.

These parameters are for example:

- (a) the character of the technical field and the average amount of effort necessary to put into practice a certain written disclosure in that technical field;
- (b) the time when the disclosure was presented to the public and the corresponding common general knowledge;
- (c) the amount of reliable technical details disclosed in a document. (point 2.3)

In **T 886/91 (Hepatitis B virus/BIOGEN INC.)**, one of the Opponents submitted that small differences in the claimed sequence compared to a known sequence are not sufficient to confer novelty to the claimed sequence. The Board did not accept this argument, since

it is well known that even a change in one amino acid can dramatically change the properties of a protein molecule. (point 8.1.2)

Further, one of the Opponents argued that there were common identical stretches in the claimed sequences and the known sequences and thus the claimed sequences should lack novelty. The Board held that this is

merely theoretical because none of the cited documents discloses or suggests any discrete fragments of the reported sequences as an identifiable entity which could be used for a comparison. (point 8.1.2)

In **T 223/92 (HIF-Gamma/GENENTECH)** two aspects are noteworthy. Claim 1 of the patent in question reads as follows:

Human immune interferon of the amino acid sequence depicted in Figure 5 hereof and alleles thereof, free from other protein with which it is ordinarily associated.

According to Figure 5, the amino acid sequence comprises about 146 amino acids, allowing calculation of the molecular weight as 17400 D.

After the priority date it was discovered that IFN- γ often occurs as a dimer or trimer. An Opponent argued that one of the prior art documents, document (21), may have described a glycosylated dimer. The Board stated:

This may or may not be the case, but it was not possible for the skilled man at the time of priority to recognise this. What was available to the public within the meaning of Article 54(2) EPC by document (21) was the information that in a culture fluid of induced lymphocytes after certain purification steps a protein is contained that has properties differing from those of the well characterised interferon-alpha and interferon-beta and has a molecular weight of 58000. (point 4.3)

Moreover, the Board considered document (21) not to be novelty destroying for the following reason:

[A]t the priority date neither the monomer, nor any oligomer was available as such, but merely infinitesimal amounts of something that included a compound showing activity typical of interferon gamma. (point 4.4)

Therefore, if only the activity of a certain protein is known from the prior art that does not describe a reproducible way of obtaining more than “infinitesimal amounts” of the protein having the activity, this disclosure might not be sufficient to defeat novelty.

In **T 412/93 (Erythropoietin/KIRIN-AMGEN)** an Appeal Board confirmed the following established principle:

[T]he fact that a product is referred to in a claim as being the result of some process, does not automatically mean that the product is novel even if it is beyond dispute that the process referred to is new. The purpose of the reference to the process was to exclude those products

which in the prior art were not obtained by the process. If, on the evidence available, the process appears capable of producing every product meeting the characteristics of the product of the prior art, the reference to the process is not a limitation for the purpose of considering novelty. The process feature in a product claim can only be relied on for establishing novelty over the prior art, where use of that process necessarily means that the product has a particular characteristic and the skilled person following the teaching of the specification would inevitably achieve that characteristic, would be aware of that characteristic and would discard any products not having it. (point 33)

In this case, the Patentee had attempted to distinguish recombinant erythropoietin over known urinary erythropoietin. The Board held that recombinant erythropoietin may not necessarily be different from urinary erythropoietin.

The Board finally accepted a claim reciting the erythropoietin to be the product of eukaryotic expression of an exogenous DNA sequence and having a higher molecular weight by SDS-PAGE than erythropoietin isolated from urinary sources.

In **T 656/94 (Colony-stimulating factor/KIRIN-AMGEN)** the Opponent-Appellant argued for a lack of novelty of the patent underlying the decision claiming *inter alia* in claim 1 of the main request:

An isolated polypeptide consisting only of part or all of the amino acid sequence 1–174 set forth in Table VII which: [...]:

In the Board's view it was clearly shown that the prior art documents disclosed a mixture of polypeptides having 174 and 177 amino acids in a molar ratio of 80:20, wherein the 177 amino acid polypeptide is a splice product with 3 additional amino acids inserted. The present invention, however, according to the Board, was directed to a single species, which was made clear by the features "isolated" and "only" in claim 1. Therefore, the Board held that the mixture disclosed in the prior art was not novelty-destroying for the present invention.

The above case is one of the rare examples where the term "isolated" actually helped the Applicant to overcome the prior art. As a rule of thumb, the term "isolated" should be avoided, as in most cases it does not help to overcome prior art.

In **T 367/95 (Antihemophilic factor/PHARMACIA)**, the underlying patent was revoked by the Opposition Division for lack of novelty. Claim 1 was directed to a fragment of Factor VIII:C further characterized by molecular weight, partial amino acid sequences and amino acid composition. In considering the prior art the Board pointed out that merely conjectural statements, such as "may be required", "seem to be", or "presumably" were not sufficient to clearly and unmistakably disclose the claimed features and thereby anticipate the claimed subject-matter. Furthermore, the Board stated that amino acid composition data was suitable to establish novelty and that any argument to the contrary based on experimental error needed to be substantiated.

In case **T 429/96 (Serine protease inhibitors/AMGEN)**, the Board had to decide on the novelty of a claim directed to a purified serine protease inhibitor consisting of a single unfragmented polypeptide chain, the inhibitor being

characterized by an amino acid sequence. The relevant prior art disclosed a composition containing the claimed inhibitor in degraded form as a mixture of fragments. The Board found the claim directed to the undegraded polypeptide chain to be novel over the mixture of degraded protein fragments.

In **T 1147/98 (Cartilage-inducing factor/CELTRIX PHARMACEUTICALS INC.)**, the appeal lay from the Opposition Division's decision to revoke the patent. On appeal, the Patentee filed new claims directed to a "homogenous" protein. Since the cited prior art documents disclosed a mixture of different relevant biochemical activities, the Board held that a "homogenous" protein was not disclosed by a mixture, and hence the claims filed on appeal were novel. (See similar finding in **T 656/94** above).

In **T 522/99 (Soybean desaturase/DU PONT)**, the Board had to decide on the novelty of a claim with product-by-process character. Claim 6 of the main request was directed to a

[r]ecombinant non-fused VP1 protein, [...], formed in *Spodoptera frugiperda* cells according to claim 3.

The Board held this claim as anticipated over a document disclosing the expression of the VP1 protein in Chinese hamster ovarian cells, thereby confirming established case law, which requires that a product defined by its production process must fulfill the patentability requirements by itself. The production process can only be considered as a limiting feature in as far as it confers particular characteristics on the product not found in the prior art.

In **T 881/01 (Alpha-amylase reagent/MODROVICH I.E.)**, the Opposition Division used technical features only disclosed in the specification to delimit the claimed subject-matter from the prior art. The Board criticized this claim interpretation and stated:

While it is true that Article 69(1) EPC second sentence states that the description and drawings shall be used to interpret the claims, this does not make it legitimate to read into the claim features appearing only in the description and then relying on such features to provide a distinction over prior art. This would not be to interpret claims but to rewrite them. The preparatory material available on the discussions leading up to the European Patent Convention, shows that the effect of Article 69 EPC and its Protocol on Interpretation was always only considered in relation to extending the extent of protection conferred beyond the strict literal meaning of the terms of the claims, and never for excluding what on the clear meaning was covered by the terms of the claims. (point 2.1)

In **T 1080/01 (Thermostable enzyme/F. HOFFMANN-LA ROCHE)**, it was argued that multiple prior art documents implicitly disclosed the claimed polymerase by means of disclosing a process that, when strictly followed, would result in the claimed protein. In this regard the Board held:

A faithful reproduction of an experiment reported in any of documents (3), (9) and (10) can only be one which reproduces as accurately as possible the very same experimental conditions the authors were using, starting from the very same material. The only deviations which may be acceptable should be those resulting from the replacement of a material which no longer exists, provided that those deviations can be proven not to have any influence at all

on the outcome of the reproduced experiment. Deviations made only for experimental convenience are not acceptable. (point 54)

Since none of the submitted documents fulfilled the criterion of accurate reproduction of the disclosed processes according to the patent, the Board did not see it proven beyond reasonable doubt that the disclosed processes in the prior art would inevitably result in the claimed product, i.e. the polymerase.

In **T 1120/01 (Cell surface antigen/OSAKA BIOSCIENCE)**, the Examining Division refused the underlying patent application *inter alia* for lack of novelty of a product claim directed to a protein. On appeal, however, the Appeal Board found that none of the cited prior art documents provided an enabling disclosure of the claimed protein, since they either failed to disclose all information necessary for the disclosed purification of the protein, or they did not disclose any purification at all. Therefore, the cited documents were not considered to anticipate the claimed protein.

In **T 90/03 (Phytase/BASF)**, the Board discussed the role of a protein preparation's purity for establishing novelty. The Board emphasized that in this regard low molecular weight compounds and high molecular weight proteins cannot be treated equally. While methods of purification of small organic molecules are common general knowledge of the skilled person, the purification of proteins is far from being standardized. In considering previous case law, the Board concluded that even though the present claims also differed from the prior art by additional technical features, the degree of purity alone would be sufficient to establish novelty (see also **T877/90** discussed above).

In **T 1303/04 (Myelin basic protein/UNIVERSITY OF ALBERTA)**, the Board emphasized once more:

[I]t is not justifiable to decide whether a document is prejudicial to novelty on the **basis of probability or plausibility**. In order to decide that the subject-matter of a claim lacks novelty, the department concerned, having taken all facts and arguments put forward during the proceedings into consideration, has to be **sure** that the decision is justified. (point 6)

In **T 1010/05 (Protein hydrolysate/VALIO)**, a method step of the process used to define a product (product-by-process) was considered to differentiate the claimed product ("hydrolysate") from the prior art ("yoghurt"). In particular, the process step of hydrolysis by pepsin and/or trypsin was considered to confer structural characteristics on the claimed "hydrolysate". These characteristics were not proven to be disclosed in the prior art, since it was not shown that these proteases or other proteases with the same cleavage characteristics were present in the prior art "yoghurt".

In **T 1414/05 (MHC complexes/SUNOL)**, the implicit structural characteristics of a functional feature helped to establish novelty over the prior art. The claimed MHC complex in question was limited by the feature "capable of modulating the activity of a T-cell receptor to induce T-cell proliferation". In contrast, the prior art disclosed MHC complexes, which suppressed T-cell proliferation. The question was whether in the absence of any other differentiating

features, the MHC complexes of the prior art would also be suitable to induce T-cell proliferation. To address this question, the Appellant submitted that for fulfilling the claimed function the peptide presented by the MHC molecule must be properly positioned, therefore giving the functional feature a structural implication. Based on this argument, the Board held that the suppressing MHC complex of the prior art would not be able to induce T-cell proliferation as required by the invention and that, therefore, the MHC complexes of the prior art were different from the claimed molecules.

In **T 847/07 (Factor VIII formulation/BIOVITRUM)**, a pharmaceutical formulation was claimed as “suitable for subcutaneous, intramuscular or intradermal administration”. Regarding the limiting effect of this claim element, the Appeal Board held:

Claim 1 has to be construed as relating to formulations that may be used for any form of administration as long as they are also suitable for subcutaneous, intramuscular or intradermal administration.

In the Board’s view the term “suitable for subcutaneous, intramuscular or intradermal administration” does however limit the meaning of the claim in so far as it excludes preparations which are not suitable for these forms of administration, such as preparations containing potentially toxic constituents or inactive factor VIII. (point 8)

Since the Respondent, however, acknowledged that the formulations of the prior art would be suitable for the above mentioned forms of administrations (even though not explicitly disclosed), and in the absence of any other limiting technical features, the Board denied novelty for the claimed subject-matter.

In **T 1898/07 (Interferon Formulations/BIOGEN)**, the Board emphasized once again (see also **T 1010/05** above) that a product-by-process claim is only patentable if the product itself fulfills the patentability requirements. The claim in this case was directed to a liquid composition. In addition to process features, the claimed liquid composition was further defined, *inter alia*, by the features: i) is contained in a syringe and ii) wherein the syringe is contained in a package. The Board held that these features do not constitute technical features describing the claimed liquid composition but merely describe the package, which contains the liquid composition. Therefore, the Board did not consider these features for the assessment of novelty.

D.III.2.e. Inventive step

T 181/88 (Assaying reagent/UNITIKA LTD.) concerns an Applicant’s appeal against the decision of an Examining Division to refuse an application having the following main claim:

A cholinesterase-assaying reagent comprising:
acetylcholine;
a thermostable acetate kinase; and
adenosine triphosphate.

The Examining Division denied an inventive step of the claimed reagent, on the basis that reagents differing from claim 1 only in the use of a non-thermostable enzyme were already described in a first document, and a second document disclosed a thermostable acetate kinase, which from a third document was known to have “high residual activity”.

The Appeal Board reversed the decision of the first instance, since there was no indication in the prior art that the assaying reagent could be improved by including a thermostable enzyme. Moreover, there was no incentive to use a thermostable enzyme, since no single step of the complex reaction was conducted under heat stress, but instead at 37°C or room temperature. Thus, the Board did not agree that replacing the conventional acetate kinase by a thermostable enzyme was obvious.

T 249/88 (Milk production/MONSANTO) concerned an appeal against the refusal of an application by an Examining Division. The claim in dispute was directed to a method for increasing the milk production of a cow by administering recombinant bovine growth hormone (bGH) including an N-terminal methionine, which is not present in natural pituitary derived bGH. The relevant prior art taught methods for increasing the milk production of a cow by administering natural (pituitary derived) growth hormone and suggested the administration of recombinant bGH, which was known from a further document. In addition, it was known that an N-terminal methionine did not affect the biological activity of human growth hormone. The Board confirmed the refusal of the application by the first instance, holding that the skilled person, in view of the cited prior art, would have considered the claimed method as an improvement of the teaching of the closest prior art documents. The Board thus concluded:

[A] person skilled in the art *would* indeed have administered the available form of recombinant bGH, i.e. the N-Met-bGH obtained according to GB-A- 1 565 190, without any modification to a cow in the reasonable expectation of obtaining the same or even a greater increase in milk production as observed when natural (pituitary derived) bGH is administered. (point 7.6)

In response to the Proprietor’s argument that a person skilled in the art would not have been able to *predict* that N-Met-bGH would increase the milk production of a cow on the basis of the cited prior art, the Board held:

The necessity of experimentally confirming a reasonably expected result does not render an invention unobvious. Absolute predictability, especially in the field of biologically active chemical compounds, is rather exceptional, but inventions relating to such compounds and their administration to living organism may nevertheless be obvious. However, if such administration were to lead to unexpected results, which is not the case here, this may provide a basis for demonstrating unobviousness. (point 8)

In **T 60/89 (Fusion proteins/HARVARD)**, an Appeal Board established that the same level of skill had to be applied when considering, for the same invention, the two questions of sufficient disclosure and inventive step (point 3.2.5 of the decision). The Board further noted:

The key question therefore is whether it was obvious for a skilled person to try the idea outlined above with a reasonable expectation of success. (point 3.2.5)

In the case underlying the decision the Board had to rule on the inventive step of a process composed of several steps, each step being known as such. The Board held:

To use known tools in a suitable combination to carry out a new method does not necessarily render this method obvious. (point 3.2.6)

T 717/89 (Hepatitis B virus E antigens/BIOGEN) was concerned with the inventive step of a process for preparing HBeAg from recombinantly produced HBcAg. The closest prior art document disclosed a process for obtaining two different forms of HBeAg from purified natural HBcAg. In the absence of any evidence that a skilled person would not have replaced a starting material having known disadvantages by an available known starting material lacking those disadvantages, the Board did not acknowledge an inventive step.

It is noteworthy that the following feature, added by the Patentee in appeal proceedings,

wherein the polypeptide displaying the antigenicity of hepatitis B virus e antigens is essentially free of primate serum polypeptides and primate liver polypeptides,

was insufficient to establish an inventive step, since

this feature is to be considered as obvious for the reason that it is nothing else than the unavoidable effect resulting from another requirement expressed in the claims, namely that HBeAg is prepared by recombinant DNA techniques which the man skilled in the art would have tried to apply in order to obtain products free of contaminating primate serum and liver polypeptides. (point 5.2)

T 877/90 (T-cell growth factor/HOOPER) concerned a patent with the following claim 1:

A T-cell growth factor derived from the peripheral mononuclear blood cells of a donor and characterized by being serum-free and mitogen-free and that the donor is human, bovine or porcine.

As discussed in D.III.2.d., the novelty of this T-cell growth factor was acknowledged over prior art which disclosed a T-cell growth factor which was not mitogen- and serum-free. The technical problem solved by the subject-matter of claim 1 was considered to be the improvement of the purity and concentration of a T-cell growth factor product. In view of known disadvantages of the known T-cell growth factor product, it was considered to be an obvious *desideratum* (point 3.1.3 of the decision) to provide a mitogen- and serum-free T-cell growth factor product as such. The Board held:

Being equipped with the information that neither mitogen nor serum are desired in a pharmaceutically acceptable end product it would have been the next obvious and evident step for the skilled person within the meaning of an obvious desideratum to further develop the substance whose activity was determined in document (17) to make the product completely mitogen- and serum-free. (point 3.1.5)

Claim 1 was thus rejected.

T 223/92 (HIF-Gamma/GENENTECH) concerns an appeal against a decision of an Opposition Division maintaining a European patent including the following claim:

Human immune interferon of the amino acid sequence depicted in Figure 5 hereof and alleles thereof, free from other protein with which it is ordinarily associated.

As discussed in D.III.2.d., the Board acknowledged the novelty of the claimed (recombinantly produced) protein over documents disclosing purification of a protein which was estimated to have a molecular weight of 58,000. In view of this document, the object of the opposed patent was considered to be the provision of authentic interferon- γ . The Appeal Board considered the first question to be whether a skilled person would have contemplated an improvement of the prior art method in order to obtain a pure protein. Since there were documents published later than the European filing date describing attempts to purify the protein rather than to express it by recombinant means, the Board concluded the “classical” method of isolating the protein was still favored by a skilled person on the priority date. However, IFN- α and IFN- β had already been produced by means of recombinant DNA. The Board thus considered whether applying the same route to IFN- γ was obvious to try with a reasonable expectation of success.

The Board observed that a person skilled in the art was confronted with “uncertainties”, since the length of the mRNA extracted from stimulated cells producing IFN- γ corresponds to 14,000 nucleotides, whereas in view of the assumed molecular weight of 58,000 a much larger mRNA was to be expected. Further, considering that the +/– method used for screening of cDNA libraries corresponding to induced and uninduced mRNA populations, the Board assumed the skilled person knew this method involves possible traps and difficulties, which are to be expected in such an extremely lengthy and complex method. The Board concluded:

If one now imagines the position of a skilled person who wants to produce and identify interferon-gamma, he would be confronted with the situation that (i) little was known about the protein as such and actually contradictory data had been published making the situation particularly confusing (see above point 5), (ii) despite the fact that an improved stimulation method was known, the quantity and quality of the mRNA available from this was extremely poor making the prospects of success for the recombinant-DNA-technique route look very poor if nothing better than this known method could be found and (iii) the decisive screening method was not to be considered as a reliable way to find what could only be described as “a needle in a haystack”.

The Board is convinced that there is no sufficient certainty that the skilled person in this situation would have tried this method with any reasonable expectation of success. In other words, while someone might have chosen the route of the recombinant-DNA-technique, he would only have attempted it despite success being very uncertain, for example because he trusted in his own luck, skill and inventive ingenuity to overcome the known and the as yet unknown problems involved, even though these problems were such that the average skilled person would expect to fail. (points 5.11 and 5.12)

Consequently, the appeals were dismissed and the patent was maintained.

T 923/92 (Human t-PA/GENENTECH) concerned the appeals of several opposing parties against the decision of an Opposition Division to maintain the patent in amended form. In the appeal proceedings, the Patentee filed auxiliary requests, with claims 1 and 2 of auxiliary request 3 relating to a process comprising the preparation of a protein having t-PA function, which in particular is capable of catalyzing the conversion of plasminogen to plasmin, binds to fibrin and, on the basis of its immunological properties, is classified as a t-PA, by expression of defined transforming DNA encoding the protein in a recombinant host organism. The closest prior art was considered to be a document disclosing the isolation of mRNA for t-PA, its fractionation and the isolation of a single fraction which was translated in oocytes into measurable protease activity. Immunoprecipitation studies suggested the protein was identical to human t-PA, but the identity of the translated proteins remained to be determined. The prior art document also provided an explicit suggestion to try the preparation of cDNA encoding human t-PA. The Board considered whether the skilled person would have attempted the preparation of cDNA encoding human t-PA with a reasonable expectation of success and confirmed that a reasonable expectation of success should not be confused with the understandable “hope to succeed”. The Board held:

However, the question here is whether the skilled person was in a position to reasonably predict, on the basis of the existing knowledge, before the starting of this research project, a successful conclusion to the project within acceptable time limits [...]. For answering this question, avoiding any hindsight, account should be taken also of the fact that, as stated in decision T 816/90 of 7 September 1993 (not published in OJ EPO), “even when it is possible to theoretically conceive a straightforward approach to solve a specific technical problem, the skilled person might be confronted with unexpected difficulties when trying to put the conceived strategy into practice.” [...] Similar considerations were taken into account in other decisions concerned with inventions in the genetic engineering field [cf., for example, T 223/92 of 20 July 1993, see point 5.15 of the Reasons and T 412/93 of 21 November 1994, see point 142 (iv) of the Reasons, both not published in the OJ EPO]. (point 51)

The Board accepted that the skilled person would have been in a position to conceive a protocol for cloning and expressing a DNA sequence encoding human t-PA. However, in the absence of any sequence information and in view of the large size of t-PA (72 kD) rendering it difficult to obtain intact full size mRNA and, thus, having an adverse impact on the probability of obtaining t-PA cDNA, the Board concluded that a skilled person would not have expected the theoretically straightforward route to be easily put into practice. The patent was thus maintained in amended form according to auxiliary request 3.

In **T 656/94 (Colony-stimulating factor/KIRIN-AMGEN)**, the Opponent-Appellant argued for a lack of inventive step of claims directed to an isolated polypeptide. The invention further related to the cloning and recombinant expression of said polypeptide. In discussing inventive step of the claims directed to the DNA encoding the polypeptide, the Board held that the use of recom-

binant DNA technology for the production of the claimed polypeptide was not obvious to the skilled person. With regard to the claims directed to the polypeptide, the Board stated that since the provision of the claimed polypeptide was only possible by way of recombinant DNA technology and since this route of production involved an inventive step, the claim to the polypeptide also involved an inventive step.

In **T 67/95 (Parvovirus Capsids/UNITED STATES OF AMERICA)** inventive step was denied. In its analysis of inventive step of a claim directed to a method for the production of empty human parvovirus capsids, the Board referred to the concept of expectation of success. In light of the prior art that disclosed the self-assembly of murine and canine parvovirus capsids, the Board held that the skilled person would have had a reasonable expectation of success that human capsids would also self-assemble. With regard to the Appellant's arguments of an ex post facto combination of two prior art documents, the Board was of the opinion that, given the objective technical problem, the skilled person would have had "no other alternative" than combining the documents. This lack of alternatives or choices is now commonly referred to in EPO case law as a "one-way street" situation, in view of which inventive step is regularly denied.

In **T 223/96 (Protein C/ELI LILLY)**, claim 7 of the main request reads:

A composition comprising a therapeutically effective amount of a polypeptide with human protein C activity produced by the method of any of claims 1 to 5 in admixture with a pharmaceutically acceptable carrier.

The Board held that the features "a therapeutically effective amount" and "in admixture with a pharmaceutically acceptable carrier" did not contribute to an inventive step since they were routine measures to be adopted by the skilled person when preparing a pharmaceutical composition. Thus the question remained whether the "product-by-process" feature "produced by the method of any of claims 1 to 5" could contribute to an inventive step. The Board did not accept the Appellant's argument that expression of protein C by recombinant DNA techniques would result in different glycosylation pattern compared to protein C isolated from natural sources, because there was no evidence that those differences were always present. According to the Appeal Board, the primary concern of the skilled person would be the biological activity of protein C irrespective of the glycosylation pattern. The claimed composition was therefore considered obvious.

In **T 1208/97 (Analogues/AMGEN)** the underlying patent claimed inter alia variants of subtilisin by the following wording:

A subtilisin analog characterized as having amino acid of a naturally occurring *Bacillus subtilisin* that has been modified by:

- a) having one or more of the amino acids present in a calcium binding site represented by Asp⁴¹, Leu⁷⁵, Asn⁷⁶, Asn⁷⁷, Ser⁷⁸, Ile⁷⁹, Gly⁸⁰, Val⁸¹, Thr²⁰⁸, and Tyr²¹⁴ of the naturally occurring *Bacillus subtilisin* replaced by a negatively charged amino acid; and

- b) having one or both of the amino acids comprising any Asn-Gly sequence of the naturally occurring *Bacillus subtilisin* deleted or replaced by a different amino acid, the analog having improved calcium binding capacity with respect to the naturally occurring *Bacillus subtilisin*.

In this case the Appeal Board commented on the question whether all embodiments of a claim have to show the claimed technical effect as follows:

[T]here is no evidence on file that for any significant area of the claims the rationale provided by the patent specification produced deterioration of thermostability. In view of the broad range of the proposed modifications proposed, it can, of course, not be excluded that some potential variant(s) covered by the claims will be unsuitable or not particularly suitable. However, this possibility, which is recognised by the skilled reader, is per se not sufficient to undermine the rationale on which the claims are based because, firstly, occasional failure is part of any scientific work, and, secondly, no evidence is available showing that the claimed technical effect can definitely not be achieved within the whole range of application or that it can be achieved only with undue burden.

For these reasons, the Board is satisfied that the claims at issue provide indeed a solution to the underlying technical problem. (point 11)

In **T 1045/98 (Eosinophilia/SCHERING)**, the Appeal Board pointed to the principle established in case law (see e.g. **T 158/96 (Obsessive-compulsive-disorder/PFIZER)** and **T 241/95 (Serotonin receptor/ELI LILLY)**) that in vitro and animal data can be sufficient evidence for a therapeutic application in humans. In this case, however, the Board furthermore pointed out that these considerations also apply to disclosure of the prior art. In the present case, this meant that a document disclosing the effects of an anti-IL5-antibody in mice was prejudicial to the inventive step of the use of IL5 antagonists in humans.

In **T 787/00 (Erythropoietin/KIRIN-AMGEN)** the Appeal Board was faced with numerous prior art documents all relating to the problem the underlying invention claimed to solve. The Appeal Board did not consider it obvious to select a single document als closest prior art from numerous confusing prior art documents as a starting point leading to the claimed solution. Rather, the selection of the closest prior art would already require applying knowledge based on the patent application in question. Further, one of the documents even taught away (“*expressis verbis*”) from the solution proposed by the Patentee.

In **T 1072/00 (Borrelia Burgdorferi/MIKROGEN)**, an Appeal Board referred to the established case law that the objective technical problem can be seen in the mere provision of an alternative and that the object does not have to be new in itself (see **T 92/92 (-/-)**). Furthermore, the Appeal Board repeated that the provided solution does not have to be an improvement over the prior art (see **T 588/93 (Porous adsorbent/-)**).

In addition, this decision also relates to the question of public availability. The Board considered a prior art document non-prejudicial to inventive step, since the bacterial strain mentioned in the document, which otherwise might have led the skilled person in an obvious manner to the claimed invention, was not deposited and hence was not publicly available, but only in the possession of the Patentee.

In **T 660/02 (Enzyme mutants/NOVOZYMES)**, the claim related to a mutant protein with particular improvements compared to the prior art. Different mutations were cited in the claim, at least one of which the mutated protein must contain. Inventive step was denied, since it had not been shown individually for each mutation that there was a causal link between the mutation and the claimed effect. In the end, inventive step of an auxiliary request was acknowledged, which claimed combinations of mutations, for which the effect was individually proven.

In **T 889/02 (Membrane cofactor protein/WASHINGTON UNIVERSITY)**, the underlying patent claimed a protein lacking a transmembrane hydrophobic region for use as a medicine. A prior art document disclosed the exact position of this region. The Board stated that while it cannot be ruled out that by removing this region the protein will lose all or part of its activity, given the general common knowledge the skilled person would have tried to solve the problem by deleting the transmembrane region. The Board thus held that the skilled person had a reasonable expectation that solubility could be achieved without total loss of activity and had no particular reasons to expect failure. The Board added that the skilled person would adopt the “try and see” attitude (see **T 91/98 (Antiviral nucleosides/WELLCOME)**). Based on these considerations the Board considered the invention to lack an inventive step.

In **T 986/02 (Anticytokine/YEDA)** in identifying the closest prior art the Board held that

the closest prior art is generally a document conceived for solving the same problem or aiming at the same objective and which requires the minimum of structural and functional modifications. Ideally, that purpose should be something already mentioned in this prior art document as a goal worth achieving. (point 4)

In **T 1146/02 (Vaccines containing a saponin and a sterol/SMITH-KLINE BEECHAM)**, the claim related to a vaccine composition comprising an antigen, a saponin and a sterol in a particular ratio. The Appellant argued that not all embodiments of this claim achieved the underlying technical effect. However, the Board held:

[I]t is of no consequence that one specific set of parameters within a claim occasionally leads to a formulation not having the advantages promised by the patent (see paragraph [0028] of the patent), so long as substantially all embodiments covered by a claim provide a solution to the problem to be solved. An occasional failure can thus be “forgiven” since there is ample evidence before the Board, not contradicted by any data from the respondent, that substantially all of the claimed formulations do provide a solution to the problems addressed by the patent. (point 49)

In **T 1190/03 (Orphan receptor/KARO BIO)**, the Board considered whether claiming a specific protein sequence of which homologs in other species or variants in the same species were already known involves an inventive step. The Board held:

Once the sequence of a receptor from one species is known, it is normally straightforward to identify and isolate the corresponding gene from a cDNA library of another mammalian species, using probes based on the known sequence. (point 7)

The Board basically applied the same reasoning for the case of cloning a different variant from the same species. Importantly, the Board made it clear that the mere fact that many variants or homologs exist, of which only one is claimed does not contribute to an inventive step.

In **T 67/05 (Tetanus vaccine/EVANS)** the Appeal Board was once again faced with the question whether all embodiments of a claim have to solve the underlying problem. In this case, the claim was directed to a process defined by parameters of a broad range. The Board stated:

The Board considers that a claim to a process defining different process parameters by broad ranges of values can formally encompass process variants which may not achieve the desired result if the extreme values of ranges are combined, as in the Appellant's example. However, in the Board's view, the skilled person would be aware that such combinations of process conditions might not generate the desired result and would not apply them. Therefore, an argument to the effect that a claim directed to a process encompasses variants not solving the problem, where that argument relies solely on rather unrealistic combinations of process conditions, does not convince the Board. (point 11.3)

As for the question as to whether the application makes it at least plausible that the underlying problem is indeed solved at all (important for the admissibility of post-published documents), the Board held that even though the parameters of the only given example lie outside the claimed range the patent made it still plausible that the problem was solved.

In **T 578/06 (Pancreatic cells/IPSEN)**, the Board pointed out that the EPC does not require experimental proof to establish that the underlying objective technical problem had been solved; the correct standard is rather one of plausibility. Furthermore, it held that the plausibility of the provided solution to the technical problem was only at issue if the case at hand allowed the substantiation of doubts in that regard.

In **T 997/06 (Insulin Preparation/NOVO NORDISK)**, the underlying patent was directed to an insulin preparation consisting of multiple components. The Board had to consider whether the claimed combination of the components warrants an inventive step. In doing so the Board held:

A mere aggregation of features must, however, be distinguished from a combination invention.

For the latter to be the case, the features must be

functionally interdependent [...] [and] achieve a technical success over and above the sum of their respective individual effects. (point 24)

In **T 1107/06 (Botulinum toxins/ALLERGAN)**, the Appeal Board, following a previous decision (**T 601/05 (Anti-TNF alpha human monoclonal antibodies/BAYER III)**), stated that if the claim explicitly referred to the effect to be achieved, the question of whether or not all embodiments fulfilling the structural limitations of the claim solved the technical problem was not to be considered under Article 56.

The previous decision **T 601/05** had pointed out that this was the case if such an additional limitation was contained in the claim, since embodiments not fulfilling the criterion (technical effect function) would not be encompassed by the claim. In this regard, for the question of inventive step, such a situation had to be differentiated from the situation in **T 939/92 (Triazoles/AGREVO)**, where the underlying technical effect was not an explicit technical feature of the claim itself, i.e. the claimed molecules were defined by structure only but not by function (or activity).

In **T 1396/06 (HLA Binding Peptides/EPIMMUNE)** the Appeal Board clarified that certainty of success is not required to deny an inventive step. The Board explained:

Rather, in spite of the understandable uncertainties which always characterize biological experiments, the skilled person would have had no reasons to adopt a sceptical attitude. He would have had either some expectations of success or, at worst, no particular expectations of any sort, but only a “try and see” attitude, which does not equate with an absence of a reasonable expectation of success [...]. (point 7)

D.III.2.f. Industrial applicability

In the last few years, the Boards of Appeal have put increased emphasis on the relevance of Art. 57 EPC in the field of DNA and protein inventions, thus creating a new obstacle for life science inventions. An Appeal Board paved the way to objections under Art. 57 EPC in **T 1329/04 (Factor 9/JOHN HOPKINS)**. Although this case was formally decided under Art. 56 EPC, the Board introduced the “plausibility concept or test” which requires that it must be plausible from the application as originally filed that an alleged function of a DNA or a protein indeed exists. The basic idea is that the invention must be complete on the filing date, and the application must contain sufficient information to make it plausible that the claimed effect exists and/or the alleged solution of the underlying problem is plausible from what is stated in the application. In the patent underlying **T 1329/04** a particular problem existed in that the alleged function of the protein encoded by the claimed DNA, in order to be a member of the TGF- β superfamily, was questioned in particular because the protein as encoded by the claimed DNA showed a different domain structure than most other known members of the TGF- β superfamily. In line with the thinking of **T 1329/04**, further decisions followed where this plausibility/credibility test of **T 1329/04** was then also applied with respect to the examination of Art. 57 EPC.

In a more recent decision, **T 870/04 (BDP1 Phosphatase/MAX-PLANCK)**, an Appeal Board had to decide on claims *inter alia* directed to purified BDP1 polypeptides of which no specific function was disclosed except for a specificity of BDP1 for HER2, a member of the epidermal growth factor family. The application also describes some further possible candidates as targets for the phosphorylation/dephosphorylation of the underlying protein. The Board

established several criteria which should be considered when assessing the requirements under Art. 57 EPC. In particular, the Board stated:

In cases where a substance, naturally occurring in the human body, is identified, and possibly also structurally characterized and made available through some method, but either its function is not known or it is complex and incompletely understood and no disease or condition has yet been identified as being attributable to an excess or deficiency of the substance, and no other practical use is suggested for the substance, then industrial applicability cannot be acknowledged ... Even though research results may be a scientific achievement of considerable merit, they are not necessarily an invention which can be applied industrially. (point 6 of the Reasons)

Under consideration of the requirements that had to be met in order to fulfil industrial application and, in particular, in view of the complexity of the cellular signal transduction pathways underlying the alleged BDP1 function, the Board denied industrial applicability. In particular, the Board held:

No doubt exists that a BDP1 polypeptide could be “made and used” as a further tool, in addition to the many already available in the art ... But the whole burden is left to the reader to guess or find a way to exploit it in industry by carrying out work in research for some practical application geared to financial gain, without any confidence that any practical application exists. (point 19 of the Reasons)

The Board then continued:

In the Board’s judgement, although the present application describes a product (a polypeptide) means and methods for making it and its prospective use thereof for basic science activities, it identifies no practical way of exploiting it in at least one field of industrial activity. In this respect, it is considered that a vague and speculative indication of possible objectives that might or might not be achievable by carrying out further research with the tool as described is not sufficient for fulfilment of the requirement of industrial applicability. The purpose of granting a patent is not to reserve an unexplored field of research for an Applicant. (item 21 of the reasons)

In a more recent decision, following **T 870/04**, the Board decided in **T 604/04 (PF4A receptors/GENENTECH)** in favor of industrial application. The claim was directed to an isolated factor 4 superfamily receptor protein and it was assumed that the claimed receptor protein belongs to a receptor family binding cytokines. An important difference to the earlier case of **T 1329/04** was that in **T 604/04**, the assumed structure was in line with the expected structure for the respective protein family. In decision **T 1329/04** one problem observed by the Board resided in the fact that the protein described therein had a structure which did **not** conform to the expected four domain members of said protein family. In the case of **T 604/04** the Board finally acknowledged industrial applicability for the following reason:

It is clear [...] that chemokines as a family were considered not only to be interesting in fundamental research but also as important for the pharmaceutical industry irrespective of whether or not their role had been clearly defined. It follows that the receptors must have been considered equally important since the mode of action of chemokines is through their receptors. It is, thus, reasonable to conclude that the polypeptides of Figures 4 and 5 which

exhibit the characteristics of receptors of members of the PF4A family of cytokines would have been regarded as important to the pharmaceutical industry, i.e. that industrial applicability may be acknowledged. (item 18 of the reasons)

D.III.2.g. Sufficiency of disclosure

As indicated in C.I.3.b.b., the EPC provides for depositing microorganisms under Rule 31 EPC to supplement a written disclosure and comply with Art. 83 EPC. Regarding the definition of a person skilled in the art who is relevant for evaluating the sufficiency of disclosure, see C.I.3.b.

Some of the most important decisions relating to sufficiency of disclosure of inventions concerning proteins are briefly summarized below. The current practice concerning antibodies is dealt with in Chapter D.IV.

T 299/86 (Monoclonal anti α -IFN/SECHER) confirmed the principle already established in **T 281/86 (Preprothaumatin/UNILEVER)**, that the disclosure of examples does not need to be identically reproducible. In **T 299/86**, one of the reasons for refusing the application by an Examining Division was that a specific hybridoma produced by using freely available cell lines and antigens had not been deposited. This hybridoma was not claimed, and its preparation was described in detail in one of the examples. It was acknowledged by the Applicant and also by the Appeal Board that the particular hybridoma in question was not repeatable without undue burden.

However, the Board confirmed the view of **T 281/86 (Preprothaumatin/UNILEVER)** stating:

[T]he requirements under Article 83 EPC are not such that a specifically described example of a process must be exactly repeatable [...] Thus the description provides support for the view that hybridomas excreting the claimed monoclonal antibody are not so rare that the process as a whole would not lead reliably to the claimed substance. In the absence of evidence to the contrary it is thus the Board's position that the description provides a sufficient disclosure repeatably to produce the claimed monoclonal antibody reliably and there is thus no need to reproduce identically the example given in the specification. (point 12)

T 158/91 (Human growth hormone/GENENTECH) concerned a process for the preparation of mature human growth hormone (hGH). An Appeal Board provided the following general statements for examination of sufficiency of disclosure:

Certainly, the question of sufficient disclosure, be it of a prior art document or a patent application in question, has to be examined in each case on its own merits. An examination as to the sufficiency of a disclosure depends on the correlation of the facts of the case to certain general parameters.

These parameters are for example:

- (a) the character of the technical field and the average amount of effort necessary to put into practice a certain written disclosure in that technical field;
- (b) the time when the disclosure was presented to the public and the corresponding common general knowledge;
- (c) the amount of reliable technical details disclosed in a document. (point 2.3)

In **T 223/92 (HIF-Gamma/GENENTECH)**, a Board of Appeal clarified that a deposit of a microorganism containing a claimed gene was only required if the written specification did not permit reproduction of the invention. The Board stated:

Finally, there is no legal requirement in the EPC which would force the Respondents to deposit a micro-organism, containing the gene coding for interferon-gamma ready for production. Rule 28 EPC, relating to the requirements of European patent applications relating to micro-organisms clearly states in paragraphs (1) and (1)(a) that in the cases where an invention concerns a microbiological process or the product thereof and involves the use of a micro-organism which cannot be described in a manner as to enable the invention to be carried out by a person skilled in the art, the invention shall only be regarded as being disclosed as prescribed in Article 83 EPC if a culture of the micro-organism has been deposited with a recognised depository institution. This prescription cannot be interpreted such that there is an obligation to deposit material to facilitate the reproduction if the invention can be repeated on the basis of the written description, even if this should be a much more cumbersome way than by merely growing the deposited micro-organism. (point 3.2)

This was confirmed in **T 412/93 (Erythropoietin/KIRIN-AMGEN)** as follows:

This need for a deposit cannot be introduced by reference to the concept of undue burden. This concept relates more to cases where the route that the reader is to follow is so poorly marked that success is not certain (see Decision T 418/89, OJ EPO 93, 20). If the route is certain but long and laborious, the Patentee is under no obligation to assist the disclosure by making actual physical samples, i.e. the “factory” available. To come to the opposite conclusion would be effectively to introduce a requirement to make the best mode immediately accessible to the public, and such a requirement is not part of the European Patent system. (point 76)

T 923/92 (Human t-PA/GENENTECH) contains an interesting statement regarding the necessity of depositing a cell line to ensure the reproducibility of a claimed protein. The cell line in question had not been deposited by the Patentee but was commonly used by the scientific community. The Opponents contested the availability of the cell line and, thus, the sufficiency of disclosure of the protein. The Board of Appeal held:

[A] large body of evidence shows that Bowes melanoma cells were generally available and freely exchanged in the scientific community among all those engaged in a research programme on t-PA (citation omitted) and that neither secrecy agreements nor contractual obligations among the research workers restricted the use or dissemination of the cells. Further, no evidence was produced that the cells would be available only to some selected laboratories for a limited time period. Thus, in the Board’s judgment, the Bowes melanoma cells were part of the state of the art already at the priority date. Under these circumstances the Board cannot agree to the Appellants’ position that it would have been the Respondents’ obligation to ensure their availability for the life-time of the patent in suit by means of a deposition under Rule 28 EPC. (point 44)

A further question discussed in the above decision was whether the sufficiency of disclosure of a protein required a certain level of expression. The Board reaffirmed earlier case law according to which it was sufficient for the requirements of Art. 83 EPC to achieve expression *at any level*.

In **T 656/94 (Colony-stimulating factor/KIRIN-AMGEN)**, an appeal was filed by one of the Opponents against the decision of the Opposition Division to maintain the patent as granted. The patent related to polypeptides that were defined by structural and functional (biological activity) characteristics. The Opponent-Appellant argued, among other things, that it would entail an unacceptable effort for the skilled person to identify those polypeptides with the claimed biological activity and further argued that only some of the peptides prepared in the examples possessed the claimed biological activity.

The Board considered these arguments “*beside the point*” since the patent would teach how to prepare the claimed peptides and would provide assays that allow the skilled person to determine whether prepared peptides would possess the claimed biological activity. So while in this case the number of theoretically possible peptides was still high, these peptides were likely to be structurally similar and possess a “*testable narrowly defined activity*”. Therefore the Board considered the claims to fulfil the requirements of Art. 83 EPC.

In **T 743/97 (Thrombolytic proteins/GENETICS INSTITUTE)**, an appeal was lodged by the Patent Proprietor against the decision of the Opposition Division. Claim 1 of a new set of claims submitted during Oral Proceedings was directed to a thrombolytic protein further characterized by functional (e.g. an improved fibrinolytic profile) and structural features. The respondents, *inter alia*, argued that it was unlikely that any embodiment falling under the scope of claim 1 would also possess the claimed functional features, i.e. display the desired technical effect and that therefore the claimed subject matter was not sufficiently disclosed.

In response, the Board pointed out that an enablement objection could not be raised merely because the description did not contain credible information that all claimed products would possess the claimed functional characteristic. The question may, however, be of relevance for inventive step, if the functional feature was a decisive factor for non-obviousness. Furthermore, the Board noted that an enablement objection was without merit because the description provides enough details for preparing and testing all variants falling under the scope of the claim without undue burden. For these reasons, the Board concluded that the requirement of Art. 83 EPC was met.

In **T 749/98 (Cellulose/NOVOZYMES A/S)**, an appeal lay from the decision of the Opposition Division to maintain the patent in amended form. Claim 1 of the main request was directed to a cellulose preparation consisting essentially of an endoglucanase component further characterized by its reactivity with an antibody raised against a specific endoglucanase.

The Board stated that at the date of filing there were several techniques available to test for the claimed biochemical property of the claimed product (e.g. Western blot and ELISA). The Board then went on to present the following argument:

Because these techniques for determining immunoreactivity give different answers and no information is given in the patent in suit as to which of them to use, the skilled person choosing anyone of them would not know when getting a positive or a negative result, whether he/she had succeeded or failed to reproduce the invention as claimed. Accordingly, the conclusion is reached that the patent in suit fails to give sufficient technical advice to isolate the claimed endoglucanase because it fails to identify the means by which to assess its claimed property. (point 5)

Largely based on the above, the Board came to the conclusion that the main request did not fulfil the requirements of Art. 83 EPC.

In **T 1080/01 (Thermostable enzyme/F. HOFFMANN-LA ROCHE)**, the underlying patent claimed a protein with a particular molecular weight as determined by SDS-PAGE. The Respondents held that the invention was not sufficiently disclosed with respect to the particular SDS-PAGE system used. However, the Appeal Board decided that “SDS-PAGE was one of the most common and routine techniques in biochemistry” and that due to this routine character of the experimental test to ascertain the claimed parameter the skilled person could carry out the invention without undue burden.

In **T 946/02 (Separation of Proteins/NOVOZYMES)**, the underlying patent claimed a method for the purification of an enzyme by crystallization in very broad terms. The Board held that the specific examples given in the patent were of no help to the skilled person to exercise the invention with other enzymes. Only upon limiting the subject-matter to the specific working embodiments, the Board acknowledged sufficiency of disclosure, since no verifiable facts leading to serious doubts could be identified which would put into question the reworking of the specific embodiments.

In **T 1067/02 (Changed epitopes/NOVOZYMES)**, a subtilisin protease was claimed characterized by an immunological potential lower than of a parent protease. Considering whether the skilled person was enabled to carry out the comparison referred to in the claim, the Board held that the information provided in the prior art on file would be sufficient to allow the skilled person to do so without requiring inventive skill or undue burden. The Board further pointed out that the question as to whether or not all variants had the same activity (lower immunological potential) was of no relevance for sufficiency of disclosure, but might be of relevance for the assessment of inventive step.

In **T 157/03 (Reducing blood loss/ZYMOGENETICS)**, the Appeal Board was faced with the question whether the medical effect claimed by means of a second medical use claim could be indeed accomplished with the claimed substance. The Board held:

In the absence of any tangible proof in the patent specification that the claimed concept can be put into practice, post-published documents may be used as evidence whether the invention was indeed reproducible without undue burden at the relevant filing date [...]. (point 9)

In **T 94/04 (Cytokine antagonists/REGENERON)**, the Board considered the contribution to the art in the provision of a theoretical concept for the

preparation of the claimed antagonists. The fact that no detailed example was provided in the patent did not violate Art. 83 EPC, since the skilled person had sufficient information from common general knowledge and the patent to prepare the claimed antagonists.

In **T 669/04 (CED-3 inhibitors/MIT)**, the patent application was directed to the use of an inhibitor of a specific protein for the manufacture of a medicament for the treatment of a series of diseases. However, neither the biological activity of the protein to be inhibited nor a structural limitation of the inhibitor was indicated in the claim. Therefore, the Board considered that the skilled person could only determine the scope of the invention with undue burden. Upon structurally limiting the claim to specific examples given in the patent, sufficiency of disclosure was acknowledged.

In **T 309/06 (Phospholipase A1/SANKYO)**, the Board acknowledged the broadly claimed subject matter and emphasized once more that the mere fact that a claim was broad was not in itself a ground for objection under Art. 83. The Board further held:

[I]t is sufficient to define the claimed product by parameters if these parameters can be clearly and reliably determined by objective procedures known in the art. (point 17)

In **T 394/06 (CASB7439 polypeptide/GLAXOSMITHKLINE BIOLOGICALS)**, the Appeal Board emphasized once more that an objection based on a lack of sufficiency of disclosure could only be raised given serious doubts substantiated by verifiable facts. Furthermore, the Board made clear that despite the fact that no experimental data was provided in the application it had no reason to doubt the therapeutic effect underlying the invention.

In **T 1074/06 (Infertility/ARS)**, the underlying patent related to the use of FSH and/or a biologically active analog for the stimulation of multiple follicular development in one claim, but also to the use of FSH and/or a biologically active analog for the stimulation of monofollicular development in another claim. Both claims had largely overlapping dosage regimens. Due to these contradictory effects within a largely overlapping application regimen, the Board considered the subject-matter not sufficiently disclosed for a skilled person wanting to put the teaching into practice for either one of the two disclosed applications.

In **T 21/07 (Endometriosis/SERONO)**, the Opponent filed an appeal against the decision of the Opposition Division. The disputed claims were phrased as Swiss-type second medical use claims for TNF antagonists. With regard to sufficiency of disclosure the Board pointed to the established case law before the Boards of Appeal and stated:

The Board would like to draw attention to the fact that, according to the case law of the Boards of Appeal and to the granting practice of the EPO, data obtained from animal models are usually accepted as evidence for the sufficiency of disclosure of a claimed human treatment, unless there is convincing evidence, i.e. verifiable facts and evidence in the sense of decision T 19/90 (see point 15 above), that the treatment does not work for human beings. (point 16)

In this case, the Board thus considered data in the rat model as sufficient to extrapolate to the therapeutic effect in humans. Furthermore, the Board was not convinced by the arguments of the Respondent that the demonstration of only one antagonist in the application was insufficient to make it plausible that all antagonists claimed achieve the therapeutic effect. Inter alia for these reasons, the Board considered the requirements of Art. 83 EPC fulfilled.

In **T 458/07 (Ion exchange chromatography method/GENENTECH)**, the Board rejected the Appellants' allegations that one example would not be enough to provide sufficient disclosure by stating:

There is no mandatory requirement for an example under the EPC. Hence, even the absence of an appropriate example would not be a reason for denying sufficiency of disclosure. (point 19)

In **T 1437/07 (Botulinum toxin for treating smooth muscle spasm/ALLERGAN)**, the Patentee lodged an appeal against the decision of the Opposition Division. The claims under dispute were directed at a Swiss-type second medical use of Botulinum toxin A. With regard to sufficiency of disclosure the Board made the following comments.

The Board considers three requirements that have to be fulfilled for enablement with regard to a second medical use claim:

- (i) the skilled person has to be enabled to obtain a compound,
- (ii) to apply the compound and
- (iii) there has to be evidence that the intended therapeutic effect can be achieved.

The Board saw all criteria fulfilled in the present case. The Respondents' argument that the treatment had not actually been carried out did not convince the Board, since according to Rule 42 (1)(e) EPC an example was not required and in the absence of convincing evidence that the effect cannot be achieved, the Board did not see any reason to doubt the therapeutic effect. Therefore, the Board saw the requirements of Art. 83 EPC fulfilled.

In **T 786/08 (Inhibitors of JNK/UNIVERSITY OF MASSACHUSETTS)**, the underlying patent claimed a protein by structural and functional features. The Examining Division refused the application due to the great number of variants encompassed by the structural definition, which the Examining Division alleged did not all possess the claimed activity. However, the Appeal Board held that the subject matter was disclosed in a manner sufficiently clear to be carried out by the skilled person, since apart from its broad structural definition the product was characterized by a narrowly defined and testable activity.

D.III.2.h. Clarity and support of claims

In the proceedings underlying **T 923/92 (Human t-PA/GENENTECH)**, claim 1 as granted reads as follows:

A process which comprises preparing cDNA from mRNA extracted from the Bowes melanoma cell line and isolating from it a DNA sequence having the restriction pattern shown in Fig. 4 hereof for the putative mature tissue plasminogen activator sequence and which encodes a 527 amino acid polypeptide *having human tissue plasminogen activator function*. (emphasis added)

During appeal proceedings, the Patentee filed auxiliary requests containing claims concerned with the preparation of derivatives of the 527 amino acid sequence, said derivatives “having human tissue plasminogen activator function”. As in the granted claim, the claims of these requests did not contain any reference to the 527 amino acid sequence nor to the nucleotide sequence encoding it. In contrast, the derivatives were defined by means of their restriction pattern and hybridization properties of the encoding cDNA.

With respect to the phrase “having human tissue plasminogen activator function” the Patentee considered any objection under Art. 84 to be without a proper legal basis, since this phrase was already present in the claims as granted. The Board observed:

[T]hat the feature “has human tissue plasminogen activator function” is quite vague and ambiguous. Although this feature was not amended during opposition proceedings, its significance and thus its clarity have to be reconsidered within the framework of the amendments to the claims in view of its influence on the decision on the issue of the sufficiency of disclosure [...]. (point 25)

The Board then explained that t-PA was a molecule with multiple functions, at least four of which were defined in the specification. The Board considered the skilled artisan to be left in doubt as to the exact meaning of the expression “which has human tissue plasminogen activator function”, and consequently attributed to this feature the broadest possible meaning, i.e. any of the features of human t-PA. The Board held:

This definition shows that the subject-matter of Claim 2 relates to a vast catalogue of derivatives of human t-PA of unspecified structure having an unspecified function of human t-PA. There is no dispute that the present description provides a disclosure of the production of human t-PA in a recombinant system. However, in the Board’s judgment, the examples and the information given are not sufficient to allow a person skilled in the art, using common general knowledge, to perform the invention without undue burden in the whole area claimed, especially in consideration of the broad functional meaning attributed to the quoted parameter. Claim 2 leaves the skilled addressee guessing as to whether any derivative of human t-PA which fulfils only one of the functions typical of this molecule is a derivative meant by the claim. In this respect the Board, in line with the quoted case law, considers the patent in suit to be insufficient and thus to contravene the requirements of Article 83 EPC. Furthermore, the area covered by the claim is not clearly defined, which is contrary to the provisions of Article 84 EPC. (point 27)

In **T 412/93 (Erythropoietin/KIRIN-AMGEN)**, an Appeal Board considered the allowability of claim 19 of auxiliary request 5 shown below:

A recombinant polypeptide having part or all of the primary structural conformation of human or monkey erythropoietin as set forth in Table VI or Table V or any allelic variant or derivative thereof possessing the biological property of causing bone marrow cells to increase

production of reticulocytes and red blood cells and to increase hemoglobin synthesis or iron uptake and characterized by being the product of eucaryotic expression of an exogenous DNA sequence and not being identical to erythropoietin isolated from urinary sources.

The Board held that the phrase “and not being identical to erythropoietin isolated from urinary sources” lacked clarity for the following reasons:

The claim does not comprise any indication of the technical feature or the degree of difference on which non identity of r-Epo with u-Epo should be based, but rather leaves this to the reader's imagination. This puts the claim clearly in the category of claims which are not clear. The whole burden on distinguishing over the prior art u-Epo is put on the reader. (point 45)

Therefore, the Board held that claim 19 of auxiliary request 5 did not comply with Art. 84 EPC.

Claim 19 of auxiliary request 11 had the following wording:

A recombinant polypeptide having part or all of the primary structural conformation of human or monkey erythropoietin as set forth in Table VI or Table V or any allelic variant or derivative thereof possessing the biological property of causing bone marrow cells to increase production of reticulocytes and red blood cells to increase hemoglobin synthesis or iron uptake and characterized by being the product of eucaryotic expression of an exogenous DNA sequence and which has higher molecular weight by SDS-PAGE from erythropoietin isolated from urinary sources.

The Board rejected the Appellant's objections to the clarity of the feature “higher” and stated:

However what is to be measured is clear. Values of the molecular weight of u-Epo measured by SDS-PAGE were part of the prior art. Frequently where something has to be measured there will be a grey area where measurement error may make it difficult to determine whether a particular product falls within a claim or not. This does not justify an objection under Article 84 EPC. (point 60)

In **T 241/95 (Serotonin receptor/ELI LILLY)**, the claims were directed to a medical treatment of conditions that were defined by being susceptible to selective occupation of a serotonin receptor. The application itself specified some conditions, however a link between these conditions and the specific receptor was not established.

The Board decided:

The selective occupation of a receptor cannot be considered in itself as a therapeutic application; the discovery that a substance selectively binds a receptor [...] still needs to find a practical application in the form of a defined, real treatment of any pathological condition in order to make a technical contribution to the art and to be considered as an invention eligible for patent protection (see reasons, point 3.1.2).

When a claim is directed to a further therapeutic application of a medicament and the condition to be treated is defined in functional terms, [...] the claim can be regarded as clear only if instructions, in the form of experimental tests or any testable criteria, are available from the patent documents or from the common general knowledge allowing the skilled person to recognise which conditions fall within the functional definition and accordingly within the scope of the claim (see reasons, point 3.1.1).

As the selective occupation of the specific receptor was not the only physiological activity of the substance, the Board held that at the time of filing no means involving testable criteria existed to assist the skilled person to identify conditions falling within the functional definition set forth in the claims. The case was remitted to the Examining Division to further examine the claims of the second auxiliary request where specific medical conditions had been specified.

In **T 285/01 (Bone resorption/WASHINGTON RESEARCH FOUNDATION)**, an Opponent alleged that the feature “of molecular weight less than 5000” in relation to peptide fragments to be detected in body fluids was unclear if the method for its determination is not stated, because different techniques for determining the molecular weight yield varying results. However, the Board ruled that in the present case the peptide fragments were small and thus the method of determination was not critical as the molecular weight could already be calculated on the basis of their formula (reasons, point 4).

In **T 610/01 (Plant growth/LONG ASHTON RESEARCH STATION)**, the Patentee submitted new claims during the Appeal proceedings which the Board had the obligation to examine for conformity with Article 84 EPC. The claim at question referred to a DNA molecule encoding a polypeptide with more than 50% homology to SEQ ID NO 2 and exhibiting GA 20-oxidase activity. The Board held that while certainly being broad, the claim did not lack a clear definition for a skilled person, as a test for the recited oxidase activity was present in the application as filed (reasons, point 7). Nor was the expression “50% homologous” found to be objectionable under Art. 84 EPC.

In **T 1146/02 (Vaccines containing a saponin and a sterol/SMITH-KLINE BEECHAM)**, the claims of the underlying patent referred to a degree of purity of one of the constituents (“[wherein] the Q21 is at least 90% pure”), said constituent being described in the application as an immunologically active saponin fraction derived from the bark of a specific plant. The Board concluded that no case of lack of clarity had been demonstrated; the Board deemed the skilled person capable of determining the level of purity of the recited saponin fraction based on HPLC peak data. The Board referred to prior art documents and the application as filed (reasons, points 5–15).

In **T 412/06 (Proteinase inhibitor/MAX-PLANCK-GESELLSCHAFT ZUR FÖRDERUNG)**, the Examining Division objected that the term “modulator” (of growth factor receptor activation) was unclear as it lacked structural definition. While the Board agreed that the term does not provide a structural definition, it held that the modulator was further defined by a functional feature, namely acting as a growth factor precursor to inhibit the activation of the extracellular domain of a growth factor receptor. The description was found to contain suitable examples how to test for the functional activity. The Board thus decided that a skilled person could determine whether a given substance would fall within the scope of a modulator as claimed. As an aside, the claim was also held to be in line with Art. 83 EPC because the Examining Di-

vision did not present reasoned arguments as to why the testing for the functional feature should amount to undue burden. The case was remitted to the first instance for further prosecution.

In **T 1599/06 (Mycobacterium vaccinating agent/UNIVERSITY OF CALIFORNIA)**, the Examining Division held that the terminology of the claims directed to a composition comprising an isolated protein was contradictory between the terms “comprising” and “at least one purified and isolated [...] extracellular protein of *Mycobacterium tuberculosis* [...]”. The term “comprising” was construed broadly, and therefore vaccination compositions of the prior art (attenuated live *Mycobacterium tuberculosis* vaccines) were considered novelty destroying. The Board, however, held that the meaning of terms in a patent claim and the resulting meaning of the whole claim must be determined from the point of view of the skilled person reading the claim in the context of the application and against the background of his/her common general knowledge (reasons point 3.1). In the present case it was clear from the description that the inventive vaccine compositions were composed of isolated purified protein components and not from whole bacteria. Hence, a composition comprising an isolated and purified protein component would be interpreted as a composition containing said component as a main constituent and not as one component in addition to several others such as in whole bacteria vaccines.

In **T 411/02 (CTL4A receptor/BRISTOL-MYERS SQUIBB)**, the question was whether the expression “capable of [exerting a certain function]” rendered the claims unclear. An Appellant argued that the ligands as defined in the claims as granted were not merely “capable” of interfering or inhibiting the interaction of the compounds or the cells, but “are” actually interfering or inhibiting such interactions, respectively. The Board however considered that the characterization of a product by “capable of” was clear within the meaning of Art. 84 EPC if the function defined was clear and testable (reasons, point 40). Therefore, no case under Art. 84 had been made out.

In **T 878/09 (Method for the detection of prion proteins/PROTH-ERICS)**, an Opponent held that the claim on file contradicted certain passages of the description and that this contradiction rendered the claim unclear. The Board in turn ruled that the claim was drafted in a way that leaves no room for interpretation. Since the claim was clear per se, there was no need to consult the description or drawings for the interpretation of this claim. The Board went on that even if the claim were considered in light of the description, the features at issue were so clearly stated in the claim that, even if there existed discrepancies between the description and the claims in this respect, they would not call in doubt the meaning of the claim (reasons, points 19 and 20). Therefore any potential contradiction between a claim and the corresponding application is irrelevant under Art. 84 EPC if the claim per se is clear and there is no need for consulting the specification in order to interpret the claim.

In **T 1815/06 (Pre-ligand association domain/THE GOVERNMENT OF THE UNITED STATES)**, the Examining Division objected to

a lack of clarity of the term “PLAD” (pre-ligand assembly domain of two specific proteins). According to the Examining Division the term had no well-recognized meaning in the art. Furthermore the specification did not remedy this deficiency, as it provided two contradicting definitions. The objection was overcome by specifying the amino acid sequence of the respective domains in the claim. The decision exemplifies that internal or laboratory designations should be avoided or at least clearly and unambiguously defined in the specification.

D.III.2.i. Product claims for proteins

As indicated in the introduction to this chapter, proteins are of commercial interest for a variety of purposes.

Proteins may be produced by chemical synthesis, by isolation from natural sources, or by transcription and translation of nucleic acids. Inventions relating to proteins produced by biological processes, i.e. isolation or transcription and translation, often face the problem of reproducibility, since living material producing the claimed protein cannot be reproduced *de novo* on the basis of the underlying written specification. Reproducibility is in particular a problem if the amino acid sequence of the protein is not known. Therefore, it may sometimes be necessary to ensure the reproducibility of a protein related invention by making the source of the protein publicly available, e.g., by depositing a microorganism producing the claimed protein.

A particular species of protein deserving special attention are antibodies. They are dealt with in the separate Chapter D.IV.

Product claims relating to proteins are discussed below. Proteins may be characterized by functional terms, by physical parameters, by the coding capacity of certain DNA, by their amino acid sequence, by a process for their production, or by citation of the deposit number of a microorganism capable of producing the protein. In most instances, proteins are characterized by more than one of the above characteristics. Examples of each type of characterization are provided below.

Applications relating to previously unknown amino acid sequences of more than 4 amino acids must include a sequence listing (Rule 30 EPC (see Annex 3)). For further details, see C.I.3.b.a as well as Annex 3.

D.III.2.i.a. Product claims characterizing a protein by functional terms

As for nucleic acids, the characterization of a protein by functional terms such as a certain activity appears to provide the broadest possible scope, since it may embrace proteins having fairly unrelated primary structures.

Claim drafting:

A product claim characterizing a protein by functional terms may have the following general wording:

Protein X being capable of ...

Examples of product claims containing functional features granted by the EPO are presented below. The functional features are underlined in the examples below.

EP-B1 – 0205555 – Claim 1:

A purified serine protease inhibitor protein consisting of a single unfragmented polypeptide chain, said inhibitor being capable of inhibiting the protease activity of at least one serine protease and being in excess of 40% homologous to a native serine protease inhibitor isolated from parotid secretions.

The claimed protein is characterized by (a) being a single intact polypeptide chain, (b) its biological activity and (c) a certain degree of homology to a protein.

EP-B1 – 0237545 – Claim 1:

A polypeptide which:

- a) has part or all of the primary structure and one or more of the biological properties typical of naturally-occurring human pluripotent granulocyte colony-stimulating factor (hpG-CSF) of the sequence set forth in Table VII,
- b) is a non-naturally occurring polypeptide; and
- c) is the product of procaryotic or eucaryotic expression of an exogenous DNA sequence.

According to feature (a), the polypeptide of this claim, although referring to a certain sequence, is only required to have *part* of the primary structure of the CSF having the sequence of Table VII.

EP- B1 – 2277997 – Claim 1:

A polypeptide having cellobiohydrolase I activity, selected from the group consisting of:

- (a) a polypeptide comprising an amino acid sequence which has at least 90% identity with amino acids 1 to 457 of SEQ ID NO: 8,
- (b) a polypeptide comprising an amino acid sequence which has at least 90% identity with the polypeptide encoded by nucleotides 1 to 1371 of SEQ ID NO: 7.

EP-B1 – 1799818 – Claim 1:

An isolated polypeptide having phytase activity and comprising an amino acid sequence which has at least 98.8% identity with amino acids 1 to 411 of SEQ ID NO: 2, whereby the identity is determined by the program “align” using the default scoring matrix BLOSUM50, the penalty for the first residue in a gap is -12 while the penalty for additional residues in a gap is -2, and whereby the phytase has a residual activity following incubation at 37°C and in a 0.1 M Glycine/HCl buffer pH 2.0 for 4 hours of at least 20%.

Interestingly, in the above claim the method for calculating percent identity is part of the product claim.

EP-B1 – 1626088 – Claim 1:

A protease, which cleaves a glycosylated amino acid and/or a glycosylated peptide from a glycosylated β -chain N-terminal of glycosylated hemoglobin without substantially cleaving a glycosylated amino acid or a glycosylated peptide from a glycosylated α -chain N-terminal of glycosylated hemoglobin, wherein the protease is;

- (i) obtained from a bacterium belonging to the genus *Lysobacter* and comprises an amino acid sequence according to SEQ ID NO:15; or
- (ii) obtained from *Bacillus* sp. ASP-842 (FERM BP-08641) and having a molecular weight of about 35kDa as determined by SDS-PAGE; or
- (iii) *Aeromonas hydrophila* (NBRCC 3820) and comprises an amino acid sequence according to SEQ ID NO:12.

EP-B1 – 1421175 – Claim 1:

A polymer-proteinase conjugate, comprising an initial Proteinase K covalently linked to three to seven polymer strands per molecule of said Proteinase K said conjugate having integrated enzymatic activity in a solution containing 0.5% SDS, 0.1 M GdnSCN or 2–4 M urea at a temperature of about 50°C that is about or greater than two times the integrated enzymatic activity of said initial Proteinase K under comparable conditions.

EP- B1 – 1409659 – Claim 1:

A variant of the BLSAVI subtilase, comprising the substitution V68A, where the variant has protease activity, and the position corresponds to a position of the amino acid sequence of subtilisin BPN', shown in Figure 1.

EP-B1 – 1496113 – Claim 1:

A gluconate dehydratase comprising an amino acid sequence having a homology of at least 95% with the amino acid sequence shown in SEQ ID No: 1, and capable of dehydrating D-gluconic acid to produce 2-keto-3-deoxy-D-gluconic acid, wherein the gluconate dehydratase maintains at least 95% of the enzyme activity thereof after being allowed to stand in 30 mM tris (hydroxymethyl) aminomethane buffer solution with a pH of about 8.5 containing 1 mM of sodium D-gluconate and 1 mM of magnesium chloride at 55°C for 2 hours.

EP- B1 – 2085472 – Claim 1:

D-serine dehydratase comprising the following protein (a) or (b):
 (a) a protein having an amino acid sequence set forth in SEQ ID NO: 1; or
 (b) a protein having an amino acid sequence having 70% or more similarity to the amino acid sequence set forth in SEQ ID NO: 1 and having a D-serine dehydratase activity, which does not react with L-serine and wherein a reactivity to D-threonine is not more than 5% when a reactivity to D-serine is 100%.

D.III.2.i.b. Product claims characterizing a protein by parameters

Parameters used for characterization of a protein are e.g. the molecular weight of the protein, its recognition by certain antibodies, its isoelectric point or the degree of homology to a reference sequence. The specification should contain sufficient information to permit determination of the parameters used to describe the protein.

Claim drafting:

A product claim characterizing a protein by parameters may have the following general wording:

Protein X having a molecular weight of ... kD and a pI of ...

Protein X having X% identity to sequence Y.

Examples of granted claims containing such parameters issued by the EPO are provided below. The parameter features are underlined.

EP-B1 – 0308378 – Claim 1:

A Tumor Necrosis Factor (TNF) Inhibitory Protein having the following features:

- (a) it inhibits the binding of TNF to its receptors and the cytotoxic effect of TNF;
- (b) when crude urine preparations thereof are chromatographed on an Ultrogel AcA 44 filtration column, the major peak of TNF inhibitory activity elutes slightly before the majority of the protein and shows an apparent molecular weight of about 40–80 kDa; and
- (c) when crude urine preparations thereof are analysed, the isoelectric point of the active protein is between pH 6 and 8 or a salt, functional derivative or active fraction thereof, said active fraction having the ability to inhibit the binding of TNF to its receptors and the cytotoxic effect of TNF.

EP-B1 – 0239425 – Claim 10:

Purified antigen of the retrovirus HIV-2 having the immunological characteristics of the HIV-2 p12 protein, immunologically recognized by antibodies raised against a retrovirus according to anyone of claims 1 to 9 and having a molecular weight of the order of 12000 daltons.

As can be seen, the above claims contain, in addition to parameters, other characteristics such as immunological characteristics.

EP-B1 – 1523553 – Claim 1:

A protease variant, which is a variant of a precursor *Bacillus lentus* subtilisin protease having the sequence shown in Figure 3, said variant being characterized by having the same net electrostatic charge at pH 7 or the same isoelectric point as said precursor protease, and comprising an amino acid sequence having the substitutions R170SA1R, R170S-G61R, R170S-N204R, R170S-S216R or R170S-G100R relative to said precursor protease, wherein the positions of said substitutions are equivalent to the specified positions in the mature *Bacillus amyloliquefaciens* subtilisin shown in Figure 3.

EP-B1 – 1157101 – Claim 1:

A protein crystal of the LTA4 hydrolase protein, characterised in that said protein crystal exhibits a three-dimensional form as defined by the parameters in table 9, defining atom 1 to atom 4876, which protein crystal is obtained when:

- a) an ytterbium salt, such as ytterbium chloride, is used as an additive during the crystallisation process;
- b) bestatin is present in the crystallisation set-up, and;
- c) liquid-liquid diffusion in capillaries is employed during the crystallisation process.

EP-B1 – 1025213 – Claim 1:

An isolated and purified epoxide hydrolase comprising an epoxide hydrolase of less than 30 kDa having an amino acid sequence that has more than 70% homology with the amino acid sequence SEQ ID NO 6, said epoxide hydrolase having 80% of its optimal enzymatic activity at a pH comprised between 7.5 and 9.5.

EP-B1 – 1865055 – Claim 1:

An isolated fraction of bromelain comprising a protein of molecular weight of about 27.45 kDa as determined by SDS-PAGE, an isoelectric point of 9.7 as determined by

isoelectric focussing and an N-terminal amino acid sequence Val Leu Pro Asp Ser Ile Asp Trp Arg Gln Lys Gly Ala Val Thr Glu Val Lys Asn Arg Gly, which fraction of bromelain is obtainable by the following method:

- (i) dissolving bromelain in 20 mM acetate buffer at pH 5.0 containing 0.1 mM EDTA sodium;
- (ii) separating the components of the bromelain by fast protein liquid chromatography on SP-sepharose HP, eluting with a linear gradient of 0 to 0.8 M sodium chloride in acetate buffer over 300 mL; and
- (iii) collecting the fraction corresponding to the third peak off the column, appearing on the ascending edge of the first main stem bromelain protease peak.

EP-B1 – 1012304 – Claim 1:

An isolated protein which has a molecular weight of about 27.45 kDa as determined by SDS-PAGE, an isoelectric point of 9.7 as determined by isoelectric focusing and an N-terminal amino acid sequence Val Leu Pro Asp Ser Ile Asp Trp Arg Gln Lys Gly Ala Val Thr Glu Val Lys Asn Arg Gly, which isolated protein is a component of bromelain obtainable by the following method:

- (i) dissolving bromelain in 20 mM acetate buffer at pH 5.0 containing 0.1 mM EDTA sodium;
- (ii) separating the components of the bromelain by fast protein liquid chromatography on SP-sepharose HP, eluting with a linear gradient of 0 to 0.8 M sodium chloride in acetate buffer over 300 mL;
- (iii) collecting the fraction corresponding to the third peak off the column, appearing on the ascending edge of the first main stem bromelain protease peak; and
- (iv) isolating the protein from the fraction obtained at step (iii).

This claim contains the term “isolated”, which should be avoided if possible.

EP-B1 – 1496113 – Claim 1:

A gluconate dehydratase comprising an amino acid sequence having a homology of at least 95% with the amino acid sequence shown in SEQ ID No: 1, and capable of dehydrating D-gluconic acid to produce 2-keto-3-deoxy-D-gluconic acid, wherein the gluconate dehydratase maintains at least 95% of the enzyme activity thereof after being allowed to stand in 30 mM tris(hydroxymethyl) aminomethane buffer solution with a pH of about 8.5 containing 1 mM of sodium D-gluconate and 1 mM of magnesium chloride at 55°C for 2 hours.

EP- B1 – 2277997 – Claim 1:

A polypeptide having cellobiohydrolase I activity, selected from the group consisting of:

- (a) a polypeptide comprising an amino acid sequence which has at least 90% identity with amino acids 1 to 457 of SEQ ID NO: 8,
- (b) a polypeptide comprising an amino acid sequence which has at least 90% identity with the polypeptide encoded by nucleotides 1 to 1371 of SEQ ID NO: 7.

EP-B1 – 1626088 – Claim 1:

A protease, which cleaves a glycosylated amino acid and/or a glycosylated peptide from a glycosylated β -chain N-terminal of glycosylated hemoglobin without substantially cleaving a glycosylated amino acid or a glycosylated peptide from a glycosylated α -chain N-terminal of glycosylated hemoglobin, wherein the protease is;

- (i) obtained from a bacterium belonging to the genus *Lysobacter* and comprises an amino acid sequence according to SEQ ID NO:15; or
- (ii) obtained from *Bacillus* sp. ASP-842 (FERM BP-08641) and having a molecular weight of about 35kDa as determined by SDS-PAGE; or
- (iii) *Aeromonas hydrophila* (NBRC 3820) and comprises an amino acid sequence according to SEQ ID NO:12.

EP- B1 – 2085472 – Claim 1:

D-serine dehydratase comprising the following protein (a) or (b):

- (a) a protein having an amino acid sequence set forth in SEQ ID NO: 1; or
- (b) a protein having an amino acid sequence having 70% or more similarity to the amino acid sequence set forth in SEQ ID NO: 1 and having a D-serine dehydratase activity, which does not react with L-serine and wherein a reactivity to D-threonine is not more than 5% when a reactivity to D-serine is 100%.

EP-B1 – 1523553 – Claim 1:

A protease variant, which is a variant of a precursor *Bacillus lentus* subtilisin protease having the sequence shown in Figure 3, said variant being characterized by having the same net electrostatic charge at pH 7 or the same isoelectric point as said precursor protease, and comprising an amino acid sequence having the substitutions R170SA1R, R170S-G61R, R170S-N204R, R170S-S216R or R170S-G100R relative to said precursor protease, wherein the positions of said substitutions are equivalent to the specified positions in the mature *Bacillus amyloliquefaciens* subtilisin shown in Figure 3.

D.III.2.i.c. Product claims characterizing a protein by the coding capacity of a certain DNA

A protein may also be characterized by a DNA encoding it. Depending on the characterization of the DNA, the claim may embrace only one specific protein or a variety of proteins containing substitutions, deletions, insertions, point mutations, etc.

Claim drafting:

A claim characterizing a protein by the coding capacity of a certain DNA may have the following general wording:

A protein being encoded by DNA X.

Examples of such claims granted by the EPO are shown below; the encoding nucleic acid is underlined.

EP-B1 – 0093619 – Claim 16 underlying decision T 923/92 (Human t-PA/GENENTECH):

A protein having human tissue plasminogen activator function and which comprises a derivative, by way of amino acid deletion, substitution, insertion, inversion, addition or replacement of the 527 amino acid sequence as encoded by the DNA product of claim 1 or claim 2.

The above claim is interesting in that it covers not only the amino acid sequence actually derivable from the DNA sequence, but also amino acid

sequences differing therefrom by way of amino acid deletion, substitution, insertion or inversion.

EP-B1 – 0220574 – Claim 1:

A recombinant human interferon-b2A in purified form obtainable by transfecting eukaryotic cells with a vector containing the cDNA sequence depicted in Figure 1, cultivating the transfected cells and isolating the interferon-b2A from the culture medium.

EP-B1 – 0318216 – Claim 1:

A polypeptide in substantially isolated form comprising a contiguous sequence of at least 10 amino acids encoded by the genome of hepatitis C virus (HCV) and comprising an antigenic determinant, wherein HCV is characterized by:

- (i) a positive stranded RNA genome;
- (ii) said genome comprising an open reading frame (ORF) encoding a polyprotein; and
- (iii) said polyprotein comprising an amino acid sequence having at least 40% homology to the 859 amino acid sequence in Figure 14.

Features (i) to (iii) of the above claim characterize the HCV, from which the specific amino acids should be derived.

D.III.2.i.d. Product claims characterizing a protein by its structure

The most important structural characteristic of a protein is its primary sequence. However, for retaining the biological activity of a protein the primary sequence does not necessarily need to be maintained unchanged. Therefore, a claim characterizing a protein by its amino acid sequence should include references to certain deviations of this sequence, such as amino acid deletions, substitutions, insertions or inversions or mutants or allelic variants or by a degree of identity to a defined sequence, as shown in the following examples.

Further structural features suitable to characterize the protein are, e.g. the glycosylation pattern of a protein, the degree of glycosylation, the presence of disulfide bridges, its existence in the form of dimers or multimers as well as the nature of association between different subunits, etc.

Claim drafting:

A claim characterizing a protein by its amino acid sequence may for instance be cast as follows:

- A protein X comprising the amino acid sequence of SEQ ID NO: Y.*
- A protein X having a higher degree of glycosylation than protein X from natural sources.*
- A protein X being composed of three subunits of protein Y.*

Examples of claims containing structural features granted by the EPO are shown below. The structural features are indicated by underlining.

EP-B1 – 0101309 – Claim 13:

A polypeptide with human H1-preprorelaxin activity, said polypeptide being selected from the following group:

- (a) a polypeptide having the amino acid sequence shown in Figure 2 A and B that corresponds to human H1-preprorelaxin;
- (b) a polypeptide that in respect to (a) is deficient in one or more amino acids;
- (c) a polypeptide in which in respect to (a) one or more amino acids are replaced with different amino acids;
- (d) a polypeptide in which in respect to (a) one or more amino acids are added to the sequence; or
- (e) a fusion polypeptide comprising an amino acid sequence consisting of all or part of the amino acid sequence of human H1-preprorelaxin shown in Figure 2 A and B as its C-terminal sequence and a portion of a procaryotic protein as its N-terminal sequence.

Part (a) of the claim is directed to the specific protein provided in said patent, whereas parts (b) to (e) allow for certain modifications. Interestingly, these modifications are mentioned as alternatives and are not necessarily cumulative.

EP-B1 – 0318216 – Claim 1:

A polypeptide in substantially isolated form comprising a contiguous sequence of at least 10 amino acids encoded by the genome of hepatitis C virus (HCV) and comprising an antigenic determinant, wherein HCV is characterized by:

- (i) a positive stranded RNA genome;
- (ii) said genome comprising an open reading frame (ORF) encoding a polyprotein; and
- (iii) said polyprotein comprising an amino acid sequence having at least 40% homology to the 859 amino acid sequence in Figure 14.

Features (i) to (iii) of the above claim characterize the HCV, from which the specific amino acids should be derived.

EP-B1 – 0226181 – Claim 1:

An angiogenic factor (bFGF) comprising a purified, human or synthetic single-chain polypeptide protein exhibiting substantial homology to the native angiogenic factor isolatable from human placental tissue (post partum), wherein said angiogenic factor has at least one active site possessing an activity selected from the group consisting of mitogenic activity, chemotactic activity, the ability to stimulate protease synthesis, and combinations thereof, the angiogenic factor comprising the amino acid sequence:

L-Y-C-K-N-G-G-F-F-L-R-I-H-P-D-G-R-V-D-G-V-R-E-K-S-()-P-H-I-K-L-Q-L-Q-A-E-E-R-G-V-V-S-I-K-G-V-C-A-N-R-Y-L-A-M-K-()-D-G-()-L-L-A-()-K-()-V-T-()-E-()-F-F-F-E-()-L-E-S-N-N-Y-N-T-Y-R-()-;

and optionally

K-L-G-S-K-T-G-P-G-Q-K-A-I-L-F-L-P-M-S-A-K;

and optionally

Y-()-S-W-Y-V-()-L-()-.

The above claim contains non-limiting features in the form of the “optionally” wording.

EP-B1 – 0239425 – Claim 16:

Antigen having the following amino acid sequence or a part of said sequence, providing that it raises a specific immunological reaction with the antibodies against HIV-2 retrovirus, according to anyone of claims 1 to 9, especially when this antigen is contacted with the serum of a patient infected with HIV-2: (...)

EP-B1 – 0148605 – Claim 20 underlying **T 412/93 (Erythropoietin/KIRIN-AMGEN):**

A recombinant polypeptide having part or all of the primary structural conformation of human or monkey erythropoietin as set forth in Table VI or Table V or any allelic variant or derivative thereof possessing the biological property of causing bone marrow cells to increase production of reticulocytes and red blood cells and to increase hemoglobin synthesis or iron uptake and characterized by being the product of procaryotic or eucaryotic expression of an exogenous DNA sequence.

EP-B1 – 1759001 – Claim 1:

A bone delivery conjugate having the structure:

Z-sALP-Y-Dn-X,

wherein X is absent or is an amino acid sequence of at least one amino acid;

Y is absent or is an amino acid sequence of at least one amino acid;

Z is absent or is an amino acid sequence of at least one amino acid;

Dn is a poly aspartate wherein n = 10 to 16; and

sALP is a soluble alkaline phosphatase.

EP-B1 – 1064019 – Claim 1:

A chemically modified mutant enzyme with one or more amino acid residues from an enzyme being replaced by cysteine residues, wherein at least some of the cysteine residues are modified by replacing thiol hydrogen in the cysteine residue with a thiol side chain, wherein the enzyme is a protease, and wherein the amino acid replaced with a cysteine is in a subsite of the enzyme selected from the group consisting of S1, S1', and S2, and wherein the thiol side chain is selected from the group consisting of:

-SCH₂ (p-OCH₃-C₆H₄).

-SCH₂ (p-COOH-C₆H₄).

and

-SCH₂C₆F₅,

and wherein said chemically modified mutant enzyme has an increased esterase to amidase ratio as compared to the corresponding wild type enzyme.

EP-B1 – 1523553 – Claim 1:

A protease variant, which is a variant of a precursor *Bacillus lentus* subtilisin protease having the sequence shown in Figure 3, said variant being characterized by having the same net electrostatic charge at pH 7 or the same isoelectric point as said precursor protease, and comprising an amino acid sequence having the substitutions R170SA1R, R170S-G61R, R170S-N204R, R170S-S216R or R170S-G100R relative to said precursor protease, wherein the positions of said substitutions are equivalent to the specified positions in the mature *Bacillus amyloliquefaciens* subtilisin shown in Figure 3.

EP-B1 – 2092061 – Claim 1:

Polypeptide isolated from plants of family Brassicaceae, in particular genus *Arabidopsis*, preferably species *Arabidopsis thaliana*, having the amino acid sequence of SEQ ID NO. 1, exhibiting at least the activity of a hydroxynitrile lyase and being (R) – selective,

characterized by one or more of the amino acid replacements in respect of SEQ ID NO. 1 set forth hereunder:

- a) Asparagine at position 12 by threonine (N12T) or alanine (N12A);
- b) Tyrosine at position 14 by cysteine (Y14C) or alanine (Y14A);
- c) Leucine at position 129 by tryptophan (L129W), wherein the replacements Y14C and L129W cause a change of enantioselectivity.

EP-B1 – 2085472 – Claim 1:

D-serine dehydratase comprising the following protein (a) or (b):

- (a) a protein having an amino acid sequence set forth in SEQ ID NO: 1; or
- (b) a protein having an amino acid sequence having 70% or more similarity to the amino acid sequence set forth in SEQ ID NO: 1 and having a D-serine dehydratase activity, which does not react with L-serine and wherein a reactivity to D-threonine is not more than 5% when a reactivity to D-serine is 100%.

D.III.2.i.e. Product claims characterizing a protein by a process for its preparation

As is the case with any other biotechnological subject-matter, it is also possible under certain conditions to draft product-by-process claims for proteins. For further general information in connection with product-by-product claims, see C.I.3.e.a.

Claim drafting:

A product by process claim relating to a protein may have the following general wording:

A protein X obtainable by a process comprising steps...

Examples of granted claims directed to proteins obtainable by a process for their preparation are shown below. The process features are underlined in the following examples.

EP-B1 – 0220574 – Claim 1:

A recombinant human interferon-b2A in purified form obtainable by transfecting eukaryotic cells with a vector containing the cDNA sequence depicted in Figure 1, cultivating the transfected cells and isolating the interferon-b2A from the culture medium.

EP-B1 – 0308378 – Claim 2:

The TNF Inhibitory Protein according to claim 1, obtainable from human urine by

- (a) submitting the fraction, which is non-dialyzable through a membrane with molecular weight cut-off at 10 KDa to lectin affinity chromatography;
- (b) eluting the protein adsorbed to the lectin;
- (c) subjecting the eluted protein to gel filtration or to ion exchange chromatography; and
- (d) recovering those fractions which inhibit the binding of TNF to its receptors and the cytotoxic effect of TNF.

EP-B1 – 1865055 – Claim 1:

An isolated fraction of bromelain comprising a protein of molecular weight of about 27.45 kDa as determined by SDS-PAGE, an isoelectric point of 9.7 as determined by

isoelectric focussing and an N-terminal amino acid sequence Val Leu Pro Asp Ser Ile Asp Trp Arg Gln Lys Gly Ala Val Thr Glu Val Lys Asn Arg Gly, which fraction of bromelain is obtainable by the following method:

- (i) dissolving bromelain in 20 mM acetate buffer at pH 5.0 containing 0.1 mM EDTA sodium;
- (ii) separating the components of the bromelain by fast protein liquid chromatography on SP-sepharose HP, eluting with a linear gradient of 0 to 0.8 M sodium chloride in acetate buffer over 300 mL; and
- (iii) collecting the fraction corresponding to the third peak off the column, appearing on the ascending edge of the first main stem bromelain protease peak.

This claim contains the term “isolated”, which should be avoided if possible.

EP-B1 – 1012304 – Claim 1:

An isolated protein which has a molecular weight of about 27.45 kDa as determined by SDS-PAGE, an isoelectric point of 9.7 as determined by isoelectric focussing and an N-terminal amino acid sequence Val Leu Pro Asp Ser Ile Asp Trp Arg Gln Lys Gly Ala Val Thr Glu Val Lys Asn Arg Gly, which isolated protein is a component of bromelain obtainable by the following method:

- (i) dissolving bromelain in 20 mM acetate buffer at pH 5.0 containing 0.1 mM EDTA sodium;
- (ii) separating the components of the bromelain by fast protein liquid chromatography on SP-sepharose HP, eluting with a linear gradient of 0 to 0.8 M sodium chloride in acetate buffer over 300 mL;
- (iii) collecting the fraction corresponding to the third peak off the column, appearing on the ascending edge of the first main stem bromelain protease peak; and
- (iv) isolating the protein from the fraction obtained at step (iii).

This claim contains the term “isolated”, which should be avoided if possible.

EP-B1 – 1824775 – Claim 1:

A debriding composition obtained from bromelain, the debriding composition comprising proteolytic enzymes having molecular weights of about 23 kDa, said composition being substantially devoid of bromelain inhibitors.

EP-B1 – 1626088 – Claim 1:

A protease, which cleaves a glycosylated amino acid and/or a glycosylated peptide from a glycosylated β -chain N-terminal of glycosylated hemoglobin without substantially cleaving a glycosylated amino acid or a glycosylated peptide from a glycosylated α -chain N-terminal of glycosylated hemoglobin hemoglobin, wherein the protease is;

- (i) obtained from a bacterium belonging to the genus *Lysobacter* and comprises an amino acid sequence according to SEQ ID NO:15; or
- (ii) obtained from *Bacillus* sp. ASP-842 (FERM BP-08641) and having a molecular weight of about 35kDa as determined by SDS-PAGE; or
- (iii) *Aeromonas hydrophila* (NBRC 3820) and comprises an amino acid sequence according to SEQ ID NO:12.

EP-B1 – 2092061 – Claim 1:

Polypeptide isolated from plants of family Brassicaceae, in particular genus *Arabidopsis*, preferably species *Arabidopsis thaliana*, having the amino acid sequence of SEQ ID NO. 1, exhibiting at least the activity of a hydroxynitrile lyase and being (R) – selective, characterized by one or more of the amino acid replacements in respect of SEQ ID NO. 1 set forth hereunder:

- a) Asparagine at position 12 by threonine (N12T) or alanine (N12A);
- b) Tyrosine at position 14 by cysteine (Y14C) or alanine (Y14A);
- c) Leucine at position 129 by tryptophan (L129W), wherein the replacements Y14C and L129W cause a change of enantioselectivity.

This claim contains the term “isolated”, which should be avoided if possible.

EP-B1 – 0220574 – Claim 1:

A recombinant human interferon-b2A in purified form obtainable by transfecting eukaryotic cells with a vector containing the cDNA sequence depicted in Figure 1, cultivating the transfected cells and isolating the interferon-b2A from the culture medium.

EP-B1 – 0148605 – Claim 20 underlying T 412/93 (Erythropoietin/KIRIN-AMGEN):

A recombinant polypeptide having part or all of the primary structural conformation of human or monkey erythropoietin as set forth in Table VI or Table V or any allelic variant or derivative thereof possessing the biological property of causing bone marrow cells to increase production of reticulocytes and red blood cells and to increase hemoglobin synthesis or iron uptake and characterized by being the product of procaryotic or eucaryotic expression of an exogenous DNA sequence.

D.III.2.i.f. Product claims comprising proteins as essential elements

As indicated in the introduction to this chapter, proteins have gained enormous economic importance in diagnosis and therapy, including prophylaxis. Typical examples of such products comprising proteins as essential elements are, for example, vaccines, kits for diagnostic purposes, microarrays, pharmaceutical compositions, etc.

Claim drafting:

A product claim relating to a kit comprising a protein may have the following general wording:

A kit for detecting compound X comprising protein Y.

A claim directed to a vaccine/pharmaceutical preparation can have the following general wording:

A vaccine/pharmaceutical preparation comprising protein X.

Examples of claims granted by the EPO and relating to embodiments comprising a protein as an essential element are shown below. The product in question comprising the protein is underlined.

EP-B1 – 0181150 – Claim 21:

A diagnostic reagent, immunogen or vaccine capable of binding an anti-HIV-I antibody in human serum characterized in that said reagent consists of an antigen comprising an immunogenic fragment of at least seven amino acids of an HIV-I env, gag or pol polypeptide, which fragment is immunologically non-cross-reactive with HTLV-I and HTLV-II and which has a sequence contained in the sequence shown in Figure 2.

EP-B1 – 0181150 – Claim 31:

An article of manufacture for use in an immunoassay for HIV-I antibodies characterized in that it comprises a solid support having bound thereto a recombinant polypeptide according to claim 22.

EP-B1 – 0309566 – Claim 13:

A diagnostic system in kit form for assaying for the presence of anti-HIV-2 antibodies in a body fluid sample comprising a package containing a polypeptide consisting essentially of no more than about 50 amino acid residues and including an amino acid residue sequence represented by the formula:

–CAFRQVC–,

said polypeptide being capable of immunoreacting with antibodies induced by HIV-2.

EP-B1 – 0309566 – Claim 28:

A diagnostic system in kit form comprising a solid support comprised of a solid matrix having operatively affixed thereto, in admixture, first, second, and third polypeptides having amino acid residue sequences represented by the formula, respectively;

AIEKYLEDDQAQLNAWGCAFRQVC

IWGCSGKLICTTAVPWNAS, and

AVERYLKDQQLGIWGCSGCKLI.

EP-B1 – 0134242 – Claim 11:

A vaccine against malaria comprising as an active ingredient the peptide of any of claims 1 to 10 and a carrier.

EP-B1 – 0013828 – Claim 6 underlying decision T 886/91 (Hepatitis B virus/BIOGEN INC.):

A means for detecting HBV infections in blood serum characterized by at least one polypeptide according to claim 4 or coded for by a DNA sequence according to claim 1.

EP-B1 – 2143790 – Claim 1:

A pharmaceutical composition comprising recombinant batroxobin having the following properties:

- (a) the batroxobin has a molecular weight of 29–32kDa;
- (b) at least 90% of batroxobin have 6 pairs of disulfide bonds which correctly match at Cys7–Cys139, Cys26–Cys42, Cys74–Cys230, Cys118–Cys184, Cys150–Cys163 and Cys1174–Cys199;
- (c) positions 146 and 225 in SEQ ID NO:1 are modified as N-glycosylation; and
- (d) the specific activity of the batroxobin is equal to or greater than 1500KU/mg protein, and a pharmaceutically acceptable carrier; wherein said composition further comprises a hydrolyzed gelatin as a stabilizer.

EP-B1 – 1421175 – Claim 1:

A polymer-proteinase conjugate, comprising an initial Proteinase K covalently linked to three to seven polymer strands per molecule of said Proteinase K said conjugate having integrated enzymatic activity in a solution containing 0.5% SDS, 0.1 M GdnSCN or 2–4 M urea at a temperature of about 50°C that is about or greater than two times the integrated enzymatic activity of said initial Proteinase K under comparable conditions.

EP-B1 – 0734437 – Claim 1:

Enzyme immobilized carrier, selected from the group comprising penicillin-G amidase (EC 3.5.1.11), glutaryl-7-ACA acylase and D-amino acid oxidase (EC1.4.3.3), which by means of covalent bond is fixed to an aminofunctional organosiloxane polymer carrier material.

EP-B1 – 1750757 – Claim 1:

A formulation comprising a chondroitinase in a sodium phosphate buffer at a concentration of about 750 to 1000 mM.

D.III.2.j. Process claims for proteins

Proteins may be obtained by any of the following routes:

- (i) chemical synthesis,
- (ii) isolation from their natural environment, such as isolation from naturally occurring cells, fungi, algae, plants or animals, and
- (iii) isolation from recombinant microorganisms programmed to express the desired protein.

The preparation of proteins by *chemical* synthesis is not considered in the following discussion.

D.III.2.j.a. Process claims involving isolation from a natural environment

Proteins are constituents of any cellular organisms and also occur as a secreted product of specialized cells, e.g. in the form of milk protein. In order to provide the pure protein, i.e. essentially without contaminants from their natural environment, enrichment and purification procedures have to be developed. In many cases these procedures are composed of several steps, each of which might be known in the art. However, a new combination of such steps may nevertheless involve an inventive step.

Claim drafting:

A general claim relating to a process for isolating a protein from its natural environment may have the following wording.

A process for isolating protein X comprising the steps of ...

Examples of such process claims granted by the EPO are the following. The sources of the proteins are underlined.

EP-B1 – 0029191 – Claim 2:

Process for preparing or enriching the protein PP11 according to claim 1, which comprises subjecting an extract obtained from human placenta by means of a saline solution to one or more of the following measures:

- a) precipitating the Protein PP11 with ammonium sulfate in the pH-range of from 5 to 8 and at a saturation of 30 to 60%;
- b) precipitating the Protein PP11 with a water-soluble acridine base at a pH-value of between 4 and 9 and a concentration of the base of from 0.2 to 0.8 g/100 ml;
- c) euglobulin precipitation at a pH of from 5 to 6 in a diluted salt solution, whereby accompanying proteins are separated and PP9 is not precipitated;
- d) preparative zone electrophoresis, whereby the >>b1-globulin fraction
- e) gel-filtration or ultrafiltration, whereby proteins in the molecular weight range of from 30000 to 90000 are isolated;
- f) adsorbing PP11 on a weakly basic ion exchanger and eluting it;
- g) immuno-adsorptive enrichment of PP11.

EP-B2 – 0049611– Claim 3 (underlying decision T 877/90 (T-cell growth factor/HOOPER):

A process for producing a serum-free and mitogen-free T-cell growth factor comprising:

- (1) separating peripheral mononuclear blood cells from a human, bovine or porcine donor;
 - (2) stimulating the cells by incubating the cells in a liquid tissue culture medium supplemented with serum and mitogen;
 - (3) separating and washing the stimulated cells to remove substantially all of the serum and mitogen;
- and
- (4) conditioning the cells obtained in step (3) by incubating the cells in the presence of a serum-free and mitogen-free liquid tissue culture medium to transfer the T-cell growth factor into the liquid medium.

EP-B1 – 1343897 – Claim 1:

A method of producing a refolded, inactive HCV NS2/3 protease, comprising the steps of:

- a) isolating said protease in the presence of a chaotropic agent;
 - b) refolding said isolated protease by contacting it with a reducing agent, and lauryldiethylamine oxide (LDAO) in the presence of reduced concentration of said chaotropic agent or a polar additive.
- Interestingly, the above claim does not indicate the starting material for the isolation step a).

EP-B1 – 1074616 – Claim 1:

Process for the preparation of the proenzyme of the protease activating blood clotting factor VII in pure and stable form, **characterized in that** the proenzyme of the protease activating blood clotting factor VII is obtained from biological fluids or those obtained in the case of preparation by genetic engineering by anion- and/or cation-exchange chromatography at a pH of between 2.5 and 7.2.

D.III.2.j.b. Process claims involving synthesis by recombinant host cells

This type of process claim has become very important over the years, since with the increasing number of available genes coding for proteins of commercial interest, there is an increasing demand for processes allowing large scale production of the desired protein in a suitable host cell. Examples for host cells as well

as the principle routes for causing them to express a gene coding for a desired protein are state of the art. Therefore, processes for recombinant production of a protein constitute in many instances processes of analogy.

Claim drafting:

A process claim relating to the recombinant production of a protein may have the following general wording:

A process for preparing protein X, comprising cultivating recombinant host cell Y and isolating protein X from the cultivated cells.

Examples of claims relating to the recombinant production of a protein granted by the EPO are the following; the recombinant process features are underlined.

EP-B1 – 0060057 – Claim 23:

A method of producing a heterologous polypeptide which comprises culturing a yeast strain of any one of claims 16 to 22, and isolating said biocompetent polypeptide from the culture medium.

EP-B1 – 0032134 – Claim 27 underlying decision **T 301/87 (Alpha-interferons/BIOGEN):**

A method for producing an α -type interferon comprising the steps of culturing a host selected from bacteria, yeasts or animals cells and transformed by a recombinant DNA molecule according to any of claims 8 to 10 and collecting said polypeptide.

EP-B1 – 0148605 – Claim 29 underlying decision **T 412/93 (Erythropoietin/KIRIN-AMGEN):**

A process for production of a polypeptide having at least part of the primary structural conformation of erythropoietin to allow possession of the biological property of causing bone marrow cells to increase production of reticulocytes and red blood cells and to increase hemoglobin synthesis or iron uptake, which process is characterized by culturing under suitable nutrient conditions a procaryotic or eucaryotic host cell transformed or transfected with a DNA sequence according to any of claims 1, 2, 3, 6, 7 and 8 in a manner allowing the host cell to express said polypeptide; and optionally isolating the desired polypeptide product of the expression of the DNA sequence.

EP-B1 – 0077670 – Claim 19 underlying decision **T 223/92 (HIF-Gamma/GENENTECH):**

A process which comprises expressing human immune interferon in a mammalian cell line transformed with the DNA depicted in Figure 5 hereof or an allelic variant thereof.

EP-B1 – 0022242 – Claim 20 underlying decision **T 347/87 (Cloning vehicle/GENENTECH):**

A method of producing human growth hormone in a manner known per se which comprises:

- (a) disposing a culture according to Claim 19 within a fermenter vessel comprising aeration and agitation means in an aqueous, nutrients-containing fermentation broth;

- (b) growing up the culture under aeration and agitation while supplying additional nutrients as required to maintain vigorous growth;
- (c) separating the resulting cellular mass from the fermentation broth;
- (d) lysing the cells to free the contents thereof;
- (e) separating cellular debris from supernatant; and
- (f) isolating and purifying human growth hormone contained in the supernatant.

Claim 19 is directed to a bacterial culture containing recombinant plasmids.

***EP-B1 – 0214971 – Claim 12* underlying decision **T 816/90 (CBHII/ALKO)**:**

A method of producing the fungal cellulase enzyme cellobiohydrolase II, said method comprising the cultivation of a yeast strain according to any one of claims 7 to 9 under conditions where the strain produces the enzyme and recovering the enzyme.

Claims 7–9 are directed to yeast strains containing a recombinant vector.

***EP-B1 – 0013828 – Claim 7* underlying decision **T 886/91 (Hepatitis B virus/BIOGEN INC.)**:**

A process for producing at least one polypeptide displaying HBV antigenicity comprising the step of culturing a host according to claim 3.

Claim 3 is directed to transformed bacterial host cells.

***EP-B1 – 0047600 – Claim 17* underlying decision **T 283/86 (–/THE REGENTS OF THE UNIVERSITY OF CALIFORNIA)**:**

A process for synthesizing bovine growth hormone characterised by incubating a microorganism transformed by an expression transfer vector comprising a deoxynucleotide sequence coding for said bovine growth hormone prepared in accordance with any of claims 8 to 12 under conditions suitable for expression of said sequence coding for bovine growth hormone and purifying bovine growth hormone from the lysate or culture medium of said microorganism.

***EP-B1 – 0054331 – Claim 9* underlying decision **T 281/86 (Preprothaumatin/UNILEVER)**:**

A process for producing preprothaumatin or any of its maturation forms prethaumatin, prothaumatin or thaumatin, which process comprises transforming a host cell by incorporating a cloning vehicle as claimed in claim 4 in said host cell, culturing the transformed cell and isolating the preprothaumatin or any of its maturation forms produced by said transformed cell.

***EP-B1 – 0185076 – Claim 14*:**

A method of making a hybrid protein as claimed in any one of claims 1 to 12, the method comprising expressing a fused gene.

***EP-B1 – 0134242 – Claim 18*:**

A process for the production of a polypeptide according to any of claims 1 to 8 characterized in that the polypeptide is produced by culturing a microorganism containing a recombinant vector and recovering the polypeptide from the culture, wherein said vector is obtainable by screening a cDNA library for an expressed protein containing the immunochemically reactive region of the sporozoite surface antigen protein using a mono-

clonal antibody and inserting the Plasmodium specific DNA encoding the repeat epitope of the immunodominant region of a circumsporozoite protein into the vector, said vector being capable of expressing the polypeptide.

EP-B1 – 1074616 – Claim 1:

Process for the preparation of the proenzyme of the protease activating blood clotting factor VII in pure and stable form, characterized in that the proenzyme of the protease activating blood clotting factor VII is obtained from biological fluids or those obtained in the case of preparation by genetic engineering by anion- and/or cation-exchange chromatography at a pH of between 2.5 and 7.2.

D.III.2.k. Use claims/purpose-limited product claims for proteins

As noted in C.I.3.e.a., use claims are interpreted as process claims. An exception are the so-called purpose-limited product claims for medical applications. Use claims may be directed to the use of proteins for biochemical processes, e.g. the use of enzymes as biocatalysts or to the use of proteins in the food industry. The most important applications of proteins are, however, in the field of pharmaceuticals, where so-called purpose-limited product claims are commonly drafted. Examples of such claims are shown in the following.

Claim drafting:

A general claim relating to the use of proteins could have the following wording:

Use of protein X for catalyzing reaction Y.

Further options for claim wording:

Protein X for use in the treatment of disease Y (or formerly, Use of protein X for preparing a medicament for the treatment of disease Y).

The latter type of claim is a second medical use claim, discussed in C.I.3.e.d.

Examples of use claims granted by the EPO are shown below; the uses/purposes are underlined.

EP-B1 – 00077670 – Claim 31 underlying decision **T 223/92 (HIF-Gamma/GENENTECH):**

The use of human immune interferon according to any one of claims 1 to 8, or as prepared by a process of any one of claims 19 to 30, in preparing pharmaceutical compositions.

EP-B1 – 0049611 – Claim 16 underlying decision **T 877/90 (T-cell growth factor/HOOPER):**

The use of a T-cell growth factor as claimed in Claim 1 or 2 to sensitise a line of cells to prepare an agent for use against parasites or bacteria.

EP-B1 – 0029191 – Claim 3:

Use of the protein according to claim 1 for preparing an antiserum for detecting and determining this protein.

EP-B1 – 0200748 – Claim 8:

The use of TNF as defined in claim 1 or 2 in making a medicament.

EP-B1 – 2007885 – Claim 1:

Use of a therapeutic polypeptide, fused directly or via a linker peptide to a polypeptide enhancing the in-vivo recovery as compared to the in-vivo recovery of the corresponding non-fused therapeutic polypeptide, and wherein the recovery enhancing polypeptide is albumin, a naturally occurring polymorphic variant or a fragment thereof, wherein the fragment is at least 20 amino acids long, for increasing the in-vivo recovery.

EP-B1 – 1330262 – Claim 1:

Enzymes from ciliates for use as a medicament, selected from the group consisting of hydrolases, lipases, proteases, amylases, glycosidases, phospholipases, phosphodiesterases, phosphatases.

EP-B1 – 0897667 – Claim 1:

Use of cellobiohydrolase-_I (CBH-_I) in an effective amount to improve:

- (i) handling properties of a dough
- (ii) the bread volume; and/or
- (iii) bread crumb structure.

EP-B1 – 1908823 – Claim 1:

Ananain or a mixture of ananain and comosain for use in treating a cancer by blocking MAP kinase pathways in a cancer cell.

D.IV. Antibodies

D.IV.1. Introduction

This chapter discusses possible ways for protecting antibodies under the EPC. Since antibodies are a kind of specific protein, many of the statements as given above under D.III. also apply to antibodies. Still, antibodies have some particular features which deserve special attention. Moreover in past years, antibodies have become extremely important for the pharmaceutical market, in which several drugs based on antibodies have entered the market.

The term “antibody” as used herein means a full antibody comprising two heavy and light chains as well as antibody derivatives such as Fab, F(ab)₂ fragments or single chain Fv fragments.

Details on the patentability requirements are provided in the following.

D.IV.2. Protecting antibodies under the EPC

As for any other subject-matter in the life science field, claims relating to antibodies must fulfill the legal requirements of the EPC. In particular, they must not fall within the exclusion provisions laid down in Arts. 52 and 53 EPC. In

addition, the claimed subject-matter has to meet the further patentability requirements of novelty, inventive step and industrial application. Furthermore, the application has to fulfill the requirements of sufficiency of disclosure and clarity and support of the claims, as discussed in C.I.3.b., C.I.3.e.b. and C.I.3.e.c.

Several decisions of the EPO relating to the above patentability requirements and the requirements of the application will be briefly discussed in connection with antibodies. The cited decisions are particularly informative and important, and should be taken into account when drafting applications directed to antibodies.

D.IV.2.a. Discoveries

According to Art. 52(2) EPC, discoveries shall not be regarded as inventions, but shall be excluded from patent protection. In their decision “**RELAXIN**” an Opposition Division dealt with the question whether the finding of a DNA coding for human relaxin or one of its biological precursors is a discovery within the meaning of Art. 52(2) EPC. In the reasons for the decision, the Opposition Division referred to the Guidelines (C-IV, 2.3 as available at that time, now G-II,5.2), stipulating:

[T]o find a substance freely occurring in nature is mere discovery and therefore unpatentable. However, if a substance found in nature has first to be isolated from its surroundings and a process for obtaining it is developed, that process is patentable. Moreover, if this substance can be properly characterised by its structure and it is new in the absolute sense of having no previously recognised existence, then the substance per se may be patentable. (point 5.1)

The Opposition Division concluded:

The above guideline is highly appropriate in the present case. Human H2-relaxin had no previously recognised existence. The proprietor has developed a process for obtaining H2-relaxin and the DNA encoding it, has characterized these products by their chemical structure and has found a use for the protein. The products are therefore patentable under Article 52(2) EPC. (point 5.2)

In conclusion, the subject-matter of the disputed patent does not represent a discovery and is hence not excluded from patentability under Article 52(2) EPC. (point 5.5)

The above finding was also confirmed by an Appeal Board dealing with the Relaxin case. In **T 272/95 (Relaxin/HOWARD FLOREY INSTITUTE)**, the Board held that the claims do not fall under Art. 52(2) EPC by referring to the then-valid Rule 23(e) (2), now corresponding to Rule 29(2) EPC (reasons, point 7).

Thus, according to present case law as well as according to the Guidelines, antibodies obtained from natural sources are considered to be naturally occurring products which may be patentable. Of course, recombinantly produced antibodies should face no problems at all under Art. 52(2) EPC.

Although the decision “**RELAXIN**” is primarily concerned with DNA-related claims, it may be assumed that antibodies obtained from natural sources such as polyclonal sera are also considered to be naturally occurring products and, thus, are to be treated in the same manner as naturally occurring DNA.

In **T 338/00 (Multimeric Receptors/SALK INSTITUTE)**, an Appeal Board confirmed the above finding in the **RELAXIN** case for a protein where a heterodimeric receptor was found to be more than a mere discovery. In particular, the Board held that the claimed receptor could be exploited in industry and hence was more than a mere description of an interesting research result.

For further discussion relating to naturally occurring products, see C.I.3.a.a.

D.IV.2.b. Morality and “ordre public”

According to Art. 53(a) EPC, inventions the exploitation of which would be contrary to “ordre public” or morality, are excluded from patent protection. There is no decision discussing the allowability of an antibody under Art. 53(a) EPC. However, the criterion provided by the Guidelines (G-II,4.1) is applied for antibodies as for any other matter:

A fair test to apply is to consider whether it is probable that the public in general would regard the invention as so abhorrent that the grant of patent rights would be inconceivable. If it is clear that this is the case, objections should be raised under Art. 53(a); otherwise not.

D.IV.2.c. Methods of treatment

According to Art. 53(c) EPC, methods for the treatment of the human or animal body by surgery or therapy and diagnostic methods practised on the human or animal body shall not be regarded as inventions which are susceptible of industrial application.

Methods of raising antibodies in the human or animal body could conflict with Art. 53(c) EPC if the method also has a prophylactic effect against certain infections (see e.g. **T 780/89 (Immunostimulating composition/BAYER)**). Whether one may delimit such a claim from a therapeutic method by way of disclaimer will have to be made on a case-by-case basis.

D.IV.2.d. Novelty

In **T 130/90 (Recombinant monoclonal antibody/UNIVERSITY OF TEXAS SYSTEM)**, an Appeal Board considered the process of producing a certain kind of monoclonal antibody to be the only possible way of distinguishing the claimed subject-matter from a prior art reference. As a consequence, the Board allowed the following claim:

A recombinant monoclonal antibody *produced* by cultivation of a quadroma cell of Claim 5 and/or a trioma cell of Claim 6 and comprising intact immunological chains and containing F(ab')₂ and Fc portions, each F(ab') portion having specific binding affinity for a respective different desired antigenic determinant, whereby the antibody has dual specificity. (emphasis added)

In the reasons for the decision, the Board emphasized that the phrasing “produced by” was necessary in order to render the subject-matter of the above cited claim novel over the prior art:

[A]s it is not possible to distinguish the antibodies of the patent in suit over the prior art antibodies of document (5) otherwise than by limiting them to the product directly obtained by the specific process of their preparation, such a feature is accepted as a distinguishing parameter for the purpose of novelty. This view is apparently also accepted by the Appellants whose auxiliary request clearly shows that in the present case they accept a significant difference of the meaning of the two expressions “produced by” and “obtainable by”, for the purpose of defining the antibodies of the patent in suit compared to those described in document (5).

The very specific circumstances of the present case, which differ from those having been the basis of the decisions of the Boards of Appeal as mentioned above under paragraph 3.3, which entered into the Guidelines for substantive examination (C-III, 4.7b) [now F-IV, 4.12], make the expression “produced by” necessary. The respective part in the Guidelines states that: “A product is not rendered novel merely by the fact that it is produced by means of a new process”. In the present case, however, as reasoned above, it is the process which renders the product novel. (point 4.12)

In the above case, the claim basically is limited to the product of the process and does not confer the claim absolute product protection.

In **T 1212/97 (Immunoglobulin preparations/GENENTECH)**, the Board discussed whether the feature “chimeric” would distinguish the claimed antibodies from the natural antibodies of the prior art. The Board agreed with the Patentee-Appellant that the natural antibodies of the prior art contain species-specific amino acid residues. However, the Board did not share the view that the chimeric antibody could be distinguished from the natural antibodies of the prior art by the fact that it carries residues specific for different species. The Board’s main argument was that at the priority date there was not sufficient knowledge about the species-specificity of individual residues, so based on a molecular analysis the skilled person could not identify the species to which an amino acid at a given position would belong. Therefore, the Board did not consider the term “chimeric” as a distinguishing technical feature.

In **T 735/00 (Anti-CRP antibodies/IATRON LABORATORIES, INC.)**, the underlying patent claimed a monoclonal antibody further characterized by the functional feature that the antibody would bind “the side face” of the target protein. The Appeal Board stated that a technical feature needs to be

precisely and reliably described in the patent in suit or in the supporting documents. (point 12)

Given these criteria and the fact that neither the application nor the supporting documents or the prior art precisely defined what the “side face” of the target protein is, the Board held that

this feature is thus vague and open to interpretation when it comes to a judgement on whether or not an antibody of the prior art falls under this term. (point 12)

Therefore, the Board did not consider the feature as a distinguishing feature over the prior art and denied novelty.

In **T 187/04 (Antikörper/KREBSFORSCHUNGSZENTRUM)**, claim 1 of the main request was directed to an antibody targeting the histidine

tail of a fusion polypeptide. The cited prior art document disclosed a polyclonal serum comprising an antibody against the N-terminal His-tag. The Board did not consider the prior art document to anticipate claim 1 of the main request since the prior art merely disclosed a mixture of antibodies (polyclonal serum) also containing antibodies that bind outside of the histidine tail, whereas the subject matter of claim 1 under dispute was functionally individualized such that the only antibodies which were claimed were those that bind the histidine tail. Therefore, the Board held that the cited prior art did not anticipate the subject matter of claim 1.

In **T 601/05 (Anti-TNF α human monoclonal antibodies/BAYER I)**, the claim was directed to a pharmaceutical composition containing a human monoclonal antibody against TNF α . The prior art disclosed sera containing antibodies against TNF α . The question was whether, due to the open language “containing a human monoclonal antibody,” the claim could be read such that it would also comprise polyclonal sera as disclosed in the prior art. The Board gave the claim a more narrow interpretation in that according to the Board

the claim had to be construed such that in addition to one kind of monoclonal antibody, the composition as claimed could not contain many further antibodies or other constituents to an extent that the composition would equal a polyclonal serum.

Therefore, the Board acknowledged novelty.

In **T 405/06 (Immunoglobulins/BRUSSEL)**, the Board discussed the requirements for a novelty-destroying anticipation. The claim in dispute was directed to an immunoglobulin comprising two heavy polypeptide chains, each lacking the CH1 region. Appellant II objected to this claim for lack of novelty over a prior art document. The prior art document disclosed an SDS-PAGE of a camel-IgG preparation identifying three components, two of which were further characterized. The relevant component, however, was only described as “an additional protein band of 40 kD”. Appellant II argued that this band corresponds to the claimed protein, since two post-published documents confirmed the identity of this band. However, the Board emphasized that

all that matters is the whole contents of the said document alone as read and interpreted by the skilled person on the background of common general knowledge, i.e. the knowledge generally available at the relevant filing date, not later. (point 29.1)

Thus, the Board did not take into account the post-published documents further characterizing the band on the SDS-PAGE and did not consider the disclosure of the prior art to anticipate the subject matter of the claimed invention.

In **T 1189/06 (Prostate-specific Antigens/ABBOTT)**, the claim in dispute was directed to an antibody specific for free PSA and further characterized by its method of preparation. The prior art cited against the novelty of this claim disclosed a specific antibody binding free PSA and also binding one of the antigens used for generating the claimed antibody and recited in the claim in dispute. Even though the antibody of the prior art (named 9B10) was not gener-

ated in the same way as the antibody of the underlying application, the Board did not consider this a distinguishing technical feature. The Board held that

the question is not whether 9B10 is identical to a specific (as yet unidentified) antibody falling within the scope of the claim, but rather whether 9B10 is at all distinguishable from an antibody which belongs to the group of antibodies which are now claimed. In this respect, in so far as the chemical structure of the antibody is not a characteristic which “tells” the way in which the antibody was isolated, it must be concluded that the process of isolation of mAb9B10 does not impart said antibody with specific and unique structural characteristics which would make it irrelevant to novelty. (point 4)

In this case the Board in essence upheld the general principle that a product (here an antibody) had to be novel over the prior art independent of its process of preparation. Therefore, the Board held that the prior art anticipated the claimed antibody.

D.IV.2.e. Inventive Step

Some general principles are already discussed under D.IV.1. The following refers to further pertinent case law.

T 499/88 (Immunoglobulins/UNILEVER) is the first of a number of decisions concerning the patentability of monoclonal antibodies. In the case underlying **T 499/88**, the Patentee appealed a decision from an Opposition Division revoking the patent which protected a process for the recovery of immunoglobulins from milk including contacting the milk with an insoluble carrier material having bound thereto a monoclonal antibody specific for certain immunoglobulin molecules. The decision was based on lack of an inventive step in view of a prior art document disclosing essentially the same process as claimed, but applying mono-specific polyclonal antibodies instead of (mono-specific) monoclonal antibodies. This document in combination with known purification processes involving monoclonal antibodies was considered to render the claimed subject-matter obvious.

The Board confirmed the decision of the Opposition Division as follows:

The disclosures of documents E2, E3 und E4 summarised above in the Board's view clearly reflect a common general knowledge of the skilled men in the art in 1980 as to the use of monoclonal antibodies in place of monospecific polyclonal antibodies for immunopurification. Since these documents do not contain any information about any disadvantages in using the monoclonal antibodies, in the Board's judgement at the priority date of the patent it did not require an inventive step for a skilled man to replace monospecific polyclonal antibodies by monoclonal antibodies. (point 4.14)

T 36/90 (Tumor cells/BOGOCH) concerned an Applicant's appeal against the refusal of an application including claims directed to a process for the quantitative *in vitro* detection of cancerous or malignant tumor cells in a cell collection regardless of the cell type of the cancerous or malignant tumor cells. The process involved the use of a specific monoclonal antibody preferentially attaching to cancerous cells. The application was also directed to a test kit comprising

this monoclonal anti-cancer antibody and to the monoclonal anti-cancer antibody as such.

The prior art already disclosed polyclonal anti-cancer antibodies which can be used *in vitro* or *in vivo* for the non-quantitative detection of cancerous cells regardless of the cell type. A severe disadvantage of the prior art polyclonal antibodies was that, due to their cytotoxicity, these antibodies were not suitable for a *quantitative* detection of cancerous or malignant tumor cells. Further, a document reviewing the essentials in the field of monoclonal antibodies described the non-cytotoxicity (due to monospecificity) of monoclonal antibodies. The Board dismissed the proprietor's argument that the prior art would not suggest that a monoclonal cancer antibody having applicability regardless of the cell-type could be prepared. In the Proprietor's opinion, everything in the review article would have led to the opposite assumption, i.e. to the cell-type specificity of monoclonal antibodies. The Board held that the knowledge of polyclonal anti-cancer antibodies described in the first prior art document, in connection with the precise knowledge of the desired property, namely non-cytotoxicity, derivable from the review article, rendered the claimed subject-matter obvious.

T 683/90 (Tumor localisation/GOLDENBERG) discusses the inventive step involved in providing a sterile injectable composition comprising a monoclonal antibody fragment specific for a tumor associated marker and detectable by an external photoscanning device. The Board again asked whether a skilled person would have considered the claimed composition in the expectation of an improvement or advantage over the prior art. The closest prior art disclosed a composition essentially as claimed, but applied complete or partial polyclonal antibodies, i.e. polyclonal antibody fragments instead of monoclonal antibody fragments. A further document described successful tumor localization and treatment using specific antibodies and suppressing the background noise due to a large excess of radiolabeled monospecific antibodies. The Board concluded that the latter document provided a strong incentive to solve the problem arising from the shortcomings of the polyclonal technique described in the prior art by making use of the technically superior monoclonal antibodies. The Board concluded that the person skilled in the art

would, therefore, certainly have tried to replace the polyclonal antibody fragments by monoclonal ones. Under these conditions the Board considers the improvement to correspond to what was to be expected by the skilled person. Consequently, the claimed solution cannot be regarded as surprising. (point 2.8)

T 906/91 (Hybridoma/E.I.DU PONT) concerns an Opponent's appeal against the decision of an Opposition Division to maintain a patent directed to a monoclonal antibody to theophylline having 5% or less cross-reactivity with caffeine. The closest prior art disclosed radioimmunoassays for theophylline using an antiserum having good selectivity for theophylline and a cross-reactivity of 4.2% with caffeine, which differs from theophylline only by one methyl group (theophylline is 1,3-dimethyl xanthine, caffeine is 1,3,7-trimethyl xan-

thine and theobromine is 3,7-dimethyl xanthine). The claimed antibody thus differed from the prior art only in being monoclonal.

The Board, having considered several documents, held:

What emerges from the foregoing is that at the priority date of the patent in suit, the advantageous properties of monoclonal antibodies over polyclonal antibodies (antisera) were common knowledge, these being the possibility of selection during their production for high specificity, a desired affinity and/or avidity, and the fact that an unlimited supply became available once they had been obtained. Accordingly, taking into account the various cautionary statements contained in the above-cited documents, the weight of their content is that at the priority date of the patent in suit it was an obvious step to replace polyclonal antibodies by monoclonal antibodies with a reasonable expectation of an improvement in properties, including that of specificity. (point 10)

The Board further examined whether any of the arguments provided by the proprietor could support an inventive step in view of the cited prior art. As outlined in point 16 of the decision, overcoming difficulties in providing the monoclonal antibodies, for example, in the “all important screening protocol”, would have been suitable. However, in the absence of any evidence to that effect, an inventive step was not acknowledged. Consequently, the patent was revoked.

T 915/93 (Monoclonal antibody therapy/ORTHO) is concerned with an Applicant’s appeal against the refusal of a European patent application by an Examining Division. Claim 1 of the application reads as follows:

A product comprising at least two ligands for sequential use in therapy or diagnosis, wherein each ligand includes a monoclonal antibody antigen binding site which is functionally equivalent (as regards antigen binding) to the antigen binding site of each of the other ligand(s), and each ligand has a distinct idio type.

The closest prior art disclosed xenosensitization due to the production of anti-OKT3 antibodies in patients. The authors of this document observed that these antibodies exhibited anti-isotypic and anti-idiotypic specificity, with the anti-idiotypic specificity being responsible for the abrogation of the therapeutic effect.

The Board confirmed the decision of the first instance. It was argued that selecting idiotypically distinct anti-T3 monoclonal antibodies for consecutive use in therapy did not require anything out of the ordinary in the field of biomedical research, since anti-T3 monoclonal antibodies were readily available. The Board concluded that it would have been obvious for a skilled person to try the suggestion offered by the closest prior art document and that he/she would have done so with a reasonable expectation of success thereby arriving in a straightforward manner at something falling within the terms of present claim 1. Consequently, the appeal was dismissed.

In **T 512/94 (Monoclonal antibody (OKT10)/ORTHO PHARMACEUTICAL CORPORATION)**, the appeal lay from the decision of the Opposition Division, maintaining a patent directed to a monoclonal antibody essentially specific for human thymocytes. In light of prior art also related to a

monoclonal antibody against human thymocytes and in the absence of any “meaningful” differences between the claimed antibody and the antibody of the prior art, the Appeal Board defined the objective technical problem as the provision of an alternative antibody directed against human thymocytes. Therefore, the Board considered the question whether the skilled person would have had a “reasonable expectation” that the problem could be solved. Given the prior art relating to the method of Koehler and Milstein for producing monoclonal antibodies, the Board held the following:

[O]nce a monoclonal antibody with essentially the same properties as desired had been isolated, the skilled person would consider the isolation of another equivalent antibody as reasonably feasible, if only by following the very same method. (point 28)

Thus the Board denied an inventive step for the provision of alternative monoclonal antibodies.

In **T 457/95 (Immunoassay/ABBOTT LABORATORIES)**, the appeal lay from the decision of the Opposition Division rejecting an opposition against the underlying patent. This appeal was largely concerned with the correct formulation of the objective technical problem. The Appeal Board noted that

the proper yardstick for defining a problem is what is actually achieved vis-à-vis the closest prior art, namely the ultimate technical effect. [...] This yardstick may change according to which art is known at the time the assessment is made. (point 6)

As can be seen from this passage the Board emphasized two points: the fact that the technical effect used for formulating the objective problem has to be actually realized and that this technical effect is determined in comparison to the closest prior art.

In **T 626/00 (Framework-mutated antibodies/WELLCOME)**, the appeal lay against the decision of the Opposition Division to revoke the underlying patent *inter alia* for a lack of inventive step. In contrast the Appeal Board considered an inventive step to be present and commented on the requirements for combining the teachings of the closest prior art and additional prior art or common general knowledge in disproving an inventive step.

When answering the question whether a skilled person would have applied a certain technical measure, it is necessary to show that there is a recognizable pointer in the state of the art to combine the known means for achieving the intended technical aim. (point 31)

The Board considered it demonstrated by multiple prior art references that the scientific community working in the field in question at the priority date was adhering to developed methods and was engaged in developing those further. Therefore, the Board concluded that a pointer as mentioned above was absent and that the skilled person would not have combined the closest prior art with the common general knowledge to solve the problem in the claimed way.

In **T 735/00 (Anti-CRP antibodies/IATRON LABORATORIES, INC.)**, the Board followed the reasoning already established by the Board in **T 512/94** and argued that the provision of an alternative antibody to the same

target as the antibodies of the prior art cannot be considered contributing to an inventive step, since at the priority date of the underlying patent in 1989 the generation of a monoclonal antibody was a matter of routine experimentation. The Board added that the presence of a surprising technical effect could help overcome this lack of an inventive step, however, that in this case no such effect could be determined. Thus, even though the claim scope was very narrow – individual antibodies defined by their corresponding deposited hybridoma cell lines – the Board decided that this claim did not fulfill the requirement of Article 56 EPC and, in the end, revoked the patent. Contrary to the USPTO, the EPO does not acknowledge structural non-predictability (here the structure of the deposited antibody) as an argument for an inventive step.

In **T 645/02 (Antikoerper/EBERHARD-KARLS-UNIVERSITAET)**, the Appeal Board commented on the issue of inventive step for monoclonal antibodies directed to targets for which monoclonal antibodies are disclosed in the prior art. While the Board acknowledged that the claimed antibody had characteristics that display “elements of surprise”, which can be understood as a surprising technical effect, it also developed a different reasoning in supporting an inventive step. Here, the Board contrasted the “theoretical possibility” of generating a monoclonal antibody with the actual provision of a specific antibody with defined characteristics, the latter warranting acknowledgement of an inventive step (as argued by the Board at least in combination with the “elements of surprise”). Furthermore, the Board referred to decision **T 737/96 (Astaxanthin/DSM)**, in which the isolation of a specific mutant from a random mutagenesis screen was not considered obvious even though using the screening method was. The Board acknowledged an inventive step because the specific properties of the antibody were not foreseeable from the prior art.

In **T 542/03 (Combination/BERLEX)**, the Appeal Board had to consider the question of inventive step of claims directed to a combination comprising an anti-hormonal compound and a binding molecule binding a cancer target. In contrast to the Appellant’s argument, the Board argued that the skilled person would have considered using the model disclosed in the prior art. Further, the Board pointed to the fact that no obstacles, difficulties or pitfalls speaking against an inventive step were encountered when using the model disclosed in the prior art. So, as a final test for inventive step, the Board considered whether the skilled person would have used the model with some expectation of success. In referring to previous case law in **T 333/97 (Somatic changes/MONSANTO)**, the Board held that the skilled person might have had at least a “try and see” attitude in approaching the model. Therefore, the Board found the claimed combination to lack an inventive step. This case shows that a “reasonable expectation of success” is not always required to deny an inventive step.

In **T 187/04 (Antikoerper/KREBSFORSCHUNGSZENTRUM)**, the Appeal Board had to decide on the inventive step of a claim directed to a monoclonal antibody binding the poly-histidine tail of a fusion peptide vis-à-vis the prior art disclosing the histidine tail as well as polyclonal antibodies against dif-

ferent metal binding peptides. The Board arrived at the conclusion that the provision of the claimed monoclonal antibody using routine methods was an obvious task for the skilled person at the priority date. Considering an auxiliary request further limiting the claimed antibody by reference to a deposit number, the Board stated that

the fact that a monoclonal antibody is provided for the first time in individualized manner is not sufficient to justify an inventive step (point 11, translated).

Thus, this decision stands in contrast to the position that was contemplated by the Board in **T 645/02**.

In **T 601/05 (Anti-TNF alpha human monoclonal antibodies/BAYER I)**, the appeal lay from a decision of the Opposition Division revoking the underlying patent. Claim 1 of the main request was directed to a pharmaceutical composition containing a human monoclonal antibody that binds to human tumor necrosis factor alpha. The closest prior art disclosed a murine monoclonal antibody binding tumor necrosis factor alpha. The Board decided that claim 1 as mentioned above could not be derived in an obvious way from the closest prior art largely based on the following argument:

Consequently, in summarizing the above (see points 8.3, 10 to 10.8), the Board concludes that at the priority date the skilled person, on the one hand, would have considered it possible to generate human monoclonal antibodies binding to TNF-alpha with low affinity. However, he/she would not have considered them as pharmaceutically useful. On the other hand, the skilled person was convinced that antibodies binding to TNF-alpha with high affinity would be pharmaceutically useful. However, he/she would not have had a reasonable expectation to succeed in generating them. Therefore, it follows that, at the priority date of the patent, the skilled person would have thought that pharmaceutically useful TNF-binding human monoclonal antibodies could not be generated and would therefore not have attempted to provide them with a reasonable expectation of success.

Thus, in this case, the technical feature “a pharmaceutical composition” and its associated technical effect of pharmaceutical usefulness contributed to the acknowledgement of an inventive step.

In **T 251/07 (Inhibition of angiogenesis/SCRIPPS)**, the claim in dispute of the underlying patent was directed at the second medical use of an antibody for the treatment of several diseases, *inter alia* certain types of cancer. The closest prior art disclosed data of this antibody inhibiting tumor growth of different types of cancer based on a different mechanism than the one disclosed in the underlying patent. The Board concluded that, based on the mechanism disclosed in the prior art, it would not have been obvious to the skilled person to apply the antibody to the claimed cancer types, since it was not disclosed in the prior art that these types (claimed by the underlying invention) were also amenable to the described mechanism.

In **T 418/07 (Human anti-TNF α antibodies/ABBOTT)**, the appeal lay from the decision of the Opposition Division to maintain the underlying patent directed to a human antibody against human TNF α further characterized *inter alia* by a high affinity towards TNF α . The prior art disclosed a murine antibody

also directed against human TNF α and methods for humanizing antibodies as well as human antibodies with low affinity towards TNF α .

The Appeal Board held that

[t]he relevant question to be answered in the context of the assessment of inventive step is whether the skilled person would [...] have the comfort of a reasonable expectation that the identification of a human antibody falling within the scope of the independent claims would be successful.

In its analysis the Board thus required the concept of reasonable expectation of success to be seen in relation to the technical features of the claim. In the current case the question was whether the provision of a human high affinity antibody could be reasonably expected. The Board denied this and stated:

Thus evaluating the “reasonable expectation of success” involves analyzing the prior art to determine the degree of confidence it gives the skilled person that an envisaged result will be obtained. If that degree of confidence is too low, the reasonable expectation turns into a mere “hope to succeed”. A skilled person working on that basis follows a non-obvious course of action.

In **T 782/07 (Human antibodies/WELLCOME)**, the appeal lay from the decision of the Opposition Division to maintain the underlying patent in amended form. Claim 1 of the main and the auxiliary requests was directed to a method for the production of a recombinant human antibody. In light of the prior art, the Board held that the skilled person would have had a reasonable expectation of success to arrive at the claimed invention. In this context the Board explained that less ambitious goals underlying the claimed invention are usually associated in the case law with higher expectations of success (reasons, point 35).

This comment alludes to the issue that broad claims may cause problems with regard to the “reasonable expectation of success” criterion in the assessment of inventive step, meaning that the less ambitious the goals (i.e. the broader the claim), the higher the expectation of success and thus, the more likely that the invention will be considered to be obvious.

D.IV.2.f. Industrial application

The requirement of “industrial application” for antibodies is basically the same as for proteins in general. Reference is therefore made to section D.III.2.f.

D.IV.2.g. Sufficiency of disclosure

As indicated in C.I.3.b.b., the EPC allows the depositing of microorganisms under Rule 31 EPC to supplement a written disclosure in order to comply with Art. 83 EPC. Regarding the definition of a person skilled in the art who is relevant for evaluating the sufficiency of disclosure, see C.I.3.b.

Some of the most important decisions relating to sufficiency of disclosure of inventions concerning antibodies are briefly summarized below.

T 299/86 (Monoclonal anti α -Interferon antibody/SECHER) confirmed the principle already established in **T 281/86 (Preprothaumatin/**

UNILEVER) that the disclosure of examples does not need to be identically reproducible. In **T 299/86**, one of the reasons for refusing the application by an Examining Division was that a specific hybridoma produced by using freely available cell lines and antigens had not been deposited. This hybridoma was not claimed, and its preparation was described in detail in one of the examples. It was acknowledged by the Applicant and also by the Board that the particular hybridoma in question was not repeatable without undue burden.

However, the Board confirmed the view of **T 281/86** stating:

[T]he requirements under Article 83 EPC are not such that a specifically described example of a process must be exactly repeatable [...] Thus the description provides support for the view that hybridomas excreting the claimed monoclonal antibody are not so rare that the process as a whole would not lead reliably to the claimed substance. In the absence of evidence to the contrary it is thus the Board's position that the description provides a sufficient disclosure repeatably to produce the claimed monoclonal antibody reliably and there is thus no need to reproduce identically the example given in the specification. (point 12)

In the opposition appeal proceedings resulting in **T 418/89 (Monoclonal antibody/ORTHO)**, the following claim was at issue:

Mouse monoclonal antibody which (i) reacts with essentially all normal human peripheral T cells, but (ii) does not react with any of the normal human peripheral cells in the group comprising B cells, null cells and macrophages.

According to the specification, the hybridoma producing a claimed monoclonal antibody could be produced by using E-rosette-positive purified normal human peripheral T cells as the antibody stimulating antigen. The Board held:

However, this fact alone is not sufficient to make the process reproducible as to monoclonal antibodies having the characteristics of claim 1. To select a hybridoma of the desired kind in any case means a huge amount of effort and, above all, *it is not certain* that this hybridoma can be selected at all. (point 3.4) (emphasis added)

The Board considers that in the circumstances of the present case, where the written description of how to produce a hybridoma is basically the known cumbersome and random general process and a specific technical teaching is provided only by identifying the type of the antigen, being E-rosette positive purified normal human peripheral T-cells, the requirements of Article 83 EPC are not met. (point 3.7)

The Patentee had deposited a hybridoma which, according to statutory declarations filed by the Opponents, did not satisfy the requirements of claim 1. The information provided by the Opponents corresponded to that disclosed in later published documents. The Patentee did not contest these results. Thus, the Board concluded:

[T]he "example" constituted by the deposition does not correspond to the written description. (point 3.11)

The Patentee filed an auxiliary request relating to the deposited hybridoma. However, the Board held:

Thus, even if one could have considered the possibility of restricting the scope of the patent to what had been deposited and thus leaving aside any information provided in the writ-

ten disclosure of the patent in suit, including the discussion of the state of the art, the problem and the solution, and the industrial application which would not at all correspond to the characteristic of the “invention” represented by the deposited hybridoma, the said “invention” would not be sufficiently disclosed because the true characteristics of the monoclonal antibodies produced by the deposited hybridoma were nowhere described and thus not available to the public. Therefore, no technical teaching is provided which would allow an examination of patentability. Thus, a mere deposit of a hybridoma without any corresponding written description does not provide a sufficient disclosure of a technical teaching within the meaning of Article 83 EPC. (point 5.3)

Further it proved to be extremely difficult to obtain antibodies from the deposited hybridomas. The Board commented on this as follows:

[T]he Board is of the opinion that a disclosure provided by a deposit of a hybridoma according to Rule 28 EPC is not regarded as being sufficient within the meaning of Article 83 EPC, if and when it is only possible to reproduce the invention after repeated requests to the depositary institution and by applying techniques considerably more sophisticated than those recommended by the depositary institution. (point 3.14)

In **T 431/96 (Monoclonal antibody/AGEN)**, the underlying patent claimed monoclonal antibodies and methods of detection of cross linked fibrin derivatives. The Board pointed out that under Art. 83 EPC the relevant question is whether the description provides enough information to enable the skilled person to obtain the claimed subject-matter without undue burden and without applying inventive skill. The Board noted that the reactivity of the claimed monoclonal antibodies is readily testable and that even though the testing might involve some tedious and time consuming work, it does not entail anything but common routine techniques for the skilled person at the priority date of the patent in suit. Furthermore, the Board pointed out that there is no obligation to deposit biological material (i.e. the hybridomas) to facilitate the execution of the invention if the invention can be repeated on the basis of the written description. Thus, sufficiency of disclosure was acknowledged.

In **T 669/97 (Chimeric Antibodies/CELLTECH THERAPEUTICS LTD)**, the underlying patent *inter alia* claimed a process for the production of a chimeric antibody comprising part of an IgG molecule and part of a non-IgG protein in mammalian cells. Appellant II challenged the underlying patent on the basis of Art. 83 EPC, citing a document disclosing a fusion protein according to the underlying invention that could not be produced in mammalian cells due to a lack of transfection efficiency. The Board, however, considered this lack of transfection as an occasional failure not allowing a conclusion as to the feasibility of obtaining the fusion protein according to the underlying invention. This is an example of the established principle that occasional failure is not necessarily detrimental to sufficiency of disclosure and a reasonable amount of trial and error is permissible.

In **T 1212/97 (Immunoglobulin preparations/GENENTECH)**, the claims in dispute were directed to a method for preparing immunoglobulins from eukaryotic or prokaryotic cells. The Appeal Board considered the subject

matter not sufficiently disclosed, since no example was given of how to produce the claimed chimeric IgGs in eukaryotic cells and the only prokaryotic example disclosed the production of IgGs in the form of inclusion bodies. The underlying claims recited the transformation of prokaryotic or eukaryotic host cells and the recovery of the immunoglobulins from the host cell. While the Board in **T 292/85** decided that the application did not have to provide instructions for all possible variants under the claim, the Board in **T 1212/97** emphasized that this case law did not apply in the present case, since the application did not provide even a single way to enable the skilled person.

In **T 792/00 (Varied binding proteins/DYAX)**, the Board commented on the issue of sufficiency of disclosure in the light of merely hypothetical examples. While the Board acknowledged the case law holding that examples are not absolutely necessary, it was of a different opinion in the present case. Here, according to the prevailing technical opinion at the priority date of the present application, the claimed subject-matter was considered impossible. In such a case, where the claimed subject-matter runs contrary to the general technical opinion, the merely hypothetical experimental protocol is not enough to enable the skilled person to carry out the invention without undue burden. This is summarized in headnote 2 of the decision:

If for an invention which goes against prevailing technical opinion the Patentee has failed to give even a single reproducible example, sufficiency of disclosure cannot be acknowledged.

In **T 411/02 (CTL4A receptor/BRISTOL-MYERS SQUIBB)**, Appellant II argued that the patent in dispute was granted on the basis of incorrect science and thus as a whole was not enabled. The Board did not accept this reasoning and held that

it is the technical teaching in a patent specification as such, and not a presumed (and possibly wrongly) scientific explanation why a certain effect is achieved if this teaching is carried out, which has to fulfill the requirements of Article 83 EPC. (point 47)

Thus, since the functional technical features of the underlying claims were enabled, it did not matter for the question of sufficiency of disclosure whether or not the underlying scientific concept was correct.

In **T 1300/05 (RET Screening Assay/PROGENICS)**, the Examining Division denied sufficiency of disclosure for the underlying application with regard to the complex functional feature in claim 1 of the main request

wherein said antibody inhibits HIV-1 envelope glycoprotein mediated membrane fusion between Hela-envJR-FL and said cell line, but does not inhibit HIV-1 envelop glycoprotein mediated membrane fusion between Hela-envLAI and Sup-T1 cells or between Hela-envLAI and Hela-CD4+ cells.

However, the Board reaffirmed the previous position as taken in other cases that laborious experiments are not identical to undue burden:

Admittedly, testing several hundred clones amounts to much work, but in the Board's judgment, it is not tantamount to undue burden, the more so that the testing method is known and that there's no doubt as to the outcome of the experiment. (point 9)

In **T 1466/05 (Pyridinoline/SEREX)**, claim 1 of the underlying patent refused by the Examining Division was directed to

an antibody reactive with pyridinoline in peptide-linked pyridinoline and not free pyridinoline which is useful in an assay to indicate bone resorption.

In essence, the Board considered the subject-matter insufficiently disclosed since the skilled person

would have to embark on a research program with the sole guidance of a desideratum, namely that the antibodies must react specifically with the pyridinoline in peptide-linked pyridinoline, but without any teaching in the application as how to achieve the desired specificity. (point 16)

While the application disclosed one specific monoclonal antibody deposited according to the instructions of the EPC, in the Board's view the application did not disclose

a screening process which would lead necessarily and directly, with a reasonable amount of trial and error, towards the specific selection of antibodies as claimed. (point 19)

While the Board considered the one specific monoclonal antibody potentially sufficiently disclosed for a claim merely directed at said antibody, however, it denied sufficiency of disclosure for the broad functionally characterized claim.

In **T 433/07 (Opsonic antibodies/HENRY M. JACKSON FOUNDATION)**, the claim under dispute was directed to a method comprising multiple steps for producing an antibody. The claim required the antibody to bind at least two serotypes of a particular staphylococcus strain. The claim however did not encompass the specific antigen, which would be required to raise an antibody possessing said functional feature. Discussing sufficiency of disclosure, the Appeal Board held that

a European patent application containing a claim referring to a method of production has to provide the skilled person with the means to produce the desired product (here with a common epitope to produce a serotype cross reactive monoclonal antibody). If this is not the case, this shortcoming can not be overcome by telling him/her exactly how the desired product has to look and which screening criteria has to be applied to find it. (point 3)

Hence, sufficiency was not acknowledged.

In **T 617/07 (Monoclonal NGF-antagonist antibodies/LAY LINE)**, one of the claims of the underlying patent was directed to a monoclonal antibody characterized by functional features as well as structural features. Appellant II held that the subject-matter of the claim was not sufficiently disclosed in the application, since it would require an undue burden to the skilled person to identify those antibodies falling under the structural definitions and fulfilling the functional features as well. The Appeal Board did not share this opinion and held that while

there is no doubt that the structural definition in claim 20 includes antibodies that do not have the desired function [...] the skilled person would be able to avoid non-functional variants based on his/her common general knowledge.

Thus, the Board did not consider it an undue burden for the skilled person to identify those antibodies that fulfill the structural as well as the functional criteria of the claim.

D.IV.2.h. Clarity and support of claims

In the case underlying **T 299/86 (Monoclonal anti α -Interferon antibody/SECHER)**, an Examining Division rejected the following claim as being unclear due to the term “specific activity”:

A monoclonal antibody to human interferon- α characterised in that in a process for the immunopurification of a crude sample of extracellular medium from stimulated Namalva cells containing interferon- α at a specific activity of 2×10^4 U/mg, an increase in the specific activity of about 5000 fold is achieved in a single pass through a 0.5 ml immunoadsorbent column produced by coupling the monoclonal antibody to CNBr-activated Sepharose at 14 mg of monoclonal antibody per ml of Sepharose.

According to the Examining Division, there existed several different methods for determining interferon- α activity, resulting in different definitions of interferon- α units. Consequently, clarity was denied.

The Board observed that the activity of human interferon- α is measured relative to an international standard reference sample of interferon- α in Reference Research Units (U) per unit mass (mg). Further, the Board was satisfied that the standard sample to which reference was made was a publicly held international standard maintained under an international treaty. The Board thus considered the term “specific activity” to have a clear meaning for a person skilled in the art. The Board further held:

Therefore, it is not necessary to incorporate the definition of the feature into the claims, because the meaning of the feature is clearly defined by the description. According to Article 84 the claims shall define the matter for which protection is sought, but they need not give a perfect instruction how the invention is to be used. Moreover, pursuant to Article 84, second sentence, EPC conciseness is a special requirement for claims. One way to draft a concise claim is by making use of features which are clearly defined in the description. There are no objections to such a method, unless the clarity of the claim is so affected that a person skilled in the art would have difficulties understanding what is meant by the claim. No such difficulties arise in the present case. (point 4)

A further issue was the definition of the claimed invention by functional features. As already established by **T 68/85 (Synergistic herbicides/CIBA-GEIGY)**, which concerned classical chemical compounds, functional features are permissible if, from an objective view point, such features cannot otherwise be defined more precisely without unduly restricting the scope of the invention and if these features provide instructions which are sufficiently clear for the

skilled person to reduce them to practice without undue burden. The applicability of this principle in the field of biotechnology was established by **T 292/85 (Polypeptide expression/GENENTECH I)**.

In view of a claim directed to a monoclonal antibody underlying **T 299/86** the Board, by referring to the two decisions cited in the preceding paragraph, held:

According to the Board's view, the prerequisites mentioned in the above decisions are fulfilled here. As to the first prerequisite (impossibility of more precise definition) the exact chemical structure of the claimed monoclonal antibody is not known and thus cannot serve as a basis for a proper definition of this antibody.

As to the second prerequisite (that the technical teaching of the chosen definition has to be clear and repeatable), it seems to be evident that the wording of a claim has to be understood in connection with the description. This principle is for example expressed in Article 69 EPC which states that the extent of the protection conferred by a European patent or a European patent application shall be determined by the terms of the claims, but the description and drawings shall be used to interpret the claims.

A common and clear way to define monoclonal antibodies is by their affinity to a certain substance. This affinity is expressed in the present claims by the ability to bind interferon- α in a certain sample to a certain degree and thus by their affinity to interferon- α . This feature can be understood as an indirect structural feature because the affinity of a monoclonal antibody depends on its stereochemical structure. (point 6)

In **T 130/90 (Recombinant Monoclonal Antibody/UNIVERSITY OF TEXAS SYSTEM)** during the Appeal proceedings, the Patentee filed amended claims comprising claims to antibodies defined as follows (emphasis added).

Main request:

13. An antibody comprising intact immunological chains and containing F(ab')₂ and Fc portions, each F(ab') portion having specific binding affinity for a respective different desired antigenic determinant, whereby the antibody has dual specificity and said antibody is derived from monoclonal source(s).

Auxiliary request:

13. A recombinant monoclonal antibody produced by cultivation of a quadroma cell of Claim 5 and/or a trioma cell of Claim 6 and comprising intact immunological chains and containing F(ab')₂ and Fc portions, each F(ab') portion having specific binding affinity for a respective different desired antigenic determinant, whereby the antibody has dual specificity.

Both claims were interpreted as product-by-process claims due to the wording of the underlined passages. The Board referred to established case law (**T 150/82 (Claim Categories/IFF)**, **T 251/85 (Polyolgemische/CPC INTERNATIONAL INC.)** and **T 248/85 (Radiation Processing/BICC)**) which held that a certain product may be defined by the process of its production if there are no other parameters available for a further definition of the product. The Board was of the opinion that if the only way of limiting a claim over the prior art is the definition of the product by the process of its production, it would be unjustified to leave the inventor without protection only be-

cause the product cannot be defined otherwise. The product-by-process claims were therefore considered allowable under Art. 84 EPC.

In **T 1300/05 (RET screening assay/PROGENICS)**, some claims, e.g. claims 10 and 11 shown below, were directed to antibodies defined by their binding characteristics and the method by which these binding characteristics could be determined.

10. An antibody determined to be capable of specifically inhibiting the fusion of a macrophage-tropic primary isolate of HIV-1 to a CD4+ cell susceptible to infection by a macrophage-tropic HIV-1, wherein such CD4+ cell is a primary human macrophage or a primary human T lymphocyte, using a method which comprises:
[steps (a) to (g)].
11. An antibody capable of specifically inhibiting the fusion of Hela-envJR-FL with primary human macrophages or primary human T lymphocytes, but not the fusion of Hela-envLAI with primary human T lymphocytes.

The Examining Division refused the application on the grounds of lack of clarity and sufficient disclosure of these claims.

The Applicant filed a new main request relating to:

1. A monoclonal antibody generated against a cell-line susceptible to infection by macrophage-tropic HIV-1 isolates, and derived from the HuT 78 T lymphoblastoid cell line, wherein said antibody inhibits HIV-1 envelope glycoprotein mediated membrane fusion between Hela-envJR-FL and said cell-line, but does not inhibit HIV-1 envelope glycoprotein mediated membrane fusion between Hela-envLAI and Sup-T1 cells or between Hela-envLAI and Hela-CD4+ cells.

The Board held that the claims of the main request defined the antibody in a clear manner, since the characteristics of the cells against which it is raised are unambiguous and its binding capacities are identified by reference to specific cell lines. In the Board's judgment, the skilled person would have no difficulties in determining whether or not an antibody falls under the scope of the claim. Interestingly, the Board also remarked on the claims that were refused by the Examining Division on the ground that the claimed antibodies may have been better defined by technical features such as sequence, epitopes and accession number. The Board remarked that the sequence of an antibody is not likely to provide any useful information as to its characteristics, because the determination of epitopes is a downstream development of the isolation of the monoclonal antibody *per se* and an accession number is not suited to characterize a family of antibodies. The Board thus found that the Examining Division's approach to clarity cannot be followed.

In **T 878/09 (Method for the detection of prion proteins/PROTH-ERICS)**, the Opponent raised clarity objections with respect to a claim directed to a method of detecting a prion protein by way of an antibody characterized by its binding epitope. The objection was, however, not directed to the language of the claim itself but to the description passages relating to the subject matter of the claim. The opponent alleged these passages were incon-

sistent with the claim language and that the claim was therefore not supported by the description. The Board, however ruled that the claim as such was clear and there was no need to refer to the description in order to properly understand and implement it. Even if there were discrepancies between the description and the claims in this respect, they would not cast doubt on the meaning of the claim.

In **T 2101/09 (Human Delta3 – Notch/MILLENNIUM)**, claims were i.a. directed to:

5. An isolated polypeptide whose amino acid sequence is at least 95% identical to the amino acid sequence of SEQ ID NO:2.
6. An antibody or antibody fragment that is specifically reactive with the polypeptide of claim 5.

Claim 6 was objected to under Art. 84 EPC by the Opponent due to the term “specifically reactive”. He reasoned that this term was broader than “specifically binding” and would not exclude antibodies cross reactive with another protein.

The Board, however, held that

in order for the claimed antibodies to be “specifically reactive with” or “selectively binding to” the polypeptide of claim 5, they must bind to epitopes that are not present in other polypeptides, in particular, not in those polypeptides which are more closely related and/or structurally similar to the polypeptide of claim 5, since – by their sequence identity and functional conformational folding – they may have the highest probability to have identical or similar epitopes. In the present case, the polypeptide of claim 5 [was] the hDelta3 protein and the structurally closest proteins [were] other members of the Delta family. Thus, the claimed antibodies [were] reactive with those epitopes of the hDelta3 protein that discriminate the hDelta3 protein from other structurally related proteins. The Board [...] is convinced that that this is a technically sensible interpretation of the term “specifically” which is in line with other decisions of the Boards (cf. *inter alia*, T 30/09 of 4 May 2012, in particular points 12 to 18 of the Reasons). (Reasons, point 8)

Furthermore, even though it could not be excluded with absolute certainty that one of the epitopes that discriminate the hDelta3 protein from structurally related proteins will be present in other *unrelated* proteins, it would be a technically sensible interpretation that antibodies raised against these epitopes are not “specifically reactive with” the hDelta3 protein and thus, not within the scope of claim 6.

D.IV.2.i. Product claims for antibodies

As indicated in the introduction to this chapter, antibodies are of commercial interest for a variety of purposes, in particular as active agents for biopharmaceuticals.

Now recombinantly produced monoclonal antibodies are by far more relevant than polyclonal sera. Still, scenarios may exist where polyclonal sera have an advantage over monoclonal antibodies. Polyclonal antibodies are generally made *in vivo* by the immune system of a host challenged with a certain antigen, whereas monoclonal antibodies are produced *in vitro*, e.g. by a hybridoma ob-

tained by fusion of an antibody producing cell from an immunized mammal with an immortalized cell or by phage display technology. The requirements for sufficiency of disclosure of polyclonal antibodies versus monoclonal antibodies differ slightly as discussed below.

Polyclonal antibodies constitute a particular kind of protein isolated from blood. In most instances where polyclonal antibodies are of commercial interest, their production can be induced by immunizing a mammal with an antigen. In that case the reproducibility of the immunizing agent must be assured. For example, if polyclonal antibodies directed against protein X are claimed, it is inevitably required that protein X also be made available, with the Applicant having the choice of safeguarding the availability of protein X by disclosing its sequence, thus allowing chemical synthesis or recombinant production, or depositing a microorganism producing it. In the case of a commercially available immunizing agent, it will be sufficient to indicate the commercial source.

Thus, in order to provide a sufficient disclosure of an invention concerning polyclonal antibodies, it is necessary to make the antigen publicly available.

In the case of *monoclonal antibodies*, the situation is more complex.

An important factor influencing the type of a claim directed to an antibody that is available is based on the question of whether or not the target protein is described in the prior art. One may distinguish between four possible case scenarios as explained in the following:

Case scenario A: The targeted protein is not prior art and consequently the prior art does not describe an antibody recognizing the target protein. In such a case, the EPO normally allows a broad generic claim directed to the antibody; the patentability of the antibody claim basically follows the patentability of the target protein.

According to fairly old case law such as **T 542/95 (TNF/YEDA)**, the Board acknowledged the patentability of broad antibody claims against a new protein. Similar findings are given in more recent decisions such as **T 604/04 (PF4a receptors/GENENTECH)** where generic antibody claims were regarded as in principle admissible even if no antibody has actually been made.

Case scenario B: In the event that the target protein is described in the prior art, but no antibodies against the target protein are described, the patentability basically depends on the characteristics of the antibodies or whether there existed specific difficulties in obtaining antibodies against the target protein. *Prima facie* it is not inventive to provide an antibody against a known protein.

According to case law such as **T 431/96 (Monoclonal antibody/AGEN)** it is routine to generate an antibody to a known antigen but if surprising characteristics are provided for the antibody, an inventive step can still be acknowledged. Similar findings can be found *inter alia* in **T 735/00 (Anti-CRP antibodies/IATRON LABORATORIES, Inc.)** and **T 645/02 (Antibodies/EBERHARD KARLS UNIVERSITÄT)**.

Case scenario C: In this scenario, the target protein is state of the art and some antibodies are already described in the prior art which detect the same tar-

get protein. Antibodies may still be patentable if they show new, unexpected properties which contribute to the solution of an underlying problem.

Case scenario D: In this scenario where the target protein is described in the prior art, the antibody in question is described in the prior art but some new surprising properties are found for the antibody, method and use claims are still available, whereas a product claim is no longer possible.

As regards unexpected properties, the Applicant of course has several options for pointing to unexpected properties, e.g. the antibody may be specific for a new epitope which specificity allows e.g. a more sensitive assay, the interaction of the antibody may trigger an interesting specific physiological reaction of the target protein, the antibody has surprisingly high binding affinity, etc.

D.IV.2.i.a. Product claims characterizing an antibody in functional terms

As for proteins, the characterization of an antibody by functional terms such as a certain activity appears to provide the broadest possible scope, since it may embrace antibodies having fairly unrelated primary structures. It is admissible to define an antibody by function only if the skilled person can identify the antibodies having a certain function without undue burden.

Claim drafting:

A product claim characterizing an antibody by functional terms may have the following general wording:

Antibody X specifically binding to ...

Antibody X capable of preventing interaction between receptor Y and ligand Z.

Examples of product claims containing functional features granted by the EPO are presented below, the functional features are marked by underlining.

EP-B1 – 0068763 – claim 13 of the Main Request and Auxiliary Request in Appeal Proceedings T 130/90 (Recombinant Monoclonal Antibody/UNIVERSITY OF TEXAS SYSTEM)

Main request:

13. An antibody comprising intact immunological chains and containing F(ab')₂ and Fc portions, each Fab' portion having specific binding affinity for a respective different desired antigenic determinant, whereby the antibody has dual specificity and said antibody is derived from monoclonal source(s).

Auxiliary request:

13. A recombinant monoclonal antibody produced by cultivation of a quadroma cell of Claim 5 and/or a trioma cell of Claim 6 and comprising intact immunological chains and containing F(ab')₂ and Fc portions, each F(ab') portion having specific binding affinity for a respective different desired antigenic determinant, whereby the antibody has dual specificity.

The product-by-process claims were considered novel, inventive and clear.

EP-B1 – 0815141 – Claim 1 in T 187/04 (Antikörper/KREBS-FORSCHUNGSZENTRUM)

An antibody against a fusion polypeptide comprising a histidine portion, wherein the antibody is directed against the histidine portion and the latter comprises 6–18 consecutive histidine residues.

Claim above found not inventive; specific deposit was considered inventive.

EP-B1 – 0972041 – Claim 6 in T 2101/09 (Human Delta3 – Notch/MILLENNIUM)

An antibody or antibody fragment that is specifically reactive with the polypeptide of claim 5 [polypeptide at least 95% identical to the amino acid sequence of SEQ ID NO:2].

The Board found that in order for the claimed antibodies to be “specifically reactive with” or “selectively binding to” the polypeptide of claim 5, they must bind to epitopes that are not present in other polypeptides, in particular, not in those polypeptides which are more closely related.

The Board further stated:

It cannot be excluded [...] that one of the epitopes that discriminate the hDelta3 protein from structurally related proteins will be present in other unrelated proteins, antibodies raised against these epitopes are not “specifically reactive with” the hDelta3 protein and thus, not within the scope of claim 6.

The claim was found clear by the Board.

EP-B1 – 0805871 – Claim 1 in T 877/03 (Anti-CD30 antibodies/ROCHE)

An antibody which binds to the CD30 antigen and

- a) releases sCD30 from Hodgkin’s disease cells to an amount of, or less than, 10%, referred to the release found without an addition of antibody;
- b) does not bind to B cell non-Hodgkin’s lymphomas or plasma cells in a manner which can be detected by immune precipitation.

The Board found the claim enabled because the antibodies could be obtained by methods which, although tedious, were nevertheless routine.

EP-B1 – 0956504 – Claim 1 in T 1466/05 (Pyridinoline/SEREX)

An antibody reactive with the pyridinoline in peptide-linked pyridinoline and not free pyridinoline which is useful in an assay to indicate bone resorption.

The antibody was found not to be enabled.

EP-B1 – 0847452 – Claim 1 in T 1300/05 (RET screening assay/PROGENICS)

A monoclonal antibody generated against a cell-line susceptible to infection by macrophage-tropic HIV-1 isolates, and derived from the HuT 78 T lymphoblastoid cell line, wherein said antibody inhibits HIV-1 envelope glycoprotein mediated membrane fusion between Hela-envJR-FL and said cell-line, but does not inhibit HIV-1 envelope glycoprotein mediated membrane fusion between Hela-envLAI and Sup-T1 cells or between Hela-envLAI and Hela-CD4+ cells.

Although much work was required to obtain the antibody, enablement was acknowledged because none of this work constituted undue burden.

EP-B1 – 0018795 – Claims 1 in T 513/94 (Monoclonal antibody (OKT3)/ORTHO PHARMACEUTICAL CORPORATION)

Mouse complement-fixing monoclonal antibody which (i) reacts with essentially all normal human peripheral T-cells but (ii) does not react with any of the normal human peripheral cells in the group comprising B cells, null cells and macrophages.

EP-B1 – 0870025 – Claim 6 in T 414/07 (Diseases of the breast/ ABBOTT)

An antibody which specifically binds to at least one epitope from an amino acid sequence selected from the group consisting of SEQUENCE ID NOS 16–22.

EP-B1 – 0811063 – Claim 16 in T 1429/08 (Chemokine receptor 88C/EUROSCREEN)

An antibody product that specifically binds a human 88C polypeptide consisting of the amino acid sequence set out in SEQ ID NO:2.

EP-B1 – 0773997 – Claim 12 in T 1980/08 (Transmembrane Htk ligand/GENENTECH)

A monoclonal antibody which binds to:
an isolated protein molecule which binds to the Htk receptor and which induces phosphorylation of the Htk receptor, the amino acid sequence of the protein molecule being the amino acid sequence for mature murine Htk ligand of SEQ ID NO: 2 or the amino acid sequence for mature human Htk ligand of SEQ ID NO: 4; or

an isolated soluble Htk ligand which binds to the Htk receptor, the amino acid sequence of the soluble Htk ligand being the amino acid sequence for mature soluble murine Htk ligand of amino acids 28–227 of SEQ ID No 2 or mature soluble human Htk ligand of amino acids 25–224 of SEQ ID No 4;

wherein the monoclonal antibody

is labelled, optionally with a radioisotope, such as ^{3}H , ^{14}C , ^{32}P , ^{35}S , or ^{125}I , a fluorescent or chemiluminiscent compound, such as fluorescein isothiocyanate, rhodamine, or luciferin, or an enzyme, such as alkaline phosphatase, beta-galactosidase or horseradish peroxidase;

is a humanized antibody;

is a human antibody;

is an antibody fusion with a heterologous protein;

is an antibody fragment which binds to the protein molecule which binds to the Htk receptor, e.g. Fab, F(ab')₂ or Fv;

is bispecific; or

is a heteroconjugate antibody.

EP-B1 – 0186833 – Claim 3:

A monoclonal antibody which specifically recognizes and binds a cytotoxin having M.W. of 17,000 6 500 D as determined by polyacrylamide SDS gel electrophoresis.

In opposition proceedings, this claim was amended as follows:

A monoclonal antibody which specifically recognizes and binds a human cytotoxin having M.W. of 17,000 6 500 D as determined by polyacrylamide SDS gel electrophore-

sis, which cytotoxin is recognized and bound by the reference monoclonal antibody produced by the hybridoma cell line CNCM I-472 deposited with the Institute Pasteur.

EP-B1 – 0323806 – Claim 1:

A chimeric monoclonal antibody consisting of variable regions of mouse origin and human constant regions, which recognizes epitopes of human carcinoembryonic antigen (CEA) not present on non-specific cross-reacting antigen NCA55 and NCA95, on biliary glycoprotein, or on granulocytes, and derivatives thereof.

EP-B1 – 0198086 – Claim 6:

Human monoclonal antibody which reacts specifically to varicella zoster virus and recognizes glycoprotein antigens having a molecular weight of 90,000 and 55,000 respectively.

EP-B1 – 0338003 – Claim 5:

A monoclonal antibody which specifically binds to an antigen on the surface of a neutrophil identified as 1D3, said 1D3 antigen having a molecular weight of approximately 48,000 daltons defined under reducing conditions and a molecular weight in the approximate range of 48,000 to 60,000 daltons defined under non-reducing conditions, said 1D3 monoclonal antibody being further characterized as not having binding specificity with respect to:

- A. human acute leukemia cells,
- B. other human peripheral blood cells, and
- C. granulocyte precursor cells in bone marrow.

EP-B1 – 1144006 – Claim 1:

An anti-CCR5 chemokine receptor monoclonal antibody or a fragment thereof, wherein the antibody or fragment thereof binds to the same epitope as that to which monoclonal antibody PA14 binds, PA14 being the monoclonal antibody produced by a hybridoma cell line deposited under ATCC_Accession No. HB-12610 and designated PA 14.

EP-B1 – 2067790 – Claim 1:

An agonist antibody which binds to the extracellular domain of and activates the kinase domain of a receptor protein tyrosine kinase (pTK) SAL-S1.

EP-B1 – 1594533 – Claim 1:

A molecular conjugate of a monoclonal antibody that binds to the human macrophage mannose receptor (MMR) linked to β human chorionic gonadotropin (β hCG), wherein the molecular conjugate is internalized and processed by antigen presenting cells (APCs), such that a T cell-mediated immune response is generated against β hCG.

EP-B1 – 1535930 – Claim 1:

An antibody specific to a central nervous System (CNS) tau protein, wherein the antibody specifically recognizes a CNS tau protein but not a peripheral tau protein and wherein the antibody specifically recognizes an amino acid sequence of a connective portion between the amino acid sequence encoded by Exon 4 of a gene encoding a tau protein and the amino acid sequence encoded by Exon 5 thereof as an epitope.

D.IV.2.i.b. Product claims characterizing an antibody by parameters

Parameters used for characterization of an antibody are, e.g. the binding affinity to its target protein, its solubility or stability in a certain solution, etc. The specification should contain sufficient information to permit determination of the parameters used to describe the antibody.

Claim drafting:

A product claim characterizing an antibody by parameters may have the following general wording.

Antibody X having binding affinity of ... to target Y

In the following claims the parameters are underlined.

EP-B1 – 2041177 – Claim 1:

An antibody or antigen-binding fragment thereof, which specifically binds human interleukin-6 receptor (hIL-6R) with a KD of 500 pM or less, as measured by surface plasmon resonance, wherein the heavy chain CDRs and the light chain CDRs comprise:

- (i) SEQ ID NO: 21, 23 and 25 as respectively heavy chain CDR1, CDR2 and CDR3 and SEQ ID NO: 29, 31 and 33 as respectively light chain CDR1, CDR2 and CDR3; or
- (ii) SEQ ID NO: 149, 151 and 153 as respectively heavy chain CDR1, CDR2 and CDR3 and SEQ ID NO: 157, 159 and 161 as respectively light chain CDR1, CDR2 and CDR3.

EP-B1 – 0186833 – Claim 3:

A monoclonal antibody which specifically recognizes and binds a cytotoxin having M.W. of 17,000 6 500 D as determined by polyacrylamide SDS gel electrophoresis.

In opposition proceedings, this claim was amended as follows:

A monoclonal antibody which specifically recognizes and binds a human cytotoxin having M.W. of 17,000 6 500 D as determined by polyacrylamide SDS gel electrophoresis, which cytotoxin is recognized and bound by the reference monoclonal antibody produced by the hybridoma cell line CNCM I-472 deposited with the Institute Pasteur.

EP-B1 – 0198086 – Claim 6:

Human monoclonal antibody which reacts specifically to varicella zoster virus and recognizes glycoprotein antigens having a molecular weight of 90,000 and 55,000 respectively.

EP-B1 – 0338003 – Claim 5:

A monoclonal antibody which specifically binds to an antigen on the surface of a neutrophil identified as 1D3, said 1D3 antigen having a molecular weight of approximately 48,000 daltons defined under reducing conditions and a molecular weight in the approximate range of 48,000 to 60,000 daltons defined under non-reducing conditions, said 1D3 monoclonal antibody being further characterized as not having binding specificity with respect to:

- A. human acute leukemia cells,
- B. other human peripheral blood cells, and
- C. granulocyte precursor cells in bone marrow.

D.IV2.i.c. Product claims characterizing an antibody by the coding sequence of a certain DNA

An antibody may also be characterized by the DNA encoding it or parts of it such as the variable regions or CDRs. Depending on the characterization of the DNA, the claim may embrace only one specific antibody or a variety of antibodies containing substitutions, deletions, insertions, point mutations, etc.

Claim drafting:

A claim characterizing an antibody by the coding capacity of a certain DNA may have the following general wording:

An antibody comprising a VL chain encoded by seq. ID no ... and a VH chain encoded by Seq ID No.

An example of such a claim granted by the EPO is shown below. Language relating to the coding sequence is underlined.

EP-B1 – 1476185 – Claim 1:

A monoclonal antibody or an antigen-binding portion thereof that specifically binds to and activates human CD40, wherein the epitope recognized by said antibody or portion does not overlap with the binding site for the CD40 ligand, wherein said antibody or portion inhibits tumor growth in vivo, and wherein said antibody comprises a heavy chain and a light chain, wherein:

- (a) the amino acid sequences of the CDR1, CDR2, and CDR3 of said heavy chain are those of a heavy chain variable domain selected from the group consisting of:
 - i) the heavy chain variable domain of 21.4.1 (ATCC Deposit No. PTA-3605);
 - ii) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 42; and
 - iii) a heavy chain variable domain encoded by the nucleotide sequence of SEQ ID NO: 41; and
- (b) the amino acid sequences of the CDR1, CDR2, and CDR3 of said light chain are those of a light chain variable domain selected from the group consisting of:
 - i) the light chain variable domain of 21.4.1 (ATCC Deposit No. PTA-3605);
 - ii) a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 44; and
 - iii) a light chain variable domain encoded by the nucleotide sequence of SEQ ID NO: 43.

D.IV2.i.d. Product claims characterizing an antibody by its structure

The most reliable structural characteristic of an antibody is the amino acid sequence of the antigen-binding portions, in particular the sequences of the CDR regions. However, for retaining the binding activity of the antibodies, the sequence need not be maintained unchanged. Therefore, a claim characterizing an antibody by its amino acid sequence should include references to certain deviations from this sequence, such as amino acid deletions, substitutions, insertions or mutants, allelic variants of the antibody or by a degree of homology to a defined sequence, as shown in the following examples.

Further structural features suitable to characterize an antibody are, e.g. its VL and VH chains or the six CDRs.

Claim drafting:

A claim characterizing an antibody by its amino acid sequence may have, e.g., one of the following general wordings:

An antibody X having the amino acid sequence of SEQ ID No ...

An antibody having a VH of SEQ ID NO. 1 and a VL of SEQ ID NO. 2.

An antibody having 6 CDR regions with SEQ ID NOs. 1–6.

In the following claims the structural features are underlined.

Exampless of such claims are shown below. Language relating to polypeptide sequences is underlined.

EP-B1 – 0327378 – Claim 1 in T 236/01 (Domain-modified antibodies/COLUMBIA UNIVERSITY)

An antibody chain having at least one binding site region and a domain-modified constant region, wherein said domain-modified constant region comprises a modification selected from the group consisting of

- (1) an insertion of at least eighty percent of the amino acids of at least one of the domains of CL, CH1, hinge, CH2, CH3, and CH4, wherein the rest of the domain-modified constant region has the same amino acid sequence as that of a constant region of a mammalian antibody,
- (2) a substitution of at least eighty percent of the amino acids of at least one of the domains of CL, CH1, hinge, CH2, CH3, or CH4 by at least eighty percent of the amino acids of at least one but less than all of said domains from a different mammalian antibody chain, wherein the rest of the domain-modified constant region has at least eighty percent the same amino acid sequence as that of a constant region of a mammalian antibody and
- (3) a deletion of at least eighty percent of the amino acids of more than one of the domains CH1, hinge, CH2, CH3, or CH4, wherein the remaining amino acids of the domain-modified constant region have at least eighty percent the same amino acid sequence as that of at least one domain of a constant region of a mammalian antibody.

EP-B1 – 0194276 – Claims 1 and 10 in T 669/97 (Chimeric antibodies/CELLTECH THERAPEUTICS LTD)

1. A process for the production of a chimeric antibody comprising at least part of an Ig molecule and at least part of a non-Ig protein, in which both parts are capable of functional activity, the process comprising:
 - a) preparing an expression vector including a suitable promoter operably linked to a DNA sequence comprising a first part which encodes at least the variable region of the heavy or light chain of an Ig molecule and a second part which encodes at least part of a non-Ig protein;
 - b) transforming an immortalised mammalian cell line, which secretes an isolated Ig light or heavy chain respectively complementary to the part of the Ig molecule encoded by the first part of the vector prepared in step (a), with the prepared vector; and
 - c) culturing said transformed cell line to produce the chimeric antibody.

10. A chimeric antibody comprising at least part of an Ig molecule and at least part of a non-Ig protein in which both parts are capable of functional activity, the antibody comprising:

- a) a first polypeptide chain comprising: (i) at least the variable region of the heavy or light chain of an Ig molecule; and (ii) at least part of a non-Ig protein, the parts (i) and (ii) being linked together by a specifically cleavable linker sequence; and
- b) a second polypeptide chain comprising at least the variable region of a complementary light or heavy chain respectively of an Ig molecule,

the first and second chains being associated together so as to form an antigen binding site.

All EPC requirements were satisfied.

EP-B1 – 0125023 – Claim 1* in 2nd auxiliary request granted of **T 1212/97 (Immunoglobulin preparations/GENENTECH)*

A non-glycosylated chimeric immunoglobulin species having specificity for a particular known antigen comprising chimeric heavy and light polypeptide chains each having a constant region from a human antibody and a variable region from a murine antibody.

EP-B1 – 214257 – Claim 1:

An anti-EpCAM antibody or a functional derivative thereof wherein the variable region of the antibody heavy chain comprises all three complementarity determining regions (CDRs) having the sequence of SEQ ID No.2; SEQ ID No. 4 and SEQ ID No. 6 and wherein the variable region of the antibody light chain comprises all three complementarity determining regions (CDRs) having the sequence of SEQ ID No.8; SEQ ID No. 10 and SEQ ID No. 12.

EP-B1 – 2143795 – Claim 1:

A murine anti-CD20 monoclonal antibody having cell growth inhibitory activities including apoptosis against human CD20 antigen expressing cells in culture of the CD20 antigen expressing cells without effector cells, wherein the amino acid sequences of the H chain variable region and the L chain variable region are SEQ ID NOS: 2 and 8.

EP-B1 – 2041177 – Claim 1:

An antibody or antigen-binding fragment thereof, which specifically binds human interleukin-6 receptor (hIL-6R) with a KD of 500 pM or less, as measured by surface plasmon resonance, wherein the heavy chain CDRs and the light chain CDRs comprise:

- (i) SEQ ID NO: 21, 23 and 25 as respectively heavy chain CDR1, CDR2 and CDR3 and SEQ ID NO: 29, 31 and 33 as respectively light chain CDR1, CDR2 and CDR3; or
- (ii) SEQ ID NO: 149, 151 and 153 as respectively heavy chain CDR1, CDR2 and CDR3 and SEQ ID NO: 157, 159 and 161 as respectively light chain CDR1, CDR2 and CDR3.

EP-B1- 00935482 – Claim 20* in **T 617/07 (Monoclonal NGF-antagonist antibodies/LAY LINE):*

Monoclonal antibody, synthetic and biotechnological derivatives thereof, able to recognize and bind the high affinity tyrosine kinase receptor of NGF [...] named TrkA, and act as antagonist for the binding of NGF to TrkA, and which prevents the functional activation of TrkA by NGF, and characterized by at least one CDR selected from: light chain CDRs defined by aa 46–55 of SEQ ID No 2, aa 71–77 of SEQ ID No 2 and aa 110–119 of SEQ ID No 2 and heavy chain CDRs defined by aa 176–185 of SEQ ID No 2, aa 200–216 OF SEQ ID No 2 and aa 249–262 of SEQ ID No 2.

D.IV.2.i.e. Product claims characterizing an antibody by a process for its preparation

As for any other biotechnological subject-matter, it is also possible, under certain conditions, to draft product-by-process claims for antibodies. For further general information in connection with product-by-product claims, see C.I.3.e.a.

Claim drafting:

A product by process claim relating to antibodies may have the following general wording:

An antibody X obtainable by a process comprising steps ...

Examples of granted claims directed to antibodies obtainable by a process for their preparation are shown below. The process features are underlined.

EP-B1 – 0186833 – Claim 4:

A monoclonal antibody according to claim 3 produced by a hybridoma cell line according to claim 1.

Claim 1 referred to in claim 4 is as follows:

A hybridoma cell line expressing a monoclonal antibody which specifically recognizes and binds a cytotoxin having M.W. of $17,000 \pm 500$ D as determined by polyacrylamide SDS gel electrophoresis said hybridoma being formed by fusion of murine myeloma cells with spleen cells from a mouse previously immunized with a pure or impure preparation of a human cytotoxin obtained from stimulated monocytes or monocyte-like cells, which is specifically recognized and bound by the reference monoclonal antibody produced by the hybridoma cell line CNCM I-472 deposited with the Institute Pasteur.

EP-B1 – 0186833 – Claim 5:

A monoclonal antibody of the type IgM said antibody being produced by the hybridoma cell line according to claim 2.

Claim 2 referred to above reads:

The hybridoma cell line of claim 1 being the cell line CNCM I-472.

EP-B1 – 0234501 – Claim 5:

A monoclonal antibody produced by culturing a hybridoma having the identifying characteristics of ATCC HB 8944.

EP-B1 – 0431171 – Claim 1 in T 735/00 (Anti-CRP antibodies/IA-TRON LABORATORIES, INC.)

A monoclonal antibody selected from the group consisting of monoclonal antibody CRP-1 obtained from hybridoma cell line CRP-1 (FERM BP-2873), monoclonal antibody CRP-2 obtained from hybridoma cell line CRP-2 (FERM BP-2874), monoclonal antibody CRP-3 obtained from hybridoma cell line CRP-3 (FERM BP-2875), and monoclonal antibody CRP-4 obtained from hybridoma cell line CRP-4 (FERM BP-2876).

EP-B1 – 0879290 – Claim 1 in T 1189/06 (Prostate-specific anti-gens/ABBOTT)

An antibody specific for free PSA produced in response to immunization by a peptide selected from the group consisting of ABT6 (SEQ.ID.NO:6) and ABT1 (SEQ.ID.NO:1).

EP-B1 – 1158003 – Claim 1 in T 30/09 (Ab to the prion PrP^{Sc}(Sc) isoform/BLOOD TRANSFUSION CENTRE)

An antibody binding exclusively to a PrP^{Sc}(Sc) isoform of the prion protein and recognizing the epitope having the three dimensional conformation provided by the protein sequence [...] of the PrP^{Sc}(SC) isoform of the prion protein while not binding to the PrP^{Sc}(C) form, obtainable by a method comprising the step of immunising an animal with a peptide consisting of the amino acid sequence [...] or [...].

Prior art disclosed antibodies against linear epitopes and having the same specificity. The object was the provision of alternative antibodies.

The Board found antibodies to a conformational epitope to involve an inventive step over antibodies to linear epitopes as disclosed in the prior art.

EP-B1 – 0018795 – claim 6 in T 513/94 (Monoclonal antibody (OKT3)/ ORTHO PHARMACEUTICAL CORPORATION)

Claim 6 as maintained was claim 8 as granted and reads as follows:

Monoclonal antibody which is produced from hybridoma ATCC CRL 8001 (OKT3).

EP-B1 – 0656946 – Claim 1 in T 405/06 (Immunoglobulins/BRUSSEL)

Immunoglobulin characterized in that it is obtainable from Camelids and in that it comprises two heavy polypeptide chains sufficient for the formation of a complete antigen binding site, or several antigen binding sites wherein the heavy polypeptide chains are devoid of a so-called first domain in their constant region (CH1), this immunoglobulin being devoid of light polypeptide chains.

EP-B1 – 0068763 – Claim 13 of the Main Request and Auxiliary Request in Appeal Proceedings T 130/90 (Recombinant monoclonal antibody/UNIVERSITY OF TEXAS SYSTEM)

Main request:

An antibody comprising intact immunological chains and containing F(ab')₂ and Fc portions, each Fab' portion having specific binding affinity for a respective different desired antigenic determinant, whereby the antibody has dual specificity and said antibody is derived from monoclonal source(s).

Auxiliary request:

A recombinant monoclonal antibody produced by cultivation of a quadroma cell of Claim 5 and/or a trioma cell of Claim 6 and comprising intact immunological chains and containing F(ab')₂ and Fc portions, each F(ab') portion having specific binding affinity for a respective different desired antigenic determinant, whereby the antibody has dual specificity.

The product-by-process claims were considered allowable under Articles 54, 56 and 84 EPC.

EP-B1 – 1144006 – Claim 1:

An anti-CCR5 chemokine receptor monoclonal antibody or a fragment thereof, wherein the antibody or fragment thereof binds to the same epitope as that to which monoclonal antibody PA14 binds, PA14 being the monoclonal antibody produced by a hybridoma cell line deposited under ATCC Accession No. HB-12610 and designated PA 14.

D.IV.2.i.f. Product claims comprising antibodies as essential elements

As indicated in the introduction to this chapter, antibodies have gained an enormous economic importance in diagnosis and therapy including prophylaxis. Typical examples of such products comprising antibodies as essential elements are, for example, pharmaceuticals, kits for diagnostic purposes, micro-arrays etc.

Claim drafting:

A product claim relating to a kit comprising an antibody may have the following general wording:

A kit for detecting compound X comprising antibody Y.

A claim directed to a pharmaceutical can have the following general wording:

A pharmaceutical composition comprising antibody X.

Examples of claims granted by the EPO and relating to embodiments comprising an antibody as an essential element are shown below. The products which comprise the antibody are underlined.

EP-B1 – 0098179 – Claim 8:

An immunoassay for theophylline which utilizes a monoclonal theophylline antibody as claimed in Claim 1 or 2.

EP0614984 –B1- Claim 1 in T 601/05 (Anti-TNF alpha human monoclonal antibodies/BAYER I)

A pharmaceutical composition containing a human monoclonal antibody that binds to human tumor necrosis factor alpha.

The claimed composition was novel over polyclonal sera to TNF-alpha.

EP-B1 – 1780273 – Claim 1:

An anti-glypican 3 antibody bound to a cytotoxic substance for use in the treatment of cancer.

D.IV.2.j. Process claims for antibodies

Antibodies may be obtained by any of the following routes:

- (i) isolation from their natural environment, such as isolation from an animal or human
- (ii) isolation from recombinant host cells programmed to express the desired antibody,
- (iii) secretion by hybridomas.

D.IV.2.j.a. Process claims involving isolation from a natural environment

Antibodies are produced by animals and humans and constitute an essential component of their blood, from which source they can be isolated as polyclonal sera.

Claim drafting:

A general claim relating to a process for isolating an antibody from its natural environment may have the following wording:

A process for isolating antibodies X from source Y comprising the steps of ...

The source of the antibody is underlined.

EP-B1 – 2075257 – Claim 1:

A process for producing a humanized antibody comprising:

- (a) immunizing a non-human animal with Fas function defects that develops autoimmune disease with an antigen that exhibits amino acid sequence homology of 90% or higher in a human and a non-human animal;
- (b) obtaining an antibody from the non-human animal; and
- (c) replacing a complementarity-determining region (CDR) of a human antibody with a CDR of the non-human animal antibody.

D.IV.2.j.b. Process claims involving synthesis by a recombinant host cell

This type of process claim has become very important over the years since with an increasing number of available genes coding for antibodies of commercial value, there exists an increasing demand for processes allowing large scale production of the desired antibody in a suitable host cell. Examples for host cells as well as the principle routes for causing them to express a gene of interest are state of the art. Therefore, in many instances processes for recombinant production of antibodies constitute processes of analogy.

Claim drafting:

A process claim relating to the recombinant production of a protein may have the following general wording:

A process for preparing antibody X, comprising the step of expressing SEQ ID Y in host cell Z and obtaining the antibody from the cultivated cells.

Examples of claims relating to the recombinant production of an antibody granted by the EPO are the following, the recombinant steps of which are underlined.

EP-B1- 0194276 – Claim 1 in T 669/97 (Chimeric antibodies/CELLTECH THERAPEUTICS LTD)

A process for the production of a chimeric antibody comprising at least part of an Ig molecule and at least part of a non-Ig protein, in which both parts are capable of functional activity, the process comprising:

- a) preparing an expression vector including a suitable promoter operably linked to a DNA sequence comprising a first part which encodes at least the variable region of the heavy or light chain of an Ig molecule and a second part which encodes at least part of a non-Ig protein;
- b) transforming an immortalised mammalian cell line, which secretes an isolated Ig light or heavy chain respectively complementary to the part of the Ig molecule encoded by the first part of the vector prepared in step (a), with the prepared vector; and c) culturing said transformed cell line to produce the chimeric antibody.

EP-B1 – 2233501 – Claim 10:

A preparation method of the humanized anti-human CD34 antibody of any of claims 1–3, comprising the following steps:

- 1) producing an expression vector using the nucleotide molecule of claims 4–6, and transforming a host cell using the obtained expression vector;
- 2) culturing said host cell;
- 3) collecting, separating and purifying the humanized anti-human CD34 antibody expressed by said host cell.

D.IV.2.j.c. Process claims involving secretion by hybridomas

Process claims involving secretion by hybridomas relate to the production of monoclonal antibodies or derivatives thereof. Given the existence of a certain hybridoma producing a certain monoclonal antibody, a process claim for producing a monoclonal antibody from such hybridoma cell will in most cases be a process of analogy.

Claim drafting:

A process claim relating to the production of monoclonal antibodies may have the following general wording:

A process for preparing a monoclonal antibody X, wherein hybridoma Y producing said antibody is cultivated and monoclonal antibody X is obtained from said medium.

EP-B1 – 1916298 – Claim 1:

A method for producing a monoclonal antibody or a monoclonal antibody-producing cell, which comprises the steps of:

- (a) inoculating a non-human animal with a minus-strand RNA viral vector carrying a nucleic acid which encodes a foreign polypeptide to be used as an antigen, a nucleic acid producing the viral vector, a cell into which the vector or the nucleic acid pro-

- ducing the vector has been introduced, wherein the inoculation is performed by palm or foot pad intracutaneous administration;
- (b) collecting an antibody-producing cell from the animal;
 - (c) fusing the collected antibody-producing cell with a myeloma to prepare a hybridoma; and
 - (d) collecting the hybridoma or a monoclonal antibody produced by the hybridoma.

D.IV.2.k. Use claims/purpose-limited product claims for antibodies

As noted in C.I.3.e.a, use claims are generally interpreted as process claims. An exception are the purpose-limited product claims in the pharmaceutical field. Use claims may be directed to the use of antibodies for biochemical processes, e.g. the use of antibodies in immuno-purification procedures. The most important applications of antibodies are, however, in the field of pharmaceuticals and diagnostics, where the special claim format of a purpose-limited product claim is used.

Claim drafting:

A general claim relating to the use of antibodies could have the following wording:

Use of antibody X for isolating protein Y,

or

Antibody X for use in a method of treating disease Y.

The latter type of claim represents a purpose limited product claim, discussed in C.I.3.e.d.

Examples of use claims granted by the EPO are shown below, and the use is underlined.

EP-B1 – 1313476 – Claim 1:

Use of an antibody for detecting the expression and/or function of sgk3 in eukaryotic cells for the diagnosis of diseases which are associated with an impaired activity of ion channels.

EP-B1 – 1853921 – Claim 9:

Use of an antibody which is binding to a therapeutic antibody which is intended for use in a human being and not binding to the immunoglobulin of an experimental animal for measuring the concentration of total, active, or antigen-bound therapeutic antibody in a sample obtained from an experimental animal.

EP-B1 – 1181318 – Claim 37:

Use of a monoclonal antibody, synthetic and biotechnological derivatives thereof, able to recognise and bind the high affinity tyrosine kinase receptor of NGF (Nerve Growth Factor), named TrkA, and act as antagonist for the binding of NGF to TrkA, and which prevents the functional activation of TrkA by NGF, in the manufacture of a phar-

macological composition for the treatment of neurological pathologies comprised within the following group: chronic pain and acute pain.

EP-B1 – 0610447 – Claim 1:

Use of an antibody recognising the CDw52 antigen for the manufacture of a medicament for the treatment of T-cell mediated inflammation of the joint synovium.

D.V. Microorganisms

D.V.1. Introduction

This chapter is concerned with the protection of microorganisms under the EPC.

The term “microorganism” as used herein includes bacteria and other generally unicellular organisms with dimensions beneath the limits of vision which can be propagated and manipulated in a laboratory (see EPO Guidelines, G-II, 5.5.1). This includes bacteriophages, viruses and unicellular eukaryotic organisms such as fungi (including yeast), protozoans, algae as well as human, animal and plant cells. It should be noted that the definition of this term provided by an Appeal Board in **T 356/93 (Plant cells/PLANT GENETIC SYSTEMS)** (see C.I.2.c) additionally includes plasmids, which however are discussed in section D.II. Many of the EPO decisions discussed below in this section relate to bacteria and viruses, either protected as such or used for a specified purpose.

Microorganisms differ from “classical” chemical subject-matter in that in many instances they are not reproducible by a person skilled in the art based on the written disclosure alone. This restricted the patent protection of microorganisms for a long time.

To overcome the above problem of providing a sufficient disclosure for a microorganism, Applicants are allowed to supplement the written disclosure by a deposit of “biological material”. The EPC regulates the requirements for a deposit of “biological material” (to which microorganisms belong) in Rule 31 EPC; the EPO accepts deposits satisfying the requirements set under the Budapest Treaty. Rules 32–34 EPC provide further regulations relating to the deposit of such biological material. The different possible modes of deposit as well as relevant case law pertaining to deposits are discussed in C.I.3.b.b (see also Annex 4).

D.V.2. Protecting microorganisms under the EPC

The EPC does not explicitly allow the patentability of microorganisms as such. In particular, neither Art. 53(b) nor Rule 31 EPC mentions microorganisms as such. Rather, Rules 31–34 EPC refer to inventions concerning *biological material*. The EPC provides a definition of “biological material” in Rule 26(3)

EPC as any material containing genetic information and capable of reproducing itself or being reproduced in a biological system. This includes microorganisms as defined above in the present section. Art. 53(b) EPC excludes from patentability plant and animal varieties or essentially biological processes for the production of plants or animals, but also states that “this provision shall not apply to microbiological processes or the products thereof.” Rule 27(c) EPC links with Art. 53(b) EPC by stating that biotechnological inventions are patentable if they concern i.a. a product obtained by means of a microbiological process other than a plant or animal variety. The EPO Guidelines in turn confirm that the product of a microbiological process may be a microorganism (Guidelines, G-II, 5.5.1):

The product of a microbiological process may also be patentable per se (product claim). Propagation of the microorganism itself is to be construed as a microbiological process for the purposes of Art. 53(b). Consequently, the microorganism can be protected per se as it is a product obtained by a microbiological process (see Guidelines at section G-II, 3.1).

Despite the EPC’s lack of an express regulation allowing the patentability of microorganisms, then, microorganisms nevertheless constitute patentable subject-matter under the EPC.

In addition to complying with the requirement of reproducibility (satisfied e.g. by a deposit as mentioned above), the claimed microorganism must also be novel, involve an inventive step and be susceptible of industrial application. Further, the claimed subject matter has to fulfill the requirements of clarity and support by the description. General information on the requirements of the application is provided in C.I.3.

Some general aspects relevant for inventions involving microorganisms will be discussed below, with particular consideration of relevant case law. This includes cases in which the EPO has applied standards for assessing the allowability of patent applications to cases involving microorganisms.

D.V.2.a. Discoveries

According to Art. 52(2) EPC, discoveries are not regarded as inventions for which European patents can be granted under Art. 51(1) EPC. Section G-II, 3.1 of the Guidelines sets out the standard as to whether a microorganism which already exists in nature should be considered an *invention* (which is patentable) or a *discovery* (which is not):

If a new property of a known material or article is found out, that is mere discovery and unpatentable because discovery as such has no technical effect and is therefore not an invention within the meaning of Art. 52(1). If, however, that property is put to practical use, then this constitutes an invention which may be patentable. ... To find a previously unrecognised substance occurring in nature is also mere discovery and therefore unpatentable. However, if a substance found in nature can be shown to produce a technical effect, it may be patentable. An example of such a case is that of a substance occurring in nature which is found to have an antibiotic effect. In addition, if a microorganism is discovered to exist in nature and to produce an antibiotic, the microorganism itself may also be patentable as one aspect of the invention.

D.V.2.b. Morality and “ordre public”

According to Art. 53(a) EPC, inventions, the publication or exploitation of which would be contrary to “ordre public” or morality, are excluded from patentability.

In decision **T 356/93 (Plant cells/PLANT GENETIC SYSTEMS)**, an Appeal Board had to decide on the question whether granting a patent on microorganisms, in that case plant cells, contravenes Art. 53(a) EPC. Applying the definitions of the concepts of “ordre public” and morality as cited in C.I.2.a., the Board reached the conclusion that none of the claims of the patent in suit comprised subject-matter which would be contrary to Art. 53(a) EPC.

D.V.2.c. Methods of treatment

According to Art. 53(c) EPC, methods for treatment of the human or animal body by surgery or therapy and diagnostic methods practiced on the human or animal body are not patentable.

Decision **T 19/86 (Pigs II/DUPHAR)** is concerned with the question as to whether the use of a live attenuated Aujeszky-virus for preparing a vaccine protecting a particular class of animals (here: sero-positive pigs) is patentable as a second medical use, if its administration to another class of the same animal (sero-negative pigs) is already known. The Board held:

Article 52(1) EPC expresses a general principle of patentability for inventions which are industrially applicable, new and inventive, and that in accordance with that principle, in all fields of industrial activity other than those of making products for use in surgery, therapy and diagnostic methods (as to which [Article 53(c) EPC] applies), a new use for a known product can be fully protected by claims directed to that use – provided that such use is new and inventive. (point 10)

Since the Board acknowledged the administration to sero-positive pigs as being new and inventive, a patent was granted.

D.V.2.d. Novelty

It is established practice of the Boards of Appeal that the disclosure of a document can be novelty-damaging only if enabled (see **T 206/83 (Herbicides/ICI)**; point 5) without undue burden to a person skilled in the art (**T 81/87 (Preprorennin/COLLABORATIVE)**; point 18). This was subsequently confirmed by **T 576/91 (Plasmid pTR2030/NORTH CAROLINA STATE UNIVERSITY)** and **T 1099/99 (Filamentous fungi/GENENCOR)**; point 3). The requirement for sufficiency of disclosure of a prior art document is identical to that of a patent application under Art. 83 EPC (**T 206/83 (Herbicides/ICI)**; point 2).

In decision **T 231/01 (Porcine virus/SOLVAY)** the claim related to a naturally occurring isolated virus causing porcine reproductive and respiratory syndrome. The virus was selected from specified deposits, for which accession numbers were provided. Certain documents cited against the claims disclosed

virus isolates, but no sequences, meaning that a novelty objection could only be raised on the basis of probability, i.e. that the disclosed viruses probably were the same as, and therefore novelty destroying for the claimed viruses. The Board held that it is not justifiable to decide whether a document is prejudicial to novelty on the basis of probability. To substantiate a novelty objection, there has to be certainty that the objection is justified. This is a good illustration of the concept in the EPO that novelty can only be lacking when there is a clear disclosure of each and every feature of a claim in a single prior art document.

Decision **T 327/04 (Influenza vaccines/DUPLIAR)** related to an influenza surface antigen vaccine from influenza viruses propagated on animal cell culture obtainable by a method involving propagation of influenza viruses on an animal cell culture and specifying a certain degree of purity. Among other things, the Board considered the novelty of the claimed subject-matter in view of a number of documents. In their assessment, the Board referred to previous decision **T 990/96 (Erythro-compounds/NOVARTIS)**, which held that conventional methods for the purification of compounds are within the common general knowledge of the skilled person. This means that a document disclosing a chemical compound and its production normally makes this compound available to the public in all desired grades of purity unless all prior attempts to achieve a particular degree of purity by conventional purification processes have failed. According to this general principle, a known compound cannot normally be made novel by simply including its degree of purity in the claim. In decision **T 327/04** the Board made an exception to this rule, because they believed that none of the cited prior art provided any evidence that the skilled person applying the purified influenza surface antigen preparations disclosed in the prior art would result in a vaccine with the recited degree of purity. In this case, the Board concluded that the purity could in fact confer novelty, and the claimed influenza virus vaccine was deemed novel.

Novelty is often disputed in cases where a microorganism is isolated from nature. Here the same considerations as outlined above for other naturally occurring products apply (see Guidelines, G-II, 3.1; see also section C.I.1). To summarize, if the Applicant is the first to properly characterize the naturally occurring microorganism in question, e.g. by a process for preparing it or by parameters allowing its reproducible preparation, the microorganism is considered to be novel.

D.V.2.e. Inventive step

D.V.2.e.a. Inventive step in cases where the microorganism is a hybridoma

Although the inventive step of applications relating to microorganisms is judged on a case-by-case basis, some general rules for the assessment of inventive step exist at least with respect to hybridoma-related applications. These are sum-

marized here, but are discussed in greater detail in section D.IV, especially section D.IV.2.e.

As a first rule, the inventive step of a generic claim relating to hybridomas secreting antibodies directed to a *new* antigen is generally acknowledged. As a second rule, such a generic claim is generally not considered to involve an inventive step once the antigen is a *known* compound. However, a claim directed to a specific hybridoma may be allowable, if there are particular reasons for acknowledging an inventive step, such as surprising properties of the antibody derived from the hybridoma or certain difficulties in obtaining it in the art.

The Appeal Boards of the EPO have decided several cases involving monoclonal antibodies as such or processes involving monoclonal antibodies, where not only the antigen, but also polyclonal antibodies corresponding to the monoclonal antibodies were already state of the art.

In **T 499/88 (Immunoglobulins/UNILEVER)** the replacement of polyclonal antibodies by monoclonal antibodies in an otherwise identical process was considered to be obvious.

In **T 36/90 (Tumor cells/BOGOCH)** a product claim directed to a monoclonal anti-cancer Recognin was considered obvious, since the prior art disclosed polyclonal anti-cancer Recognins and the technology required to produce monoclonal anti-cancer Recognins. Further, the polyclonal anti-cancer Recognins were known to have certain disadvantages (cytotoxicity) which the monoclonals were expected to avoid.

Considering **T 499/88 (Immunoglobulins/UNILEVER)** and **T 36/90 (Tumor cells/BOGOCH)**, it appears that if polyclonal antibodies are already known, claims involving hybridomas producing monoclonal antibodies will involve an inventive step only under extraordinary circumstances.

If the prior art discloses monoclonal antibodies recognizing a specific antigen, a claim relating to a new hybridoma still may be allowable if the cell line in question secretes an antibody against that antigen having an unexpected advantage over antibodies of the prior art. This was confirmed in **T 355/92 (-/BOEHRINGER MANNHEIM GMBH)**. In the case underlying this decision a monoclonal antibody to the glycoprotein hormone FSH having less than 0.3% cross-reactivity to the closely related glycoprotein hormones LH, TSH and hCG, was claimed. There were several prior art documents disclosing monoclonal antibodies to FSH, which, however, showed a considerable degree of cross-reactivity with the three related glycoprotein hormones. The Board acknowledged an inventive step of the claimed antibody since all cited documents conveyed the expectation that monoclonal antibodies to FSH having even less than 0.1% cross-reactivity could not be prepared. Additionally, in the immunization protocol applied by the Applicant unusual adjuvants had been employed, which was considered to be the reason that monoclonal antibodies of high specificity were obtained. Thus, the immunization method was also considered to support an inventive step of the claimed hybridomas.

D.V2.e.b. Inventive step in cases where the microorganism is not a hybridoma

The following decisions issued by Appeal Boards of the EPO relate to inventive step in applications involving microorganisms other than hybridomas.

In the case underlying **T 261/89 (–/MERCK & CO., INC.)** a patent relating to a process for the propagation of hepatitis A virus was revoked due to lack of an inventive step over a document disclosing a method differing from the claimed process only with respect to the incubation period. Since the Patentee failed to support a surprising effect of the longer incubation period, an inventive step could not be acknowledged.

The subject-matter of the application underlying **T 630/92 (Salmonella vaccines/LELAND STANFORD JUNIOR UNIVERSITY)** was a method for preparing a non-virulent vaccine from virulent pathogenic cellular microorganisms. The prior art disclosed a method for preparing non-virulent single auxotrophic mutants of *S. typhimurium* carrying a non-reverting deletion. In order to provide safe strains with an even lower reversion rate, the Applicant prepared double auxotrophic mutants carrying in addition to a first deletion mutation a second deletion mutation. The Board examined the question whether a person skilled in the art would have considered in a straightforward manner the repetition of the procedure already described in the prior art for a second independent gene, in order to reduce the reversion frequency and to arrive at something falling within the terms of the present claims. The Board held that in view of the prior art:

The skilled person not only had the motivation further to improve the existing live vaccine by introducing an additional mutation in a second independent gene, but he would have done it by using the known technique [...] with a reasonable expectation of success. (point 3.2 (f)2c)

Therefore, an inventive step was not acknowledged.

In the microorganism field a common consideration in evaluating inventive step is whether or not the skilled person would have transferred the teaching for one microorganism to another. The following decisions illustrate the thinking which the EPO Boards of Appeal have applied to such questions.

In decision **T 342/98 (A. orizae/NOVOZYME)** the Board assessed inventive step of a method for the expression of a protein product in the organism *Aspergillus orizae*. The method involved providing a recombinant cloning vector, transforming this into the *A. orizae* host and culturing the *A. orizae* host in a culture medium. The closest prior art taught the transformation of foreign genes into *A. niger* using a transformation method already designed for *A. nidulans*, and that transformation was successful because a new phenotype resulted. A further document classified *A. niger* and *A. orizae* in the same class of organism. Based on this common classification, the Board held that it would have been obvious for the skilled person to substitute *A. orizae* for *A. niger*. In the Board's words, this substitution represented a "one way street", because no other substitution option existed. Having determined that the idea to substitute *A. orizae* for *A. niger* was obvious for the skilled person to try, the Board then considered

whether, following this idea, the skilled person would have expected that such transformation would have successfully resulted in *A. orizae* able to produce the transformed product. Here, the Board considered that *A. niger* and *A. orizae* were phylogenetically closer to one another than either of them were to *A. nidulans*. Since the prior art showed a successful technology transfer between *A. nidulans* and *A. niger*, the skilled person would have expected a successful technology transfer all the more between *A. niger* and *A. orizae*. The Board believed that substituting one microorganism for the other as claimed was obvious to try, and that doing so would have given the skilled person a reasonable expectation of success. This two-tiered analysis is often used in the EPO in assessing the inventive step of biotech inventions. Applying it here to the process involving *A. orizae*, the Board denied inventive step.

T 430/96 (*Aspergillus*/GIST – BROCADES N.V.) involved a similar claim regarding transformation of *Aspergillus niger*, as well as similar legal issues involving inventive step assessed by considering obviousness to try and reasonable expectation of success. In this case, the Board held that in order for a claim to be considered obvious, it was not necessary to predict success, but rather only necessary that there is a reasonable expectation of success. Success in transferring relevant technical teaching therefore need not be certain, but only reasonably expected.

Decision **T 78/95 (*Penicillium Chrysogenum*/ANTIBIOTICUS)** illustrates that the two requirements “obvious to try” and “reasonable expectation of success” discussed above need not always be confirmed together. The claims related to a selectable transformation technique for *P. chrysogenum* involving selection of an auxotrophic strain of *P. chrysogenum*, transforming this with a plasmid containing DNA from a fully prototrophic strain of *P. chrysogenum*, where the plasmid has been selected according to previous prototrophic transformation of a suitable auxotrophic strain of a host microorganism. The Board held that the transfer of a teaching from a document describing the claimed method for a related organism rendered the claimed subject-matter obvious to try. However, the Board held that at the priority date, the genetics of *P. chrysogenum* was still an unexplored area of research, so that the skilled person entering this area was faced with a number of uncertainties and problems. For these and other reasons, the Board held that even though the claimed subject-matter was obvious to try, the skilled person still had no reasonable expectation of success in trying it, and confirmed inventive step. This decision illustrates how the confirmation that something is obvious to try does not always mean that there is also a reasonable expectation of success.

In decision **T 441/93 (Cloning in *Kluyveromyces*/GIST BROCADES)**, the claims related to a process for preparing a strain of *Kluyveromyces* yeast involving transforming the *Kluyveromyces* cells with a vector defined in terms of certain sequence elements, and propagating the resultant transformed cells in a growth-sustaining medium. The claims also were directed to the use of *Kluyveromyces* as a host for the transformation and expression of foreign genes.

Finally, the claims were directed to a *Kluyveromyces* expression vector, defined as in the main process claim. In assessing inventive step, the Board considered a document relating to the transformation of *S. cerevisiae* with different kinds of recombinant vectors. The Board held that the skilled person would not have any assurance from the prior art that he could develop a process for the transformation of *Kluyveromyces* protoplasts with a reasonable expectation of success, because he would see that the transfer of existing technology set up for one field of research would require scientific research rather than routine work (see point 33 of the decision). The Board therefore acknowledged inventive step. This decision illustrates that the ability to transfer the teaching from one technical field into another is not in itself enough to deny inventive step. If such transfer involves performing scientific research rather than mere routine work, then this transfer may indicate an inventive step.

D.V.2.f. Sufficiency of disclosure

For a general discussion of sufficiency of disclosure, see C.I.3.b. and C.I.3.b.b.

D.V.2.f.a. Necessity of a deposit

When is it necessary to deposit a microorganism in order to ensure sufficiency of disclosure? Is this necessary any time a deposit is named in the description, regardless of whatever else the description may disclose? Or is it only necessary when a deposit is cited and the description otherwise does not provide enough information to perform the invention? Knowing that microorganisms are fundamentally patentable, Applicants often ask questions like these. EPO case law has addressed such questions. The following is a sampling of relevant decisions on this question.

EPO case law has repeatedly held that there is no general obligation to deposit microorganisms, provided the written disclosure is sufficient to repeat the claimed teaching. This question was addressed in decision **T 361/87 (Microorganisms/NABISCO)**. The claims in this case related to a method for preparing fructose involving, among other things, the use of α -amylase, glucoamylase and glucosyltransferase obtained by cultivating a *Basidiomycetes* fungus. The application referred to certain deposits within this class of fungi which were not available to the public during certain periods after the publication of the application. But the application also disclosed generic methodology enabling the skilled person to obtain any member of the claimed class. The Board held that the claimed invention is not limited to the use of the particular strains indicated, and that even without a reference to these strains, the description alone provides all the information necessary for the skilled person to carry out the invention. The fact that the Applicant indicated specific strains thus went beyond the requirements for sufficiency of disclosure, which were already satisfied by the general methodology described. Accordingly, any intermittent unavailability of the specified strains could not adversely affect sufficiency of disclosure, and the

Board acknowledged that the claimed subject-matter was sufficiently disclosed. This decision illustrates that, even in the face of deposits with deficiencies, the general methodology of the description can be enough to ensure sufficiency of disclosure in microorganism inventions.

A completely enabling description can make deposits unnecessary. This concept was further illustrated in **T 223/92 (HIF-gamma/GENENTECH)** where a Board of Appeal stated:

Finally, there is no legal requirement in the EPC which would force the Respondents to deposit a micro-organism, containing the gene coding for interferon-gamma ready for production. Rule 28 EPC [former EPC rule corresponding to current Rules 31–33 EPC], relating to the requirements of European patent applications relating to micro-organisms clearly states in paragraphs (1) and (1)(a) [corresponding to respective paragraphs (1) and (1)(a) of current Rule 31 EPC] that in the cases where an invention concerns a microbiological process or the product thereof and involves the use of a micro-organism which cannot be described in a manner as to enable the invention to be carried out by a person skilled in the art, the invention shall only be regarded as being disclosed as prescribed in Article 83 EPC if a culture of the micro-organism has been deposited with a recognised depository institution [Rule 31 EPC now states that the deposit must be made on the same terms as those laid down in the Budapest Treaty]. This prescription cannot be interpreted such that there is an obligation to deposit material to facilitate the reproduction if the invention can be repeated on the basis of the written description, even if this should be a much more cumbersome way than by merely growing the deposited micro-organism. (point 3.2)

The above principle was again confirmed in **T 412/93 (Erythropoietin/KIRIN-AMGEN)**. In that case an Appeal Board dealt with the question whether a deposit is obligatory if repeating the invention in the absence of a deposit is very laborious. The Board held:

The need for a deposit cannot be introduced by reference to the concept of undue burden. This concept relates more to cases where the route that the reader is to follow is so poorly marked that success is not certain (see Decision T 418/89, OJ EPO 93, 20). If the route is certain but long and laborious, the Patentee is under no obligation to assist the disclosure by making actual physical examples, i.e., the “factory” available. To come to the opposite conclusion would be effectively to introduce a requirement to make the best mode immediately accessible to the public, and such a requirement is not part of the European patent system. (point 76)

The guiding principle in considering whether a deposit is necessary is that a deposit is only necessary when the microorganism in question was not previously available to the public. This point was illustrated in decision **T 423/04 (Staphylococcal antigens/JACKSON FOUNDATION)**, relating to an antigen preparation which was isolatable from a strain identified by deposit number. In that case, the Opponent had contested sufficiency of disclosure on the basis that no deposit had been made. However, the Patentee produced multiple affidavits to show the availability of the relevant strain on the priority date, as well as after that date. The Board held these affidavits are sufficient to establish the availability of the referenced strain on the priority date. Sufficiency of disclosure was therefore acknowledged, even in the lack of a corresponding de-

posit for the microorganism, because the Patentee proved the public availability of the microorganism.

However, if there exists any doubt at all that the prior art provides the skilled person with the information required to identify a particular microorganism referenced in a claim, then it is advisable to deposit the microorganism before filing. The importance of this was demonstrated in decision **T 549/05 (*Aspergillus niger*/DA BARRA)**, relating to a process for preparing a particular enzyme using strain 489 of *Aspergillus niger*. This strain was described in the application as originating from the soil of sugar cane plants in Brazil. It was selected from over 2000 strains in a database based on its high production of the particular enzyme referenced in the claim. The Board held that this information was not enough to enable the skilled person to obtain the very same specific strain of *A. niger* 489 as referenced in the claims without undue burden. The claimed invention was therefore judged insufficiently disclosed in the absence of a corresponding deposit. This decision illustrates that even a description of how or where a particular microorganism was isolated may not be enough to ensure sufficiency of disclosure without a corresponding deposit. If there exists any doubt as to the availability of a microorganism, then it should be deposited before filing! Failure to do so could jeopardize the validity of the resulting patent.

The timing of microorganism deposits can be crucial for patent validity. In decision **T 328/04 (Humoral immunity/DARTMOUTH COLLEGE)**, the question of sufficiency of disclosure depended on whether or not the biological deposit had been filed on time. The claim related to a pharmaceutical composition comprising a gp39 antagonist, including antibodies defined by ATCC accession numbers. The Board concluded that the information concerning the file number of the culture deposit according to (current) Rule 31(1)(c) EPC had not been filed in time, so the patent could not rely on deposit information for the purposes of disclosure. This decision illustrates the importance of observing the time limit for submission of information regarding the depository institution and the accession number of the deposited biological material. According to Rule 31(2) EPC, this information must be provided a) within 16 months after the filing or priority date, with compliance acknowledged as long as the information is communicated before completion of the technical preparations for publication of the patent application; b) by the date of submission of a request for early publication of the patent application; or c) within one month after the EPO has communicated to the Applicant that the right to inspect the files under Art. 128(2) EPC exists. The ruling time limit according to a), b) or c) above is the earliest-expiring time limit. This ruling was consistent with the holding of earlier Enlarged Board of Appeal decision **G 2/93 (Hepatitis A virus/UNITED STATES OF AMERICA II)**.

If a microorganism is obtained by classical selection techniques using defined conditions without applying mutagenizing agents and if the Applicant is in a position to demonstrate the reproducibility of the selection process, a deposit might not be required.

According to **T 212/92 (–/TEIJIN LIMITED)** this concept was even applied to hybridomas, where the Patentee could show that in fact only a few hybridomas secreting antibodies of different specificity were obtained upon repeating the protocol disclosed in the application. In particular, in this case an Examining Division had refused a claim directed to a method for quantifying human pulmonary surfactant. The method relied on two specific monoclonal antibodies designated PC6 and PE10, which were recited in the claim. The description described PC6 and PE10 as being directed to different epitopes of pulmonary surfactant. The reason for the refusal was that the skilled person, having followed the protocol provided in the application, would certainly produce a large number of antibodies with specificities for different epitopes on the human pulmonary surfactant molecules, but would be unable to select which of these antibodies had identical epitope specificities to the PC6 and PE10 antibodies, as the specificities of PC6 and PE10 were not sufficiently disclosed in the application as originally filed. The Appeal Board reversed the Examining Division's decision, since the disclosure provided some information as to the epitope and, further, since the Applicant had shown that upon repeating the protocol disclosed in the application, only three monoclonal antibodies were obtained, two of which corresponded to PC6 and PE10.

D.V.2.f.b. Other requirements for sufficiency of disclosure

Generally, Rule 31 EPC requires that the Applicant and Depositor are the same party. Rule 31(1)(d) EPC includes special requirements which must be fulfilled in the case that this is not so: In this case, the name and the address of the Depositor must be stated in the application, and the EPO must be furnished with evidence that the Depositor has authorized the Applicant to refer to the deposited biological material, i.e. microorganism, in the application and has given his unreserved and irrevocable consent to the deposited material being made available to the public. Decision **T 118/87 (Amylolytic enzymes/CPC INT.)** dealt with a case in which Applicant and Depositor were not the same legal entity. While the Board confirmed that in principle, Applicant and Depositor must be one and the same (point 6 of the decision), it also held that the Applicant and Depositor, when formally different legally entities, may be considered one and the same because the Applicant was a parent company and the Depositor was a subsidiary of that parent. So although the subsidiary company was the formal Depositor, the Applicant (parent company) alone had control of the deposits. For the Board, this was the relevant question: Which party had ultimate control over the deposit? This decision illustrates the principle that control over the deposited biological material, e.g. microorganism, is the relevant question in considering whether the information contained in a deposit has been made available to the public, and the requirements of Art. 31 EPC have been fulfilled.

While the EPC provides special provisions for ensuring sufficiency of disclosure of inventions relating to biological material, including microorganisms, this

does not mean that other established standards for sufficiency of disclosure developed in the EPO cease to apply. This was demonstrated in decision **T 2224/08 (Producing L-amino acids with MalK mutants/AJINOMOTO)**, which related to a method of producing an L-amino acid utilizing a microorganism. The Opponent had alleged insufficient disclosure because the patent allegedly provided no instructions as to how to assess certain parameters of the claim. Specifically, these parameters were allegedly effected by mutations, however the patent showed the effect of such mutations only for one specific bacterial strain. The Opponent argued that it would unduly burden the skilled person to identify other mutants having the claimed characteristics. The Board disagreed, stating that the patent showed one way of producing amino acids by a microorganism having the features required by the claims. This was the standard to apply for assessing sufficiency of disclosure. The Opponent's argument was essentially that the claim was too broad, but a broad claim does not necessarily mean insufficient disclosure. Normally, for allegations of insufficient disclosure, the burden of proof is on the Opponent. The Board noted (point 4 of the decision) that there is no evidence as to why the disclosed procedures would not work with other strains than the exemplified one. Allegations of insufficient disclosure are normally only justified in the face of serious doubts supported by verifiable facts. The Board found no verifiable facts presented by the Opponent, and therefore found the claimed subject-matter sufficiently disclosed. This decision illustrates how the simple fact that an invention relates to microorganisms does nothing to change the established standard for sufficiency of disclosure developed in the EPO.

In decision **T 48/85 (Coccidiosis vaccines/NATIONAL RESEARCH DEVELOPMENT CORPORATION)**, the claim related to a process for the production of an attenuated strain of *Eimeria necatrix* involving passaging of pathogenic *Eimeria necatrix* in embryonated eggs a specified number of times. The application had been refused as insufficiently disclosed on the basis of prior art suggesting that the claimed method would not work. The Board concluded that the claimed subject-matter was in fact sufficiently disclosed because a deficiency would only arise if the skilled person was unable to recognize the necessary conditions and steps, as a matter of general knowledge, which might be needed to bring about the desired result (point 5 of the decision). The Board saw no suggestion that the examples in the patent would not be reproducible in themselves. Also, the method in the document in question was an enabling disclosure as long as one was not distracted from repeating it in view of other unsatisfactory features in that publication. Importantly, the Board stated that no example in a publication or patent becomes non-repeatable for the reason only that the product was not specifically tested for its identity, provided the alleged product can indeed be obtained on the basis of instructions (point 6 of the decision). Finally, the Board applied the common standard for sufficiency of disclosure, that an error in the description (or in the prior art) is immaterial to the question of sufficiency of disclosure if the skilled person could recognize the error and rectify it

using his established general knowledge. The Board believed that none of the deficiencies in the paper cited could disable the skilled person, or render the instructions irreproducible, let alone cast doubt on the disclosure of the application (point 8 of the decision). This decision again demonstrates how Boards of Appeal have applied the established standard for assessing sufficiency of disclosure to process claims involving the production of microorganisms.

In decision **T 1010/01 (Acellular vaccine/MEDEVA B.V.)**, the claim was directed to an acellular vaccine comprising antigens from *Bordetella pertussis* in a specified range of weight ratios to provide synergistic vaccine potency. In previous opposition proceedings, Opponents had contested sufficiency of disclosure, referring to the examples of the patent. In its decision, the Board pointed out that the disclosure of the patent is not limited to its examples (point 5 of the decision). Although the Board held that the examples only suggested, but did not show, the claimed synergism, it is common practice in proceedings before the EPO, in particular where the issue is sufficiency of a patent disclosure in relation to pharmaceutical compositions or vaccines, that a decision about the presence or absence of a given biological effect be made on the basis of all sorts of evidence,

including ... data filed after the filing date of the application, provided that they render the intended effect credible". (point 13)

Normally, sufficiency of disclosure is judged based on the information present on the relevant date of the application or patent. This decision demonstrates that, especially in inventions relating to pharmaceutical compositions or vaccines, it may also be possible to provide post-published data in support of sufficiency of disclosure, provided the data support the technical effect stated in the patent. This can be important for Applicants in cases where further data corroborating the effect described in the application has been generated after filing.

Decision **T 857/01 (Herpes simplex virus/GENERAL HOSPITAL)** related to a medical use of a herpes simplex virus 1 vector with a specific mutation, and having certain functional features, in treating a neurological deficiency of the central nervous system. The Board started its assessment of sufficiency of disclosure under Art. 83 EPC by stating that the disclosure of an invention is one of the fundamental requirements for the grant of a patent. In order for an invention to be sufficiently disclosed, it has to be possible for the skilled person to achieve the desired result without undue burden and without exercising any inventive skill. Based on the disclosure of the post-published documents, the Board believed that the regulation of gene expression is not a straightforward task that can be routinely carried out by a skilled person. Rather, because it is a complex problem requiring a different solution for every gene of interest, and also requiring extensive research and experimental work (point 10 of the decision). In the Board's view, in order to put the invention into practice would require the skilled person to start an independent research project, something which precludes sufficiency of disclosure. The Board denied sufficiency of dis-

closure. This decision is a good illustration of the principle that the requirement for independent research to put the claimed subject-matter into practice, possibly involving an inventive step, is an indicator of insufficient disclosure. Generally, there must exist a proper balance between the contribution to the state of the art and the scope of the claim.

This concept of balance between the technical contribution and claim scope is at the core of the patent system and was confirmed early by the EPO. For instance, in **T 81/87 (Preprorennin/COLLABORATIVE)** an Appeal Board had to decide on the allowability of the following claim under Art. 83 EPC:

A transformable living cell selected from the group consisting of fungi, yeast, bacteria, and mammalian cells containing genetic material derived from recombinant DNA material and capable of expressing bovine rennin.

An Examining Division had refused this claim as lacking support by the description, which exemplified only the use of cells of *Escherichia* and *Saccharomyces* species. Since there was not enough information as to how expression might be achieved in different hosts, the Examining Division considered the disclosure insufficient under Art. 83 EPC. The Board disagreed, acknowledging sufficiency of disclosure due to the limiting functional feature of “capability for expression”:

As regards the use of cells of various origins according to Claims 1 and 2, the disclosure repeatedly emphasises that these are such as to enable expressions of proteins. It was known at the time of filing that in addition to bacterial cells, various fungi, e.g. yeast cells, were suitable for the purpose. The specification itself refers to various preferred *Escherichia* and *Saccharomyces* strains in this respect. Thus, the terms in the claims are not without formal support since *it would be unfair to restrict the claims to the exemplified strains in the disclosure excluding those which may be used in the future. From the disclosure, it is implied for the skilled person that only those cellular organisms are relevant for use which are capable of providing expressions of the desired proteins (citation omitted). (point 4; emphasis added)*

The Board’s consideration of fairness illustrates the above fundamental principle that a balance must exist between the contribution to the art and the scope of a claim.

The correlation between disclosure and scope was especially clearly articulated in **T 242/92 (Invasive microorganisms/LELAND STANFORD JUNIOR UNIVERSITY)**, in which a Board had to decide on the sufficiency of disclosure of the following claim:

A bacterium capable of invading mammalian cells having invasive phenotype attributable to a single membrane protein, the said protein being expressed as a result of the introduction of exogenous DNA into said bacterium or progenitor thereof.

The application provided one example according to which the non-invasive bacterium *E.coli* could be made invasive by transfer of a gene from *Yersinia*. The invasive bacterium *Shigella* was known to encode the proteins conferring invasiveness by two genes and, thus, was not suitable. The Examining Division had therefore decided that the process leading to the product was not generally applicable and reproducible and refused the application.

The Board of Appeal disagreed, holding in its decision:

In the present case it is not disputed that the information in the application is sufficient to carry out the invention in respect of the *Yersinia inv* gene. The mere fact that only one way of carrying out the invention is indicated does not in itself offer grounds for considering that the application is not entitled to broader claims. At the present stage no concrete evidence is available that the skilled person would be unable to extend the particular teaching of the description to a broader field by using routine methods. *In view of the contribution to the art by the present Applicant it would be unjustified, in the absence of well-founded reasons, to restrict the claims to the specifically exemplified embodiments.* (point 3; emphasis added)

D.V.2.f.c. Reproducibility with certainty

As a general rule, if a generic broad claim relating to a large number of microorganisms, e.g. a whole species, is considered patentable, it is not necessary to deposit a specific microorganism selected therefrom. However, if due to the prior art the generic claim is restricted to a specific microorganism, a deposit might be required to ensure sufficiency of disclosure of the specific microorganism.

Microorganisms which have been obtained by mutagenesis or by fusion are commonly considered as non-reproducible, since their preparation might require screening of millions of microorganisms to identify a single one having the identical characteristics as the claimed one without *any certainty* that this result will be achieved. The importance of the concept of certainty was emphasized in **T 412/93 (Erythropoietin/KIRIN-AMGEN)** and **T 418/89 (Monoclonal antibody/ORTHO)**. In the case underlying the latter decision a hybridoma secreting a monoclonal antibody had been deposited. However, the properties of the deposited antibody were different from those disclosed in the specification. The Board did not acknowledge the deposit and therefore decided on the sufficiency of disclosure of a mouse monoclonal antibody disclosed only in writing, which was characterized by functional terms. The Board held:

The description of the patent in suit provides information concerning a general process for the production of hybridomas and monoclonal antibodies whereby the only feature being particularly directed to the present case is the use of E-rosette positive purified normal human peripheral T-cells as the antibody stimulating antigen. However, this fact alone is not sufficient to make the process reproducible as to monoclonal antibodies having the characteristics of Claim 1. To select a hybridoma of the desired kind in any case means a huge amount of effort and, above all, *it is not certain* that this hybridoma can be selected at all. (point 3.4) (emphasis added)

The concept of reproducibility with certainty was also illustrated in several further Board of Appeal decisions. In decision **T 780/95 (Antigenic preparations/EVANS MEDICAL)** the claims related to a purified *Bordetella pertussis* antigen which is extracted together with adenylate cyclase activity under given extraction conditions, and which is characterized by various parameters, including a ratio of Pro:Glu of substantially 1:1 as determined by amino acid analysis. The Board started by setting the relevant standard: in order to evaluate sufficiency of disclosure, it had to be established whether or not a product having the

technical features recited in the claims, including a Pro:Glu ratio of substantially 1:1, can be achieved by the skilled person without undue difficulty when following the instructions in the patent, optionally supplemented by the common general knowledge of that person (see point 3 of the decision). In the Board's view, if the skilled person were not able to perform a meaningful measurement, including of the Pro:Glu ratio, he would be prevented from knowing whether the protein he was looking for has been obtained or is present in a mixture. The Board saw this as equivalent to being unable to carry out the invention (see point 6 of the decision). The Board considered multiple methods described in the patent with regard to whether these methods would allow the skilled person making use of his common knowledge to obtain the claimed antigen. For many technical reasons, the Board came to the conclusion that the methods described in the patent would not have put the skilled person in the position of reproducibly and certainly achieving the claimed subject-matter. Since reproducibility was uncertain, the Board denied sufficiency of disclosure.

The need for certainty in reproducibility was especially well illustrated in decision **T 727/95 (Cellulose/WEYERSHAEUSER)**. The claimed subject matter in this case related to a method of producing a reticulated cellulose as defined in claim 1 involving culturing under specified conditions an *Acetobacter* microorganism having the ability of specific microorganisms designated by ATCC accession number to produce a cellulose product under given conditions. In the Board's view, the fact that the claim related to *Acetobacter* microorganisms having certain abilities of the deposited microorganisms designated by ATCC accession number meant that the claim covered not just those microorganisms identified by ATCC accession number, but also a host of other different microorganisms. Certain of the Patentee's statements suggested that finding these microorganisms might be a matter of luck. The Board viewed the finding of other stable *Acetobacter* strains in nature which were high-producers of cellulose a chance event; and relying on chance events for reproducibility constitutes undue burden in the absence of evidence that such chance events occur and can be identified frequently enough to guarantee success. The Board summarized by stating that there must exist other reliable means for producing such strains for sufficiency of disclosure to be acknowledged (see point 11 of the decision). In the EPO, then, the skilled person must not only know what to do to gain success but he must also know that doing it will lead to success, rather than just the possibility of success. In this case, the Board saw success as only a possibility rather than certainty, so it denied sufficiency of disclosure.

In the proceedings relating to **T 740/90 (Yeast/LESAFFRE)** an Opponent contested sufficiency of disclosure. Claim 1 of the patent was directed to an active dry baker's yeast characterized by a certain degree of gas development in four different tests. Claim 2 was directed to a specific deposited yeast strain. The Opponents had attempted to reproduce the gas development experiments set out in claim 1 and in more detail in the specification using the deposited yeast according to claim 2, but failed to obtain the results indicated in claim 1. How-

ever, since the Opponents had not applied the conditions set out in the patent for conducting the experiments, the Board held that the Opponent did not provide any proof of non-reproducibility of the invention. Since the patent contained an example of preparing a dry baker's yeast according to claim 1, sufficiency of disclosure was acknowledged. In its failed attempt to contest certain reproducibility, the Opponent illustrates the principle that the burden of proof for insufficient disclosure rests with the Opponent.

In **T 886/91 (Hepatitis B virus/BIOGEN INC.)**, the Board applied similar thinking to their assessment of sufficiency of disclosure. In that case, the claim related to recombinant DNA molecules contained in deposited strains, as well as HBV antigenicity. Both of these aspects had been contested by Opponents under sufficiency of disclosure, but the Board pointed out that since the parties did not show that the patent failed to disclose the claimed invention sufficiently clearly and completely for it to be carried out by a skilled person, then the claimed subject-matter is sufficiently disclosed. Again, any objection under sufficiency of disclosure, regardless of who presents it, must be backed up by substantiated doubts supported by verifiable facts if it is to succeed.

D.V.2.g. Clarity and support of claims

D.V.2.g.a. Functional features in claims

As outlined in C.I.3.e.b, functional terms are allowable if there is no other way to precisely define the invention without restricting the scope of protection in an undue manner. A number of early decisions discuss the allowability of functional terms. A typical example thereof is provided by **T 26/82 (–/BAYER AG)**, where a claim having the following wording was allowed by an Appeal Board:

A process for the preparation of 6-amino-6-deoxy-L-sorbose, characterized in that 1-amino-1-deoxy-D-glucitol is oxidized with oxygen accompanied by the action of suitable aerobic or facultatively aerobic microorganisms or of extracts thereof. (underlining denotes functional feature)

The allowability of functional terms was also confirmed in **T 81/87 (Preprorennin/COLLABORATIVE)**. In that decision, a claim having the following wording was considered allowable under Art. 84 EPC:

A transformable living cell selected from the group consisting of fungi, yeast, bacteria and mammalian cells containing genetic material derived from recombinant DNA material and capable of expressing bovine rennin.

The Board held:

As regards the use of cells of various origins according to Claims 1 and 2, the disclosure repeatedly emphasises that these are *such to enable expressions of proteins*. It was known at the time of filing that in addition to bacterial cells, various fungi, e.g. yeast cells, were suitable for the purpose. The specification itself refers to various preferred *Escherichia* and *Saccharomyces* strains in this respect. Thus, the terms in the claims are not without formal support, since it

would be unfair to restrict the claims to the exemplified strains in the disclosure excluding those which may be used in the future. *From the disclosure, it is implied for the skilled person that only those cellular organisms are relevant for use which are capable of providing expressions of the desired proteins [...].* (point 4) (emphasis added)

In the proceedings underlying **T 391/91 (Ice nucleating/UNIVERSITY OF CALIFORNIA)** an Examining Division had refused a process claim for preparing a certain microorganism, since the DNA used to transform the desired host cells was characterized by functional terms only. An Appeal Board reversed the decision of the Examining Division and summarized the criteria for the allowability of functional terms as follows:

[T]he essential technical features may be expressed in general functional terms, if, from an objective point of view, such features cannot otherwise be defined more precisely without restricting the scope of the invention and if in relation to these features the description provides instructions which are sufficiently clear for the expert to put the invention into practice with no more than a reasonable amount of experimentation (see, for example, T 68/85 OJ EPO, 1987, 228). (point 3.1.2)

Further, the Board concluded:

The skilled person is not obliged to use the described donor strains or to isolate DNA fragments of specific lengths or of specific sequences or to use the same host cells. As there is no reason to doubt that it is possible to generalize the specific teaching of the present examples, it would be unfair to the Appellant to require a restriction of Claim 1 by incorporation therein of the specific features of the examples.

...

The function of the examples is primarily that of providing a guidance for the successful execution of the invention in its broader outline. The skilled person is likely to refer to the examples in order to design a strategy to cut the genomic DNA of the donor organism, in order to test the INA, in order to construct a suitable expression vector and to choose a suitable host system. However, the skilled person can use any suitable variant capable of providing the same effect of the invention (see T 292/85 OJ EPO, 1989, 275). This might be tedious, but it is nothing out of the ordinary in this field and involves only routine trials. (point 3.1.2)

In decision **T 923/92 (Human t-PA/GENENTECH)** the granted claims related to a process involving preparing cDNA from mRNA extracted from a specific melanoma cell line. The claims recited a polypeptide having human tissue plasminogen activator function. The Board held that the functional feature of having human t-PA function lacked clarity because t-PA had multiple known functions. Without knowing which one was intended, it was impossible to determine the scope of the claim.

D.V.2.g.b. Clarity and the view of the skilled person

One of the main questions in considering clarity of claims is whether or not the skilled person can definitely recognize the boundary, i.e. scope of the claims. This was clear for instance in **T 744/08 (Recovery of virus/XANOVA)**, where the claims related to the process of harvesting a herpes virus from an infected cell culture. Among other things, the claims specified that the process is

“without a cell-disruption step”. The Board considered that in the absence of a definition for this feature in the application, the meaning of this feature was ambiguous. Does it mean that the claim requires no cell disruption at all? Or rather that only a minimal, not excessive or acceptable level of cell disruption is allowed. If the latter, then how much is acceptable? The Board held that the skilled person could not determine the scope of the claim, and rejected the claim as unclear. This is a good illustration of how the EPO views clarity in the sense of Art. 84 EPC: if the bounds of the claim are determinable, then the claim is clear. If they are not determinable, then the claim is unclear and not allowable. When drafting a patent application, it is therefore advisable to include definitions for as many terms as possible so that support exists for optionally limiting claims, if required, by incorporating a clear definition into the claims.

Decision **T 1084/00 (HIV-3 variants/INNOGENETICS)** related to an HIV-3 retrovirus strain, the essential morphological and immunological properties of which were defined by reference to a deposited retrovirus, identified by accession number. Another claim related to a nucleic acid molecule containing cDNA corresponding to the entire RNA genome of the HIV-3 retrovirus strain, and was defined as specifically hybridizing with the nucleotide sequence of the HIV-3 strain identified by accession number under stringent hybridization conditions. The Board held that the definition of the claimed HIV-3 strain by reference to a deposited HIV-3 strain satisfied the requirements of clarity. The Board believed that the “stringent hybridization conditions” were known to the skilled person and were anyway defined in the description, so the meaning of this term was clear as well. Finally, the Board considered the term “specific hybridization”, and referred to decision **T 190/99 (-/-)**, which stated that when considering a claim the skilled person should exclude interpretations which are illogical or do not make technical sense and should in general seek to understand rather than misunderstand the claims. The Board believed that the only sensible interpretation of the term “specific hybridization” was that the hybridization is limited to the deposited HIV-3 strain and that strains HIV-1 and HIV-2 do not hybridize. The Board therefore held that the claims were clear in the sense of Art. 84 EPC.

The above view regarding clarity under Art. 84 EPC and the limits of the claim was perhaps made clearest in decision **T 960/98 (Detergent composition/UNILEVER PLC)**. Although not related to microorganisms, it is included here because of the lucidity with which the Board articulated the above concepts in their opinion. The claims in this case recited a viscosity range, and Opponents had argued that the claimed invention was insufficiently disclosed because in the absence of measurement conditions it was impossible for the skilled person to establish the limits of the claims. As a result, the skilled person could not know when his actions fell within the claims. In its opinion (point 3.4.4) the Board noted that the Opponents had not asserted that the skilled person would have difficulty measuring the viscosity, but that the skilled person could not establish the limits of the claim. Varying results obtained using differ-

ent temperatures or measurement methods do not necessarily disable the skilled person from carrying out the invention (Art. 83 EPC). In the present case the objection related to the question of whether the invention is correctly defined in accordance with Art. 84 EPC. The question of whether the boundaries of the invention can be determined, then, is the relevant question when assessing clarity under Art. 84 EPC.

D.V.2.h. Product claims for microorganisms

Claims relating to microorganisms may cover whole genera of species or descendants of a selected single cell. Generally, claims directed to a certain microorganism, particularly a microorganism identified by its deposit number, are of fairly limited scope. Therefore, terms such as “having the identifying characteristics of ...” or “and mutants and variants of ...” are often included in claims. Both terms frequently trigger objections in the EPO under clarity and/or sufficiency of disclosure. However, at least the term “mutants and variants” may be considered admissible, providing the extent of mutation and variance is defined and reproducible with certainty.

When including mutants or variants in the claim language, it is therefore highly advisable to define these terms in the specification. There is no fixed definition as to what percentage of homology on the basis of nucleic acid or amino acid sequences is required, for example, for a microorganism to be considered an admissible mutant or variant of a claimed microorganism. The introduction of a function that must be fulfilled by the mutants may help to get a claim directed to such mutants allowed.

For claims directed to a microorganism characterized by possessing a certain DNA or expressing a certain protein it is generally advisable to include fallback positions in the specification, for example, referring to a 80%, 90%, 95% and/or 99% homology/identity on the nucleic acid or amino acid level. Specific fallback positions not included in the application cannot admissibly be added later, even if they fall within originally disclosed ranges. For instance, even if the original application discloses a homology range of 95–99%, but does not specifically disclose a homology of 97%, it is not generally possible later to add “97%”. It is therefore advisable to include as many specific fallback positions as possible in the original application.

Furthermore, with regard to the clarity of claims directed to microorganisms, the EPO frequently objects to claims as being unclear when the claim attempts to define the claimed subject-matter by an internal designation. This objection may be overcome by including, e.g. the deposit number. In the absence of a deposit, the claimed microorganism must be characterized as precisely as possible, for example, by including a reference to restriction maps or the nucleic acid sequence of the DNA rendering the microorganism patentable or by including the process for its preparation.

In applications drafted in the US, it is common to characterize the claimed microorganism as being “isolated” or “purified”. This kind of characterization is not required under EPO practice (nor, indeed, advised, as discussed in previous chapters). A claim directed to a microorganism, e.g. a fungus, is inherently considered to refer to the fungus outside its natural environment, and is understood to cover a fungus made available to the public by isolation and suitable characterization.

D.V.2.h.a. Product claims characterizing a microorganism in functional terms

This type of product claim often concerns “classical” microorganisms, i.e. microorganisms of a type already available in the era before genetic engineering. Most of the claims relate to microorganisms involved in the production of biological compounds, e.g. amino acids, antibiotics or monoclonal antibodies, etc. or to microorganisms used for fermentation purposes.

Claim drafting:

A claim characterizing a microorganism by functional terms may have the following general wording:

Microorganism X being capable of ...

Examples of claims granted by the EPO and defining a microorganism by functional terms are provided below. Functional terms are underlined.

EP-B1 – 0197497 – Claim 1:

A yeast for making bread which belongs to the genus *Saccharomyces cerevisiae*, is su-
crose non-fermentable, is incapable of decomposing fructooligosaccharide and has suit-
ability for making bread.

EP-B1 – 0227367 – Claim 1:

A murine-derived hybridoma cell line capable of producing in the medium of its
growth a monoclonal antibody capable of specifically binding with hpG-CSF in an an-
tigen/antibody reaction.

In the above claim, the cell line is characterized by producing a certain antibody.

EP-B1 – 0278959 – Claim 1:

A substantially pure culture of ATCC 53522 or a mutant thereof capable of protect-
ing seeds from a damping off disease.

The above claim characterizes the microorganism by its capability to protect seeds as well as by its deposit number. The culture may be a mutant of the cited deposited culture.

EP-B1 – 2157170 – Claim 1:

A microorganism comprising one or more exogenous nucleic acid sequences encod-
ing at least one wax synthase (EC 2.3.1.75), one thioesterase (3.1.2-, 3.1.1-), and a fatty
acyl-CoA synthase (EC 2.3.1.86).

The remainder of the claim examples below in this section relate to plant cells. As discussed above, plant cells are considered to be microorganisms.

EP-B1 – 2319932 – Claim 1:

A transgenic plant cell comprising an isolated polynucleotide that encodes a protein that enzymatically degrades a herbicide selected from the group consisting of a phenoxy auxin herbicide and an aryloxyphenoxypropionate herbicide, wherein said polynucleotide hybridizes under stringent conditions with the full complement of a nucleic acid molecule that encodes SEQ ID NO:9, wherein said plant expresses said polynucleotide and produces said protein.

EP-B1 – 2292765 – Claim 8:

A genetically modified plant or part thereof of cells therefrom comprising an isolated nucleic acid molecule of any one of Claims 1 to 3, preferably wherein the genetically modified plant or part thereof or cells therefrom exhibits altered flowers or inflorescence, further preferably wherein the plant part is selected from the group comprising sepal, bract, petiole, peduncle, ovaries, anthers, flowers, fruits, nuts, roots, stems, leaves and seeds.

EP-B1 – 2224009 – Claim 8:

A plant, a plant cell, or a seed, comprising a nucleotide sequence encoding microbial Neu5Ac lyase operatively linked with a regulatory region that is active in the plant.

EP-B1 – 2093283 – Claim 1:

A plant cell comprising in its chloroplasts enzymatic activities for converting glycolate into malate, wherein said plant cell comprises in its chloroplasts a first polypeptide having glycolate oxidase activity, a second polypeptide having malate synthase activity and a third polypeptide having catalase activity.

EP-B1 – 1799813 – Claim 8:

A carrot root host cell producing an IgG4 antibody, comprising a polynucleotide encoding the IgG4 antibody, wherein said antibody comprises a human antibody natural signal peptide sequence.

D.V2.h.b. Product claims characterizing a microorganism by a certain DNA or plasmid

The essential feature in claims of this type is a certain DNA or plasmid, conferring special properties to a microorganism. Very often the claims refer to other DNA/vector claims.

Claim drafting:

A general form of a product claim characterizing a microorganism by a certain DNA may have the following wording:

A microorganism transformed with DNA X.

Examples of claims granted by the EPO defining a microorganism by a DNA contained therein are provided below. References to the relevant DNA or plasmid are underlined.

EP-B1 – 0323806 – Claim 42:

A host cell which is transformed with recombinant DNAs according to any of the claims 31–39.

EP-B1 – 0148605 (underlying decision T 412/93 – Erythropoietin/KIRIN-AMGEN) – Claim 13:

A procaryotic or eucaryotic host cell transformed or transfected with a DNA sequence according to any of claims 1, 2, 3, 6, 7 and 8 in a manner allowing the host cell to express said polypeptide product.

In addition to referring to certain DNA sequences this claim recites the functional characteristic of allowing the host cell to express the polypeptide.

EP-B1 – 0200746 – Claim 1:

A plant cell which is resistant to a herbicidal glutamine synthetase (GS) inhibitor, wherein said resistance is caused by plant cell levels of GS activity which, when present in an otherwise herbicidal GS-inhibitor sensitive plant cell, render said cell substantially resistant to said herbicidal GS-inhibitor, said plant cell carrying a DNA sequence combination which comprises:

- (a) a first DNA sequence coding for a glutamine synthetase (GS) having the sequence shown on page 13, operably linked to
- (b) a second DNA sequence capable of increasing the levels of expression of said first DNA sequence such that when such combination is present in an otherwise herbicidal GS-inhibitor sensitive plant cell, said cell is substantially resistant to said herbicidal GS-inhibitor.

The above claim characterizes the microorganism by its resistance to a GS inhibitor and the presence of certain DNA sequences.

EP-B1 – 0246678 – Claim 1:

A substantially normally sporulating *Bacillus* which contains mutated subtilisin and neutral protease genes so as to be incapable of excreting enzymatically active subtilisin or neutral protease.

EP-B1 – 0383431 – Claim 1:

An attenuated enterovirus or rhinovirus having an attenuating mutation at least at a position which is, or corresponds with, position 471 of the genome of poliovirus type 3 Leon strain where the numbering of the positions of the said genome is set by numbering the positions at the beginning and end of the following nucleotide sequence as positions 470 and 484 respectively: AUCCUAACCAUGGAG.

The above claim is an example of a claim relating to a virus characterized by a certain mutation.

EP-B1 – 2334799 – Claim 1:

A thermophilic recombinant bacterium comprising a heterologous gene encoding a glycerol dehydrogenase, wherein the heterologous gene encoding a glycerol dehydrogenase has been incorporated into the chromosome.

EP-B1 – 2129390 – Claim 1:

A recombinant turkey herpesvirus comprising a hemagglutinin gene of avian influenza virus and the cytomegalovirus immediate early promoter, wherein said hemagglutinin gene is under control of said promoter.

The remainder of the claim examples below in this section relate to plant cells. As discussed above, plant cells are considered to be microorganisms.

EP-B1 – 2458010 – Claim 3:

A plant cell comprising the recombinant construct of claim 2.

EP-B1 – 2390339 – Claim 5:

A cell or an oilseed plant or a transgenic seed comprising in its genome the recombinant DNA construct of Claim 4.

EP-B1 – 2333088 – Claim 7:

A transformed plant cell comprising at least one expression cassette according to claim 5.

EP-B1 – 2350290 – Claim 6:

A plant, cell, or tissue comprising a recombinant vector of claim 5.

EP-B1 – 2333072 – Claim 6:

A recombinant microbial cell comprising at least one copy of an isolated nucleic acid molecule according to any one of Claims 1 to 3.

EP-B1 – 2333072 – Claim 8:

A recombinant plant cell comprising at least one copy of an isolated nucleic acid molecule according to any one of Claims 1 to 3.

D.V2.h.c. Product claims characterizing a microorganism by parameters

Microorganisms may be characterized, e.g. by their growth or fermentation properties or by other reliable parameters such as their lipid content or the G/C content of their DNA, optionally in combination with a taxonomic designation.

Claim drafting:

A claim characterizing the microorganism by parameters may have the following general wording:

A microorganism X having a reduced/increased content of ...

A microorganism X having the following growth characteristics ...

An example of an allowed product claim is shown below. The parameters are underlined.

EP-B1 – 2418276 – Claim 1:

Microorganism strain of the species *Escherichia coli* comprising a gene coding for a frecombinant protein and a mutated gene coding for the host protein YddS (putative

hemin-binding protein, Swiss Prot # Q8XAU4 57 kDa, putative dipeptide transport protein), characterized in that said recombinant protein is secreted during a fermentation and said mutated gene coding for said YddS host protein has been mutated so as to cause reduced expression of said host protein compared to the wild-type gene on which said mutated gene is based such that the host protein encoded by the mutated gene is produced and secreted in an amount which is reduced by 100% compared to production and secretion in a wild-type cell.

D.V.2.h.d. Product claims characterizing a microorganism by a process for its preparation

Product-by-process claims are only allowable if the microorganism cannot be characterized by its structure or by parameters such as growth requirements, metabolic capabilities, etc. without unduly limiting the scope of the claim. This claim type may be appropriate in the case of microorganisms attained by cross-ings, fusions or growth under selective conditions.

Claim drafting:

A product-by-process claim relating to a microorganism may have the following general wording:

A microorganism obtainable by selecting ...

Examples of claims granted by the EPO defining a microorganism by a process for its preparation are provided below. The corresponding process language is underlined.

EP-B1 – 0198086 – Claim 7:

A mouse-human hybridoma or a cell line arising therefrom which is obtainable by fusing a human antibody producing cell with a mouse myeloma cell and which produces herpes simplex virus-reacting human monoclonal antibody of IgG type having a molecular weight of about 160,000 which has the property of reacting to glycoprotein B in the cell membrane and cytoplasm of a cell infected with herpes simplex virus types 1 and 2 but scarcely reacting to a cell which is not infected.

EP-B1 – 0338003 – Claim 1:

A hybridoma cell line produced by a hybridoma technique which produces a monoclonal antibody which specifically binds to the 1D3 surface antigen of neutrophils and which does not specifically bind to other human peripheral blood cells or to human acute leukemia cells and which does not significantly bind to granulocyte precursors in bone marrow, said 1D3 antigen having a molecular weight of approximately 48,000 daltons defined under reducing conditions and a molecular weight in the approximate range of 48,000 to 60,000 daltons defined under non-reducing conditions.

Both claims above characterize the claimed hybridoma by a process for its preparation and the specificity of the antibody produced by the claimed hybridoma.

EP-B1 – 2173886 – Claim 5:

A virus like particle (VLP) produced by the method of any of claims 1 to 4 comprising an influenza virus hemagglutinin (HA) protein and one or more than one lipid derived from a plant.

The method of claim 1 related to producing a virus-like particle (VLP) involving introducing a nucleotide sequence encoding influenza hemagglutinin (HA) into a plant, incubating the plant to allow expression of the VLPs, harvesting the plant, and purifying the VLPs of a given size range.

D.V2.h.e. Product claims characterizing a microorganism by its deposit number

The characterization of a microorganism by its deposit number is the very last resort, if claims having a broader scope are not allowable.

Claim drafting:

A claim characterizing a microorganism by its deposit number may have the following general wording:

A microorganism X being deposited at ... under deposit No ...

The characterization of a microorganism by its deposit number is exemplified by the following claims granted by the EPO. The relevant deposit accession numbers are underlined.

EP-B1 – 0103646 – Claim 1:

Yeast strain SAV-301 (FERM BP-261) of *Saccharomyces cerevisiae*.

EP-B1 – 0204009 – Claim 1:

A biological pure culture of *Hyphozyma roseoniger* ATCC 20624.

EP-B1 – 0234501 – Claim 1:

A hybridoma which has the identifying characteristics of ATCC HB 8944.

The claim is intended to cover not only hybridomas derived directly from the cited ATCC strain, but also hybridomas having the “identifying characteristics” of the deposited hybridoma.

EP-B1 – 0292272 – Claim 1:

A culture of a sporogenic, crystalliferous mutant of *Bacillus thuringiensis* having the identifying characteristics of a strain selected from NRRL B-18195, NRRL B-18196 and NRRL B-18197, wherein the strain is characterized as having the ability to produce bipyramidal crystals composed of toxic protein and requiring a leucine and valine containing nutrient medium for growth, sporulation and crystal production.

This claim characterizes the claimed *Bacillus thuringiensis* by (1) identifying characteristics of deposited strains, (2) a certain capability and (3) growth requirements.

EP-B1 – 2327764 – Claim 1:

A Newcastle Disease Virus clone comprising the DNA nucleotide sequence of Seq. ID. No. 1 or as deposited with European Collection of Cell Cultures as Accession Number 06112101 on Nov. 21, 2006.

EP-B1 – 2256210 – Claim 4:

Trichoderma atroviride strain FKI-3737 (FERM ABP-11099 corresponding to FERM BP-11099).

EP-B1 – 2241616 – Claim 1:

A biologically pure culture of *L. rhamnosus* HN001 AGAL deposit number NM97/09514 dated 18 August 1997.

EP-B1 – 2559753 – Claim 1:

An L-valine-producing *Corynebacterium glutamicum* strain KCCM11201P.

EP-B1 – 2374868 – Claim 1:

A *Fusarium* strain which is *Fusarium solani* KCCM90040 [Accession No. KCCM10881P].

EP-B1 – 2166083 – Claim 1:

A novel *Lactobacillus paracasei* subsp. *paracasei* SG96 strain, which has been deposited in China General Microbiological Culture Collection Center (CGMCC), with accession number: CGMCC 2697.

D.V.2.i. Process claims for microorganisms

In the following section, process claims for preparing a microorganism as well as process claims involving use of a microorganism are discussed.

D.V.2.i.a. Process claims for preparing a microorganism

Generally, microorganisms may be obtained by isolation from their environment, which is often done by growing them under selective conditions, by transformation using a specific DNA or, for example in the case of hybridomas, by fusion of different cells.

Claim drafting:

A claim directed to a process for preparing a microorganism may have the following general wording:

A process for preparing microorganism X, wherein a cell Y is transformed with DNA Z.

Examples of process claims for preparing microorganisms granted by the EPO are provided below:

EP-B1 – 0323806 – Claim 49:

A process for the preparation of a host cell according to claim 42 or 48, characterized in that a suitable cell is transformed with one or two vectors by electroporation, calcium treatment, microinjection or protoplast fusion.

Claims 42 and 48 referred to in this claim are directed to a host cell transformed with certain recombinant DNAs or to a host cell being transformed with recombinant DNAs and secreting chimeric monoclonal antibodies as defined in claim 1. The process itself is a process of analogy.

EP-B1 – 0103646 – Claim 2:

A method of constructing a killer yeast comprising fusing a karyogamy deficient mutant yeast harboring killer plasmids to the spore produced by meiosis of a diploid or polyploid homothallic yeast before the homothallic spores undergo two cell divisions and selecting the desired cells from those cells which bud from the fused cells by subjecting to tetrad analysis to see the killer-behaviour of the cells.

This claim relating to the construction of a specific yeast comprises the process steps of fusing selected partners at selected times and selecting derived cells exhibiting a certain behavior.

EP-B1 – 0179871 – Claim 1:

A method for continuous production of HTLV-III virus which comprises infecting a cell culture of highly susceptible permissive cells consisting of a neoplastic aneuploid OKT4-positive T-cell line with said virus, selecting cells which preserve the capacity for permanent growth after infection with said virus, growing said cells under conditions suitable for cell growth and recovering said virus produced by said cells.

This method for the continuous production of HTLV-III virus comprises the process steps of infecting, selecting, growing and recovering.

EP-B1 – 0318216 – Claim 71:

A method of growing hepatitis C virus (HCV) comprising providing cells infected with HCV, and propagating said cells *in vitro*, wherein said HCV is characterized by:

- (i) a positive stranded RNA genome;
- (ii) said genome comprising an open reading frame (ORF) encoding a polyprotein; and
- (iii) said polyprotein comprising an amino acid sequence having at least 40% homology to the 859 amino acid sequence in Figure 14.

EP-B1 – 0383434 – Claim 7:

A process for the preparation of an attenuated enterovirus or rhinovirus as defined in claim 1, which process comprises:

- (i) introducing the desired mutation by site-directed mutagenesis into a sub-cloned region, which includes the position it is wished to mutate, of a cDNA of an enterovirus or rhinovirus;
- ii) reintroducing the thus modified region into the complete DNA from which the region was derived; and
- (iii) obtaining live virus from the cDNA thus obtained.

Claim 1 of this patent is directed to a certain attenuated enterovirus having an “attenuating mutation” at a certain position.

EP-B1 – 0198086 – Claim 1:

A process for preparing a mouse-human hybridoma which produces human antiviral antibody, characterized by sensitising a human antibody-producing cell with a virus or a

protein or glycoprotein from a virus *in vitro* in the presence of a mitogen, and fusing the sensitised cell with a mouse myeloma cell.

**EP-B1 – 0112342 (underlying decision T 391/91 – Ice nucleating/
UNIVERSITY OF CALIFORNIA) – Claim 1:**

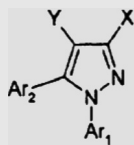
A method for producing unicellular microorganism host cells having ice nucleation activity (INA), or enhanced INA activity, which comprises:

isolating from a donor microorganism expressing an INA phenotype a DNA segment including a single gene encoding an expression product responsible for said INA phenotype; introducing said DNA segment into said host cells so that the gene will be expressed therein;

producing therefrom a culture of said cells which have additional DNA encoding INA and thereby have acquired INA, or enhanced INA, as compared to the host cells before introducing said DNA.

EP-B1 – 2118269 – Claim 1:

A method for producing an isolated, single plant cell comprising an intact cell wall, wherein said method comprises culturing plant cells comprising intact cell walls in medium containing glycerol and a tubulin de-polymerizing compound selected from the group consisting of dinitroanilines and a compound according to the following formula:



wherein

X = CO₂R, CH₂CO₂R, CH₂CH₂CO₂R, (CH₂)₃CO₂R, OCH₂CO₂R, OCH(CH₃)CO₂R, OC(CH₃)₂CO₂R, CH₂OCH₂CO₂R, CH₂CH(CO₂CH₂CH₃)CO₂R or OCH(CO₂CH₂CH₃)CO₂R

Y = CN, Cl, Br, F, or NO₂

Ar₁ = unsubstituted phenyl, unsubstituted pyridine, 1–3 substituted phenyl, 1–3 substituted pyridine, or substituted with halogen or CN

Ar₂ = unsubstituted phenyl, unsubstituted pyridine, 1–3 substituted phenyl, 1–3 substituted pyridine, or substituted with halogen or CN; and

R = H or 1–5 carbon linear or branched ester.

The “microorganism” in the above claim is a plant cell.

EP-B1 – 2428581 – Claim 1:

A method for identifying a first group of microorganisms and a second group of microorganisms, expressing the same enzymatic activity, comprising the following steps:

- incubating said first and second groups of microorganisms in a reaction medium comprising a first enzyme substrate and a second enzyme substrate, said first and second enzyme substrates being metabolized by the same enzymatic activity;
- identifying said groups of microorganisms.

This claim above is directed to a method of “identifying” a group of microorganisms based on certain stated functional characteristics. While not a classical method of production claim, it still results in obtaining (by “identifying”) microorganisms having the desired functions.

EP-B1 – 2121918 – Claim 1:

A method for preparing a mutant microorganism producing a high concentration of L-threonine in high yield, using site-specific mutation, the method comprising:

- (a) disrupting in a microorganism a gene encoding repressor of lac operon, a gene encoding homoserine O-succinyltransferase, a gene encoding diaminopimelate decarboxylase and a gene encoding L-threonine dehydrogenase;
- (b) mutating in a microorganism a gene encoding aspartokinase I and aspartokinase III to prevent the inhibition of aspartokinase I and aspartokinase III activities; and
- (c) inducing in a microorganism substitution of a promoter of L-threonine operon or acetyl CoA synthetase with a strong promoter.

D.V2.i.b. Process claims involving use of a microorganism

The following considers process claims which make use of certain microorganisms in order to obtain a desired result.

Claim drafting:

A general claim directed to a process involving a microorganism may have the following wording:

A method for producing compound X, wherein microorganism Y is incubated in culture medium and compound X is isolated from said culture medium.

Examples of process claims involving use of microorganisms granted by the EPO include the following. The steps of using the microorganisms are underlined.

EP-B1 – 0103646 – Claim 4:

A method of making wine, characterized by using the killer yeast constructed by the method according to claim 2.

EP-B1 – 0264074 – Claim 13:

A method for preparing Met-IGF-I, which comprises:

- a) transforming a host cell with a vector as claimed in any of Claims 1 to 9;
- b) growing said transformed host cell under conditions suitable for expression;
- c) lysing the transformed cell, and
- d) isolating Met-IGF-I from the lysate.

As can be seen from the above claim, the method steps are transforming, growing, lysing and isolating. This type of claim is quite common in the field of genetic engineering, in order to claim processes for preparing recombinant proteins.

EP-B1 – 0227260 – Claim 19:

A method for producing a desired product, said method being characterised in comprising the steps of:

- (1) ligating a DNA sequence encoding said desired product to a DNA sequence including a regulatory DNA sequence which is substantially identical to a regulatory DNA sequence which regulates the expression of a DNA sequence which encodes a pro-

- tease in a *Bacillus* species, preferably *B. subtilis*, to form a ligated DNA sequence, expression of said DNA sequence encoding said desired product being under the control of said regulatory DNA sequence;
- (2) transforming said ligated DNA sequence into a *Bacillus* cell, preferably a *B. subtilis*;
 - (3) prior to or after steps (1) and (2), introducing into said bacterial cell an enhancing DNA sequence capable of effecting enhanced expression of said gene encoding said desired product, said enhancing DNA sequence comprising a first and a second sequence, said second sequence being a *Bacillus* sequence which is not a portion of a *sacQ* sequence, said first sequence comprising a portion of a *sacQ* DNA sequence which, when combined with said second sequence is effective to cause said enhancing, said first and second sequences together comprising less than the entire *sacQ* sequence;
 - (4) culturing said *Bacillus* cell in a culture medium, and
 - (5) recovering said desired product from said *Bacillus* cell or culture medium.

This claim is directed to the expression of a desired product in *Bacillus* cells, wherein expression is regulated by a *Bacillus* protease regulatory DNA sequence and expression is enhanced by an enhancer comprising a portion of *sacQ* DNA sequence and a further DNA sequence. The process steps are ligating, transforming, introducing, culturing and recovering.

EP-B1 – 0204009 – Claim 5:

A process for preparing a diol of the formula (3), which comprises cultivating a biologically pure culture according to any of claims 1 to 3 under aerobic conditions in an aqueous nutrient medium containing one or more of the compounds ..., wherein R is ...

The process step of this claim is cultivating a biologically pure culture which was defined in three preceding claims.

EP-B1 – 0292272 – Claim 6:

A method for controlling Lepidopteran insects comprising subjecting the insects to an effective amount of a sporogenic, crystalliferous mutant of *Bacillus thuringiensis* as claimed in any one of claims 1–4.

EP-B1 – 0278959 – Claim 6:

A method for protecting plants in a growing medium from a damping off disease comprising placing in the growing medium in the immediate vicinity of the plant to be protected bacteria which is ATCC 53522, a mutant thereof capable of protecting seeds from a damping off disease or a mixture of said mutants or of one or more said mutants and ATCC 53522.

EP-B1 – 1972602 – Claim 1:

A method for mass cultivation of exclusively planktic mixed algae/bacteria cultures in open, flat round basins provided with shield scrapers (3) while peripherally feeding culture media (7) and a central extraction funnel with three extraction points, wherein for cultivating mixed algae/bacteria cultures floating components are periodically extracted via a central overflow (8), fractions settling at the level of the funnel floor are extracted via a lower extraction point (9), and the planktic algae/bacteria fraction is extracted from the free water and fed back to the periphery of the basin via a central extraction point (6) disposed between the overflow and the lower extraction point (9).

EP-B1 – 1891206 – Claim 1:

A method of producing secondary metabolites using *Taxus* cell culture, by culturing the plant cells in a culture medium for plant cell culture containing a saccharide mixture of fructose and sucrose, as the sole carbon source, to increase the productivity of secondary metabolites, wherein the plant cell culture is conducted by adding the saccharide mixture at the cell growth phase and the secondary metabolite production phase, and wherein the contents of the saccharide mixture is 2 to 12% (w/v), the saccharide mixture contains sucrose and fructose in the mixture ratio by weight of 1:2 to 2:1, and the secondary metabolite is paclitaxel.

EP-B1 – 1851305 – Claim 1:

A method for large-scale production of a polypeptide in eukaryote cells contained in a serum-free culture liquid, said method comprising

- (i) a propagation phase for said cells, where the cells are propagated in a first cell culture liquid, and
- (ii) a production phase for said cells, where the cells are present in a second cell culture medium liquid,

wherein each of the cell culture liquids comprise a plant protein hydrolysate, and wherein the ratio between the concentration of the plant protein hydrolysate (C_1) in the first cell culture liquid and the concentration of the plant protein hydrolysate (C_2) in the second cell culture liquid is at least 1.5:1 ($C_1:C_2$).

EP-B1 – 1799813 – Claim 17:

A method of producing a recombinant antibody, the method comprising:

- (a) generating a suspension culture comprising carrot root cells being genetically modified to express the recombinant antibody; and optionally
- (b) recovering the recombinant antibody from said suspension culture thereby producing the recombinant antibody;

wherein said carrot root cells express assembled, functional human IgG4 antibodies, wherein said antibodies comprise human antibody natural signal peptide sequence, and wherein said antibodies have a higher level of binding affinity for an antigen than a corresponding antibody produced in mammalian cell culture.

EP-B1 – 2230302 – Claim 1:

A method for producing L-cysteine, L-cystine, a derivative or precursor thereof, or a mixture of these, which comprises culturing a bacterium belonging to the family *Enterobacteriaceae* in a medium and collecting L-cysteine, L-cystine, a derivative or precursor thereof, or a mixture of these from the medium, wherein said bacterium is able to produce L-cysteine, and has been modified so that expression of the *ydjN* gene coding for *ydjN* protein is reduced by introducing a missense mutation, a nonsense mutation, or a frame shift mutation into the coding region of the *ydjN* gene on a chromosome, by deleting a part of, or the entire coding region of the *ydjN* gene on a chromosome, or by modifying an expression control sequence of the *ydjN* gene, or the *ydjN* gene is disrupted.

EP-B1 – 2259753 – Claim 3:

A method for producing L-valine, comprising culturing KCCM11201 P of claim 1 in a culture medium.

EP-B1 – 2154238 – Claim 2:

A method for producing a fermented food or drink product comprising the step of: fermenting raw materials of a food or drink product using the *Lactobacillus pentosus* according to Claim 1, in order to obtain a fermented food or drink product.

D.V.2.j. Use claims/purpose-limited product claims for microorganisms

As noted in C.I.3.e.a, use claims are interpreted as process claims.

Claim drafting:

A claim relating to the use of a microorganism may have the following general wording. The latter example is a medical use claim in purpose-limited product format.

Use of microorganism X for preparing compound Y.

Microorganism X for use in a method of treating disease Y.

Examples of allowed use claims are shown in the following. The purposes of use are underlined.

EP-B1 – 1838859 – Claim 10:

Use of a plant cell according to claim 1... for the production of a modified starch.

This claim has been edited to remove subject-matter not relating directly to a plant cell. In this claim, the plant cell (understood as the microorganism) is used as a “factory” for making modified starch.

EP-B1 – 1767639 – Claim 1:

A plant cell transformed with a gene encoding the protective R7 antigen against leucocytozoonosis development for use in conferring immunity against *Leucocytozoon caulleryi* on an animal through oral administration, wherein the plant cell is to be administered to animals whose antibody tier against said antigen has been increased by vaccination.

In the above medical use claim, the plant cell itself is used as a therapeutic agent for conferring immunity against a specific organism. The medical use claim is written in purpose-limited product format, as allowed under Art. 54(4) and (5) EPC 2000.

EP-B1 – 2124976 – Claim 1:

A composition for use in a method for inhibiting the growth of a methicillin-resistant *Staphylococcus aureus* in vivo comprising an effective amount of at least one lactic acid bacterium strain selected from the group consisting of *Lactobacillus acidophilus* I-1492, *Lactobacillus casei* and a mixture thereof and a pharmaceutically acceptable vehicle.

In the above medical use claim, a specified bacterial strain or strain mixture is used as a therapeutic agent for inhibiting the growth of a separate specified bacterial strain. Again, the medical use claim is written in purpose-limited product format, as allowed under Art. 54(4) and (5) EPC 2000.

EP-B1 – 2124976 – Claim 10:

Use of a composition comprising an effective amount of at least one lactic acid bacterium strain selected from the group consisting of *Lactobacillus acidophilus* I-1492, *Lactobacillus casei* and a mixture thereof and a pharmaceutically acceptable vehicle in the manufacture of a medicament for treating a methicillin-resistant *Staphylococcus aureus* infection.

The purpose in this medical use claim is equivalent to that of the above claim, only the claim is formulated as a traditional “Swiss-type” medical use.

EP-B1 – 2123291 – Claim 1:

An agent comprising *Lactobacillus amylovorus* cells as an active ingredient, for use in a method of improving or preventing periodontal disease.

This medical use claim is formulated in purpose-limited product format, as allowed under Art. 54(4) and (5) EPC-2000.

EP-B1 – 2123291 – Claim 13:

Use of an agent as defined in any one of claims 1 to 9 in the manufacture of a medicament, food, feed or beverage for improving or preventing periodontal disease.

This medical use claim is formulated as a traditional “Swiss-type” medical use.

D.VI. Plants

D.VI.1. Introduction

This chapter addresses the possibilities for protecting plants and parts of plants taking into consideration the established practice of the EPO and relevant case law.

As used herein:

The term “plants” includes natural plants, hybrid plants, and transgenic plants.

The term “natural plants” includes naturally occurring wild plants and cultivated plants obtained by a conventional plant breeding process.

The term “hybrid plants” means plants which are obtained by hybridization, i.e. a genetic recombination process between genomes of plants which are derived from different populations and which cannot be stably propagated without losing some traits.

The term “transgenic plants” means plants which contain a foreign DNA sequence that is normally not observed in the plants. Usually the foreign DNA is introduced into the plants by genetically engineering single plant cells which are then grown to the complete transgenic plants. The foreign DNA can be, for example, a regulatory sequence controlling the expression of another gene or the protein-coding sequence itself.

The term “parts of plants” includes highly differentiated plant parts such as plant organs, e.g. roots, leaves, and propagating material, e.g. seeds, seedlings, etc. “Parts of plants” also includes and poorly differentiated plant parts such as plant tissue and cells. Plant components such as plant genes and proteins, are separately discussed in D.II and D.III.

D.VI.2. Protecting plants under the EPC

General patentability requirements for plants apply as for any other kind of invention. As above, this applies for the basic patentability requirements of novelty, inventive step and industrial applicability, as well as the requirements for the application, for example, sufficiency of disclosure (Art. 83 EPC) and clarity (Art. 84 EPC). Certain of these aspects are discussed below in the context of specific decisions of the EPO Boards of Appeal. Because of the particular importance of sufficiency of disclosure (Art. 83 EPC) and clarity (Art. 84 EPC) for applications relating to plant inventions, these topics are addressed in greater detail in subchapters D.VI.2.c (for sufficiency of disclosure) and D.VI.2.d (for clarity) below.

D.VI.2.a. Morality and “ordre public”

Art. 53(a) EPC excludes from patentability inventions, the commercial exploitation of which would be contrary to “ordre public” or morality. These terms were interpreted in decision **T 356/93 (Plant cells/PLANT GENETIC SYSTEMS)** and later confirmed in decision **T 315/03 (Transgenic animals/HARVARD)**. Essentially, the “ordre public” in the sense of Art. 53(a) EPC is interpreted as meaning the protection of physical security and the physical integrity of individuals as part of society, including protection of the environment. The concept of “morality” in the sense of Art. 53(a) EPC is interpreted as related to the belief that some behavior is right while other behavior is wrong. This belief is founded on the totality of the accepted norms deeply rooted in, for the purposes of the EPC, European society and civilization. Inventions which are not in conformity with the conventionally accepted standards of conduct pertaining to this culture are excluded from patentability under the “morality” aspect of Art. 53(a) EPC.

A further discussion of this exclusion provision can be found in section D.VI.2.g.a, there with specific reference to transgenic plants.

D.VI.2.b. Plant varieties and essentially biological processes

Art. 53(b) EPC sets out several fundamental provisions relating to the types of subject-matter for which protection under the EPC is available, and the types for which it is not. Art. 53(b) EPC reads as follows:

European patents shall not be granted in respect of [...] plant or animal varieties or essentially biological processes for the production of plants or animals; this provision shall not apply to microbiological processes or the products thereof.

Art. 53(b) EPC thus first removes from patent protection plant and animal varieties, and essentially biological processes for the productions of plants or animals, and then provides an exception to such removal, expressly allowing protection for microbiological processes and the products thereof.

Each of these exclusions, as well as the exclusions from exclusions will be dealt with separately below.

D.VI.2.b.a. Plant varieties

As outlined earlier in B.I. and C.I.2.b, Art. 53(b) EPC excludes plant varieties from patentability. The definition of the term “plant variety” has previously been the subject of a number of early decisions of the Boards of Appeal, in particular, **T 49/83 (Propagating material/CIBA-GEIGY)**, **T 320/87 (Hybrid plants/LUBRIZOL)** and **T 356/93 (Plant cells/PLANT GENETIC SYSTEMS)**.

The EPC now provides a formal legal definition of the term “plant variety” in Rule 26(4) EPC, which reads as follows:

“Plant variety” means any plant grouping within a single botanical taxon of the lowest known rank, which grouping, irrespective of whether the conditions of the grant of a plant variety right are fully met, can be:

- (a) defined by the expression of the characteristics that result from a given genotype or a combination of genotypes,
- (b) distinguished from any one other plant grouping by the expression of at least one of said characteristics, and
- (c) considered as a unit with regard to its stability for being propagated unchanged.

This rule makes clear the Legislator’s intention that in order to be considered a plant variety, the plant in question must be both genetically homogenous as well as stable in its propagation.

Rule 26(4) EPC is substantially identical to Art. 1(vi) of the UPOV Convention of 1991 as well as to Art. 5(2) of the EC Regulation 2100/94 on Community Plant Variety Rights (CPVR), which establishes protection for plant Breeder rights relating to plant varieties. Unifying the definition for “plant variety” in the UPOV Convention, CPVR and the EPC has the effect that where protection for a “plant variety” is possible outside the EPC, it is excluded from patentability under the EPC. Conversely, where protection is possible for a non-varietal plant under the EPC, protection under e.g. CPVR is impossible because this regulation applies only for varietal plants. As a Board of Appeal succinctly noted in decision **T 1854/07 (Oil from seeds/CONSEJO SUPERIOR)**:

The extent of the exclusion for patents is the obverse of the availability of plant variety rights. (see point 7)

Enlarged Board of Appeal decision **G 1/98 (Transgenic plants/NO-VARTIS II)** provided further clarification regarding the exclusion of plant varieties under Art. 53(b) EPC. This decision stated that a claim encompassing plant varieties is not excluded from patentability under Art. 53(b) EPC as long it does not individually claim these varieties. This has the effect that it is fundamentally possible to obtain patent protection in the EPO for a genus of plants which may include individual plant varieties, as long as the subject-matter of the claim is not directed to a single plant variety.

This is now expressly regulated in Rule 27(b) EPC, which states that

Biotechnological inventions shall also be patentable if they concern [...] plants or animals if the technical feasibility of the invention is not confined to a particular plant or animal variety.

This principle has been applied in several decisions. In **T 1854/07 (Oil from seeds/CONSEJO SUPERIOR)**, for instance, the claims related to sunflower seeds of a defined oil content, obtainable by crossing and breeding methods. The claims were thus directed to a seed product defined in terms of how the seed product was made, and in which the referenced production method constituted an essentially biological process in the sense of Art. 53(b) EPC. In considering whether the claimed seed products were a “plant variety” in the sense of Art. 53(b) EPC, the Board applied the definition of Rule 26(4) EPC. The Board concluded that while the claimed seeds have certain common traits (specified fatty acid composition), these common traits do not constitute the seeds’ “genotype” which defines its entire genetic makeup. The question of whether or not the plant/seed is a “plant variety” in the sense of Rule 26(4) EPC, however, turns on the question of a uniform genomic makeup. The shared traits of the claimed seeds were not therefore enough to qualify them as plant varieties which would be excluded from patentability.

The Board therefore held that the claimed seeds were not excluded from patentability as plant varieties under Art. 53(b) EPC (point 13 of the decision). Significantly, the Board held that this applies, even though the claims may embrace plant varieties. This view is entirely consistent with **G 1/98**, according to which a claim which embraces certain plant varieties will still not be excluded under Art. 53(b) EPC as long as the claim is not directed to a specific plant variety.

Similarly, in **T 775/08 (Glyphosphate tolerant alfalfa/MONSANTO)** the claims related to a seed of a glyphosphate alfalfa plant, including a representative plant J-101, which had been deposited. The Board acknowledged that the deposited strain J-101 represented a plant variety in the sense of Rule 26(4) EPC. But since the claim was not limited to J-101, and also encompassed other strains, the broader claim was not excluded from patentability under Art. 53(b) EPC.

In **T 2239/08 (Rice/BAYER)** the claims related to a transgenic rice plant, cell, tissue or seed with specified transgene sequences which are present in specific rice varieties, specified by deposit number. As above, the Board held that while the deposited rice is a plant variety in the sense of Rule 26(4) EPC, the claims went further than just this variety, so following the holding of **G 1/98**, the claims were not excluded under Art. 53(b) EPC.

In **T 788/07 (Brassica/PIONEER)** the claims related to a hybrid seed with an inheritable and stable fertility restorer gene for male sterility, produced by a cross between a number of strains identified by deposit number, and with certain specified characteristics in the plant leading to specified characteristics in the plant’s oilseeds. The Board held that the seeds or resulting plants could not

be considered as units with regard to their “suitability for being propagated unchanged” as required by the definitions of “plant variety” in Rule 26(4)(c) EPC. The seeds/plants were therefore not considered “plant varieties” and were accordingly not excluded varieties under Art. 53(b) EPC. This decision illustrates how each and every requirement of Rule 26(4)(a), (b) and (c) EPC must be fulfilled if a plant is to be considered a “plant variety” excluded from patentability under Art. 53(b) EPC.

G 1/98 also held that in examining a claim to a process for the production of a plant variety, Article 64(2) EPC is not to be taken into consideration. Art. 64(2) EPC stipulates that if the subject-matter of the European patent is a process, the protection conferred by the patent extends to the products directly obtained by such process (but not to identical products obtained by some other process than that claimed). So a claim to a process of producing a specific plant would cover, besides the process itself, that specific plant in as far as it was made by the claimed method. The holding of **G 1/98** means that even if this specific plant is a “plant variety” in the sense of Rule 26(4) EPC, the process claim will not be excluded from patentability under Art. 53(b) EPC. **G 1/98** therefore suggests that process claims should be treated differently (i.e. more liberally) than product claims in regard to the exclusion of “plant varieties” under Art. 53(b) EPC.

Finally, the Enlarged Board stated in decision **G 1/98** that the exclusion of plant varieties in Art. 53(b) EPC applies to plant varieties (when claimed as products) regardless of the way in which these varieties are produced. Decision **G 1/98** therefore makes clear that the question of whether or not a plant is considered to be an excluded plant variety depends only on whether or not it meets the criteria set out in the definition of Rule 26(4) EPC.

The relevant European case law in connection with plants focuses on the exclusion provisions of Art. 53 EPC. Therefore, the exclusion provisions and the above definition of “plant varieties” represent major aspects of the discussion in the following subchapters.

D.VI.2.b.b. Essentially biological processes

Besides excluding plant and animal varieties (i.e. products), Art. 53(b) EPC also excludes “essentially biological processes for the production of plants or animals”. It should be noted that this exclusion of such processes applies for the production of any kind of plants, not just plant varieties. This exclusion is to be interpreted narrowly, especially in view of the fact that it does not apply to microbiological processes or the products thereof (Art. 53(b), second half sentence EPC).

The term “essentially biological” is formally defined in Rule 26(5) EPC, which states that

[a] process for the production of plants or animals is essentially biological if it consists entirely of natural phenomena such as crossing or selection.

A difficulty with this provision arose in interpreting the terms “crossing” and “selection”, specifically when considering whether these actions are intended to be interpreted in a transitive or an intransitive sense. The Legislator intended to give these terms in Rule 26(5) EPC a transitive meaning, i.e. that plants or animals are crossed or are selected by human intervention. However, these terms also carry an intransitive meaning equivalent to what happens in nature, where plants self-cross, for example, by pollination, and self-select, for example, by differential survival of plants having advantageous characteristics for thriving in their environment. The definition in Rule 26(5) EPC was thus deemed insufficient.

Questions regarding the definition of the term “essentially biological” were referred to the Enlarged Board of Appeal in the two decisions **T 83/05 (Broccoli/PLANT BIOSCIENCE)** dated 22 May 2007 and **T 1242/06 (Tomatoes/STATE OF ISRAEL)** dated 04 April 2008. The Enlarged Board of Appeal consolidated their response to these two referrals in respective decisions **G 2/07 (Broccoli/PLANT BIOSCIENCE)** and **G 1/08 (Tomatoes/STATE OF ISRAEL)**, the headnotes of which are identical and read as follows:

1. A non-microbiological process for the production of plants which contains or consists of the steps of sexually crossing the whole genomes of plants and of subsequently selecting plants is in principle excluded from patentability as being “essentially biological” within the meaning of Article 53(b) EPC.
2. Such a process does not escape the exclusion of Article 53(b) EPC merely because it contains, as a further step, or as part of any of the steps of crossing and selecting, a step of a technical nature which serves to enable or assist the performance of the steps of sexually crossing the whole genomes of plants or of subsequently selecting plants.
3. If, however, such a process contains within the steps of sexually crossing and selection an additional step of a technical nature, which step in itself introduces a trait into the genome or modifies a trait in the genome of the plant produced, so that the introduction or modification of that trait is not the result of the mixing of the genes of the plants chosen for sexual crossing, then the process is not excluded from patentability under Article 53(b) EPC.
4. In the context of examining whether such a process is excluded from patentability as being “essentially biological” within the meaning of Article 53(b) EPC, it is not relevant whether a step of a technical nature is a new or a known measure, whether it is trivial or a fundamental alteration of a known process, whether it does or could occur in nature or whether the essence of the invention lies in it.

By the wording of its opinion, the Enlarged Board of Appeal makes clear that the exclusion of “essentially biological processes” under Rule 26(5) EPC is intended to apply to the transitive meaning of “crossing” and “selection” by which plants (or animals) are crossed and are selected, as the objects of human intervention. In their further holdings, the Board drew a clearer dividing line between processes which are “essentially biological” and those which are not by requiring that the “essentially biological” process is a) non-microbiological and b) consists of the steps of sexually crossing the whole genomes of plants and of subsequently selecting plants.

The EPO Guidelines provide some helpful examples of situations in which the holdings of **G 2/07 (Broccoli/PLANT BIOSCIENCE)** and **G 1/08 (Tomatoes/STATE OF ISRAEL)** might apply. Some of these examples relate to animals, suggesting that the holding of **G 2/07 (Broccoli/PLANT BIOSCIENCE)** and **G 1/08 (Tomatoes/STATE OF ISRAEL)** with regard to the term “essentially biological process” should not be restricted to plants, but should also apply to animals. According to the Guidelines, a method of crossing, inter-breeding or selectively breeding animals such as horses, involving merely selecting for breeding and bringing together those animals (or their gametes) having certain characteristics would be “essentially biological” and therefore unpatentable. This method would remain essentially biological and unpatentable even if it would contain an additional feature of a technical nature, for example the use of a genetic molecular marker to select either parent or progeny. However, a process involving inserting a gene or trait into a plant by genetic engineering does not rely on recombination of whole genomes and the natural mixing of plant genes, and would therefore be patentable. Further, a process of treating a plant or animal to improve its properties or yield or to promote or to suppress its growth, for instance, a method of pruning a tree, would not be an essentially biological process for the production of plants or animals since it is not based on the sexual crossing of whole genomes and subsequent selection of plants or animals. The same would apply to a method of treating a plant characterized by the application of a growth-stimulating substance or radiation. As a final example, the EPO Guidelines note that the treatment of soil by technical means to suppress or promote growth of plants would also not be excluded from patentability.

From the above holdings of the Enlarged Board of Appeal in decisions **G 2/07** and **G 1/08**, taken together with the examples provided in the EPO Guidelines, it is clear that the EPO views the sexual crossing of whole genomes of plants (or animals) and the subsequent selection of the resulting organisms as the crucial criteria in determining whether or not a process is “essentially biological” and therefore excluded from patentability under Art. 53(b) EPC.

However, the case law has recently raised the question of whether a plant product produced by an “essentially biological process” should also be excluded from patentability for the reason that the product was made by an excluded method. The question is therefore whether or not the exclusion of essentially biological processes “spills over” to products made by such processes. Art. 53(b) EPC does not explicitly exclude products of essentially biological processes from patentability. Two recent decisions have referred such questions to the Enlarged Board of Appeal for review. **T 1242/06 (Tomatoes II/STATE OF ISRAEL)** dated 31 May 2012 and **T 83/05 (Broccoli II/PLANT BIOSCIENCE)** dated 08 July 2013 have each considered, and have referred to the Enlarged Board of Appeal to clarify, whether the exclusion of essentially biological processes for the production of plants in Art. 53(b) EPC can preclude the allowability of a product claim directed to plants or plant materials such as plant parts when

the product is claimed in product-by-process format (see section C.I.3.e.a for an explanation of product-by-process format). Specifically: is a claim directed to a plant or plant material (other than a plant variety) allowable if its process features define an (excluded) essentially biological process for the production of plants?

The decisions **T 1242/06** (dated 31 May 2012) and **T83/05** (dated 08 July 2013) provide a number of reasons for and against such a spillover effect to the products of excluded processes which are “essentially biological” in character. These considerations, both pro and contra, are pending before the Enlarged Board under case numbers **G 2/12 (Tomatoes II/STATE OF ISRAEL)** and **G 2/13 (Broccoli II/PLANT BIOSCIENCE)**. As this book goes to press, the Enlarged Board’s opinion in these matters has not yet appeared.

By the bare wording of Art. 53(b) EPC only three things are excluded from patentability: a) plant varieties, b) animal varieties and c) essentially biological processes for the production of plants or animals. The questions referred to the Enlarged Board of Appeal essentially ask whether this list should be expanded to contain a fourth exclusion: products of essentially biological processes for the production of plants or animals when the claims to these products are defined in terms of (excluded) methods of production. In the authors’ opinion, exclusions from patentability must be interpreted narrowly. In fact, the narrow interpretation of patentability exclusions has considerable precedent in past holdings of the Boards of Appeal, for instance in **T 866/01 (Euthanasia Compositions/MICHIGAN STATE UNIV.)**. Following this view, a statutory exclusion from patentability such as that laid down in Art. 53(b) EPC must be interpreted at face value, and narrowly, such that the only subject-matter excluded from patentability is that explicitly set out in the exclusion, and no other. Supporting this view is the notion that the Legislator had a very clear idea of which subject matter was to be excluded and which was not. This clear idea informed the Legislator’s decisions during drafting, meaning that in interpreting an exclusion provision one may assume that both inclusions as well as omissions were the explicit intention of the Legislator. In stating that

European patents shall not be granted in respect of [...] plant or animal varieties or essentially biological processes for the productions of plants or animals [...].

the Legislator thus intended that the only product claims which should be excluded from patentability are those directed to “plant or animal varieties”, and that the only process claims which should be excluded from patentability are those directed to “essentially biological processes for the productions of plants or animals”, i.e. regardless of whether or not the plants or animals resulting from the essentially biological process are plant or animal varieties. We note that Art. 53(b) EPC does not exclude from patentability “products of essentially biological processes for the production of plants or animals”, corresponding to the fourth potential category mentioned above. By not including this fourth category in Art. 53(b) EPC as subject-matter excluded from patentability, the au-

thors believe that the Legislator did not intend such subject-matter to be excluded from patentability.

Certain EPO Boards of Appeal have held consistently with the authors' view above. For instance, in **T 1854/07 (Oil from seeds/CONSEJO SUPERIOR)**, mentioned above, the Board considered what relationship, if any, exists between the question of whether a certain plant is to be classified as a "plant variety" in the sense of Art. 53(b) EPC and Rule 26(4) EPC and, on the other hand, the method by which the plant in question was produced. There, the Board stated:

[D]ecision G 1/98 makes clear beyond doubt that whether or not a plant is considered to be a plant variety depends only on whether or not it meets the criteria set out in the definition in Rule 26(4) EPC [...] The method for its production, be it by recombinant gene technology or by a classical plant breeding process, is not relevant for answering this question. It is not called into question that a plant variety may be the product of crossing and selection [...], but [...] it cannot be derived from decision G 1/98 that a plant by definition is not a variety when the claimed phenotype has been obtained by introduction of a transgene, whereas it is automatically a variety when the plant having the desired phenotype is achieved in a more traditional way, for example by mutagenesis or by crossing and selection.

The method by which a plant in question (and the same assumedly applies for animals) is produced, then, should have no bearing on the exclusion of this plant from patentability under Art. 53(b) EPC. The only products excluded from patentability under Art. 53(b) EPC are plant and "animal varieties" under Rule 26(4) EPC, and regardless of how produced. Conversely, the only methods excluded from patentability under Art. 53(b) EPC are "essentially biological methods" under Rule 26(5) EPC. This view is in standing with the narrow interpretation of patentability exclusions mentioned above, according to which the subject-matter excluded by the language of a provision is limited to that which the provision expressly states. A further consideration is that adding plants produced by essentially biological processes to the "list" of exclusions in Art. 53(b) EPC would effectively put the Enlarged Board of Appeal in the role of the Legislator. This is certainly not its function. The Enlarged Board of Appeal may interpret the law, but it may not amend it.

It should be stressed that the above is merely the personal opinion of the authors of the present book, and that as this book goes to press, the Enlarged Board of Appeal has not yet issued its opinion in response to the referred question of law.

D.VI.2.c. Sufficiency of disclosure in plant inventions

The following considers in greater detail how the Boards of Appeal have viewed the requirement of sufficiency of disclosure for inventions relating to plants. The majority of the plant-related applications filed in the EPO relate to transgenic plants. The decisions discussed below reflect this. In several instances outlined below, the holdings of the Boards of Appeal emphasize that the suffi-

ciency standards generally applicable for other types of inventions apply to plant inventions as well.

In the decision **T 694/92 (Modifying plant cells/MYCOGEN)**, the claims were directed to a method for genetically modifying a plant cell by inserting a particular gene, the resulting plant cell, as well as a plant or plant tissue grown from the modified plant cell. In the second headnote of that decision, the Board reiterated a basic principle governing sufficiency of disclosure, namely that the scope of the claims must be balanced by the skilled person's ability to put the whole claim into practice without undue burden. In point 5 of the decision, the Board applied the long-standing principle that the patent must provide at least one way to carry out the invention over its whole scope. In some cases, depending on the nature of the invention, this may require at least one example, even if the EPC itself has no formal requirement for examples. In that case, the Board noted that the claim was very broad, applying to the modification of any plant cell and the insertion of any plant structural gene. Given this breadth, the Board held that the patent did not provide sufficient disclosure

for the skilled person to reliably achieve without undue burden the technical effect of expression in any plant cell of any plant structural gene under the control of any plant promoter and that, consequently, they [experimental evidence and technical details in the description] do not provide sufficient support for a claim, such as present claim 1 broadly directed to such a method. (point 19 of the decision)

This decision illustrates the EPO's consistent stance on sufficiency of disclosure, applied to a transgenic plant invention, namely that the broader the claims are, the more crucial become supporting instructions which allow the skilled person to perform the claimed invention over its whole range. Therefore, in drafting broad claims, whether relating to plants or otherwise, the guiding principle in conforming with the requirements of sufficiency of disclosure should be whether the amount of disclosure provided in the patent is commensurate with the scope requested in the claims.

Decision **T 149/98 (Resistance development/BAYER)** related to cells of a plant with at least two specific genes stably inserted into the genome, and controlled by the same or different promoters. Each gene encoded a different related protein, allowing two different proteins to be produced in the plant cells. The claims also related to a plant as well as specific brassica, tomato, potato, tobacco, cotton or lettuce plants containing a combination of transgenes. Here, even though the patent did not report field experiments, the Board found no reason to believe that the claimed invention could not be put into practice (point 12 of the decision). This decision illustrates the principle, mentioned above, that the EPC contains no formal requirement for examples or experimental data so that, depending on the nature of the invention, the lack of such things in the patent need not necessarily preclude sufficiency of disclosure.

The above general principle of **T 149/98** was further illustrated in the decision **T 984/00 (Ti-plasmid vectors/MAX-PLANCK-GESELLSCHAFT)**,

relating to the cell of a plant containing a foreign DNA stably integrated into its genome. The application further related to a plant composed of such cells, as well as the seed of such a plant. The Board believed the application's contribution to the art resided in the provision of cells in general, containing a desired foreign DNA, but free of all of the genes of the T-region of wild type Ti-plasma, and therefore, free of any deleterious genes of the T-region. While the Board acknowledged that the breadth of the invention may justify further research and possible invention in identifying optimal combinations of plants, desired foreign coding DNA and promoter, it also stated that the application cannot be expected to list all possibilities (point 16 of the decision). This holding illustrates that the Applicant/Patentee may rely on a certain amount of extrapolation on the part of a skilled person in support of sufficiency of disclosure, which the Board acknowledged as being present in this case.

In decision **T 78/01 (Insect resistant plants/MYCOGEN)**, the claims related to a plant comprising plant cells which are genetically modified to contain a particular structural gene under the control of a plant-expressible promoter. The expression of this gene rendered the plants containing it resistant to insect attack. The Board identified three main issues which would guide the assessment of sufficiency of disclosure under Art. 83 EPC: 1) the availability of plant vectors; 2) the availability of the insecticide structural gene to be inserted and 3) transformation and regeneration of monocotyledonous plants. These questions reflect the importance of the availability of the materials needed to implement a plant invention (especially a transgenic plant invention) in order to comply with the requirements of Art. 83 EPC. In the end, the Board denied sufficiency of disclosure because it believed that the skilled person would be unduly burdened in elucidating uncertain results which the documents on file indicated would be encountered in an attempt to perform the invention. Among other things, this decision indicates the importance of making sure that all materials needed to perform a plant invention are available to the skilled person. If they are not, then compliance with the requirements of Art. 83 EPC dictate that these be provided in the patent.

Decision **T 612/92 (Monocotyledonous plants/RIJKSUNIVERSITEIT LEIDEN)** dealt with a process for incorporation of foreign DNA into the genome of monocotyledonous plants by infecting protoplasts with specific bacteria containing a specific DNA sequence. By infection, the DNA sequence present in the bacteria was transferred to the monocotyledonous plants. In this case, the Board held that the invention's contribution to the field is a new application of a known technique, and the relevant question for assessing sufficiency of disclosure was whether or not the process could be carried out over the whole range of the claim (point 10 of the decision). Point 11 of the decision referred to established case law of the Boards of Appeal, making it clear that the standard applicable for sufficiency of disclosure for this (transgenic) plant definition was no different as already applied by previous Boards of Appeal in other non-plant-related cases. In this case, while the Board acknowledged that a process analo-

gous to that claimed existed for dicotyledonous plants, the patent contained no instructions how to adapt the process known for dicotyledons to monocotyledons, and therefore unduly burdened the skilled person in performing the invention over its entire scope. Sufficiency of disclosure was therefore denied.

The need, discussed above, to include in the patent application a disclosure of any and all information needed to perform the invention if not known from the prior art was further illustrated in decision **T 891/02 (Potato starch/BASF)**. This case related to a method of increasing the formation of amylose-type starch in potato plants by suppressing the formation of amylopectin-type starch. The method included the introduction of a gene construct into the genome of the potato tissue, with the construct comprising a specified promoter, a transcription start site and the first exon of the gene encoding for a specified protein, where the exon is inserted in the antisense direction. In its opinion, the Board considered fundamental aspects of sufficiency of disclosure, applying them to this transgenic plant case:

The disclosure of the invention for which protection is sought is one of the fundamental requirements for the grant of a patent. This requirement is based on the legal principle according to which the inventor is granted a temporary exclusivity to the invention in return for the disclosure of the technical teaching to the public. In the European Patent Convention, the disclosure requirement is formulated in Article 83 EPC which states that a European patent application must disclose the invention in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art. (point 2 of the decision)

In point 6 of the decision, the Board considered the availability of the sequences needed to put the application into practice. For example, the genomic and enzyme DNA sequences were essential for the skilled person's ability to carry out the claimed invention. The Board noted that at least one of the necessary sequences was not available at the priority date of the application, and in the absence of the sequence information for the required enzyme gene, the skilled person who wanted to prepare the gene construct needed to perform the invention as claimed would first have to isolate the required gene from the potato. In the end, the Board deemed this an undue burden, and denied sufficiency of disclosure. This decision again illustrates the importance of the prior availability of genes required for performing the invention in plant inventions, particularly inventions relating to transgenic plants. If not already available, the application must disclose the necessary genes/information.

Decision **T 1052/98 (Gene switch/SYNGENTA)** related to a method of controlling the expression of a foreign gene or series of genes in a transgenic plant. In this method, the coding region was put under the control of a promoter of a gene specifying a specific subunit of maize glutathione-S-transferase gene (GSTII). The gene transcription was then induced by applying a chemical inducer to the plants. Here, the Board held that the mere listing of general procedural steps, in the absence of any concrete data and technical information concerning the GSTII promoter, cannot be considered sufficient for a clear and complete disclosure under the terms of Art. 83 EPC (point 1 of the decision).

In fact, the Board held that even if each individual experimental step *per se* could be considered feasible with a certain amount of trial and error, the total amount of experimental effort needed to successfully advance step by step toward the desired final goal was undue for a skilled person (point 3 of the decision). This decision illustrates, for a transgenic plant invention, that even when the steps underlying the claimed process are known *per se*, the disclosure may still be insufficient if it would be unduly burdensome for the skilled person to determine how these steps should be linked to reliably lead to the claimed invention.

D.VI.2.d.Clarity in plant inventions

The Boards of Appeal have issued a number of decisions relating to the standard which must be met for an invention relating to plants to comply with the clarity requirements in the EPO. The following summarizes some of these holdings, illustrating in several instances, and using examples of transgenic plants, that the clarity standards generally applicable for other types of inventions apply to transgenic plant inventions as well.

T 984/00 (Ti-plasmid vectors/MAX-PLANCK-GESSELLSCHAFT) related to a transgenic cell of a plant which contains a foreign DNA stably integrated into its genome. As part of the definition of the foreign DNA, claim 1 specified that the foreign DNA is “substantially free of internal T-DNA sequences of a wild type Ti-plasmid”. The Examining Division had objected to this term as a functional interpretation equating the expression to the absence of genes controlling neoplastic growth. The Board interpreted the term “substantially free” as meaning that the language of the claim makes clear that a structural interpretation is appropriate to the effect that substantially only the border regions and any desired promoter sequence remains in the foreign DNA to be incorporated (point 6 of the decision). In the Board’s view, the skilled person would isolate the T-DNA borders using restriction enzymes which do not cleave at the exact limit between the desired border and the T-DNA, with some nucleotides belonging to the internal T-DNA possibly remaining associated with the border regions but without any deleterious effect. The Board concluded that the use of the term “substantially” in the claim would be understood by the skilled person in this sense, so this term was clear (point 7 of the decision). It should be noted that the Board acknowledged clarity in this case due to the special circumstances prevailing when using restriction enzymes. Generally, however, when drafting claims, it is helpful to avoid such relative terms as “largely” or “substantially” etc., as such terms allow room for interpretation which could (and often do) lead to a lack of clarity.

In decision **T 610/01 (Plant growth/LONG ASHTON RESEARCH STATION)**, the claims were directed, among other things, to transgenic plants, plant cells and progeny containing a DNA molecule encoding a polypeptide more than 50% homologous to a certain specified sequence, and exhibiting

GA20-oxidase activity. In assessing clarity, the Board stated that the reference to a certain percentage homology to a given sequence results in a claim of very wide scope. One of the main considerations in assessing whether the requirements of Art. 84 EPC, with respect to clarity, are satisfied is whether it is possible for the skilled person to reliably establish the scope, i.e. the bounds of the claim. Are these bounds definite or indefinite? If definite, then the claim is clear in the sense of Art. 84 EPC; if indefinite, then it is not. In this case, the Board came to the conclusion that the skilled person could identify the claimed molecules in a straightforward manner. Thus, a broad claim in itself does not preclude clarity as long as the skilled person can determine what this breadth is. This is a useful guiding principle in drafting claims for transgenic plant inventions, in which the scope of the claims often depends, at least in part, on the definition of a genetic sequence to be incorporated into the plant.

In decision **T 1006/02 (Selection of transformed cells/SYNGENTA)**, the Board considered whether the terms “co-introduced” and “expressible” are unclear. The Board found both terms clear. In the case of the term “co-introduced”, the description of the patent in question provided a formal definition of this term, to the effect that the two nucleotide sequences which are “co-introduced” are coupled to each other or otherwise introduced together in such a manner that the presence of the co-introduced nucleotide sequence in a cell indicates that the desired nucleotide sequence has entered the cell. The Board saw this as an unambiguous definition. With regard to the term “expressible” the Board found this term not unusual for a skilled person in the field of genetics, where it is common to refer to a genetic sequence in terms of the encoded protein product (points 20–22 of the decision). This decision illustrates the importance of providing formal definitions for as many terms as possible when drafting a patent application. Many times, the EPO may require that these formal definitions be recited in the claims in order to render the claimed subject-matter clear. In other cases, however, as in the present case, it is sometimes sufficient to simply refer to the formal definition in the description in support of clarity.

In decision **T 1165/03 (Soybean transformation/MONSANTO)**, the Board considered the clarity of claims directed to soybeans with a “foreign” gene and an “exogenous” gene. The question was whether there was any difference between the terms “foreign” and “exogeneous” and, if so, what this difference was. In its opinion, the Board considered that when two different terms were used in the specification, this meant that these terms were intended to have different meanings. Otherwise, so the Board, the Patentee would have used only a single term. However, in the lack of any formal definition of the terms “exogenous” and “foreign”, it was not clear what the intended difference in meaning should be. In the lack of any meaningful difference between these terms, derivable from the patent, the Board assigned the broadest possible meaning to the term “foreign” and this negatively impacted the assessment of novelty. This is a good illustration of the importance of using consistent terminology throughout the description and claims when drafting a patent application, and also of the

importance of defining the terminology used. When there exists an unresolvable discrepancy between two terms, and even when there is doubt regarding the meaning of a single term, and the description provides no definition, the EPO typically interprets the terms in question as broadly as possible in assessing patentability.

D.VI.2.e. Natural plants

The meaning of the term “natural plants” as used herein is provided in the introduction of this chapter (D.VI.1).

D.VI.2.e.a. Product claims for natural plants

The attempt to obtain patent protection for a natural plant by means of a product claim encounters several obstacles.

First, without further characterization representing a new technical teaching, a wild plant which is merely found in nature is not regarded as an invention but rather as a discovery. Since European patents are only granted for inventions and not for discoveries (Art. 52(2)(a) EPC), a product claim directed to such an uncharacterized wild plant as such is not allowable. The exclusion of discoveries from patentability is discussed in C.I.1.a.

Second, and the above notwithstanding, Art. 53(a) EPC excludes inventions from patentability, the commercial exploitation of which would be contrary to “ordre public” or morality, and could present an additional bar to the allowability of a product claim directed to a natural plant. The interpretation of “ordre public” and “morality” is discussed above in section D.VI.2.a.

If a plant invention does not fall under the above exclusion provisions, it must fulfill the further requirements for patentability, namely the invention must be novel (Art. 54 EPC), involve an inventive step (Art. 56 EPC) and be susceptible of industrial application (Art. 57 EPC). So as long as the claimed plant is not itself excluded from patentability as a “plant variety” under Art. 53(b) EPC, the same principles as apply to any conventional chemical invention remain valid for plant inventions as well.

In addition to the above patentability requirements, the requirements of the application must also be fulfilled. In particular, the application must disclose the invention in such a manner to enable the skilled person to carry out the invention (Art. 83 EPC), and the claims must be sufficiently clear for the skilled person and must also be supported by the description (Art. 84 EPC). General information on these requirements of the application is provided in C.I.3.b, C.I.3.e.b and C.I.3.e.c.

An interesting point in connection with the disclosure of plant inventions in accordance with Art. 83 EPC is whether propagating material of a plant can be deposited in accordance with Rule 31 EPC (see Annex 4 and C.I.3.b.b). While earlier EPO case law (**T 356/93 (Plant cells/PLANT GENETIC SYS-**

TEMS)) held that this term is not limited to bacteria and yeasts, but also includes fungi, algae, protozoa and human, animal and plant cells, the previous version of Rule 31 EPC was limited to deposits of “microorganisms”. The current version of Rule 31 EPC allows deposits for “biological material”. In line with Art. 2(1)(a) EPC of the European Biotech Directive, Rule 26(3) EPC defines the term “biological material” as

any material containing genetic information and capable of reproducing itself or being reproduced in a biological system.

Decision **T 315/03 (Transgenic animals/HARVARD)** held, albeit for an animal, that

[t]here can be no doubt that any animal consists of a material containing genetic information and is capable of reproduction. An animal is therefore a product consisting of biological material in accordance with [current Rule 26(3) EPC]. (point 5.2)

Applying the same thinking to plants (or reproduction-capable parts thereof such as seeds or seedlings) must result in the same conclusion: any plant (or reproduction-capable part thereof) qualifies as “biological material” in the sense of Rule 26(3) EPC which, as such, falls under the definition of what may be deposited under Rule 31 EPC. Consistent with this thinking, the Board in **T 1854/07 (Oil from seeds/CONSEJO SUPERIOR)** considered seeds and plants interchangeably in interpreting Art. 53(b) EPC (see point 4 of the decision). Plants or parts thereof qualifying as “biological material” under Rule 26(3) EPC may therefore be deposited in order to comply with the requirements of sufficiency of disclosure.

Plant cells can be deposited under Rule 31 EPC, as has been discussed in D.V.1.

In inventions relating to natural plants, the question of reproducibility can affect the assessment of sufficiency of disclosure under Art. 83 EPC. Specifically, the chance of such events occurring may have a bearing on whether or not the claimed subject matter is sufficiently disclosed; if the chances of the required event occurring are low, or beyond the experimenter’s control, then this can adversely affect the skilled person’s ability to put the claimed invention into practice, lowering the chances of the claimed subject-matter being regarded as sufficiently disclosed.

This was clear, for example, in decision **T 1026/02 (Oilseed Brassica/PI-ONEER HI-BRED INTERNAT., INC.)**. The claimed subject matter in this case related to a *Brassica* plant or a part thereof comprising a homozygous fertility restore gene for *Ogura* cytoplasmic male sterility. Upon pollination, the claimed plant yielded oil seed of a specified chemical composition. In its decision, the Board reiterated the general principle that the disclosure of an invention for which protection is sought is one of the fundamental requirements for the grant of a patent (point 1 of the decision). The Board considered that the separation of two closely linked genes by mitotic crossing-over events using a

plant breeding program based on crossing and selection, and the segregation of the traits in question into the progeny, is a fortuitous event (point 9 of the decision). Essentially, the Board considered that the skilled person's success in putting the claimed invention into practice depended on luck and the chances of the skilled person being lucky in his attempts to put the invention into practice were further reduced by the fact that, in that case, proprietary seed lines were used (point 9 of the decision). The Board concluded that

relying on fortuitous events or chance for reproducibility amounts to undue burden in the absence of evidence that such chance events occur and can be identified frequently enough to guarantee success (point 10),

and held the application insufficiently disclosed.

While this principle of course applies for any type of invention, it appears especially relevant for inventions relating to natural plants, in which success can depend on the likelihood of certain genetic events occurring.

A similar principle, although leading to a different result, was illustrated in decision **T 542/04 (Soybean products/E. I. DU PONT DE NEMOURS)**. The claims in this case related to soybeans with a genotype conferring a heritable phenotype of a specified seed stachyose content. The soybeans were non-viable as a result of mechanical processing such as dehulling, cracking or grinding, and the seeds were obtainable from progeny lines prepared by a plant-crossing method to ensure homozygosity for a specified gene. The claims were also directed to a number of methods for using the soybeans, making various soy protein products, various soy protein products themselves as well as even pet food products containing the soybeans. In the Board's view, the relevant question for assessing sufficiency of disclosure was whether the patent provided sufficient information for the production and identification of further soybean lines comprising alternative alleles of the specified gene described and for the identification of these alleles. Since the claimed method involved plant-crossing steps, a relevant question was whether a suitable allelism test was known in the prior art or disclosed in the application. The Board concluded that the skilled person could determine the allelism of any newly identified and isolated mutant soybean line having low raffinose saccharide content with the specified alleles (point 17 of the decision). The Opponent in this case had alleged – without evidence – that reworking the examples of the patent would not result in the claimed soybean lines which would also provide suitable starting material for the method defined in claim 1, meaning that reproducing the subject matter of the examples of the patent would depend on chance events. The Board did refer to past cases in which the dependence on chance events precluded sufficiency of disclosure, but concluded here that the patent provided plenty of information as to the steps which must be performed at each stage of the crossing and checking process. Thus, in the absence of evidence to the contrary and while upholding the general principle that the dependence on chance events is damaging to sufficiency of disclosure, the Board acknowledged sufficiency of disclosure.

Claim drafting:

Although a product claim directed to a natural plant may not be allowed by the EPO if considered a discovery (see above), the wording for such a claim could, in principle, be as follows:

Plant X having characteristics a, b, c, ...

wherein the characteristics a, b, c, ... are the intrinsic or extrinsic features and/or parameters of the plant which can be precisely defined. If the plant cannot be sufficiently defined by characteristics, the claim may comprise process steps for the preparation of the plant. Such a product-by-process claim could have the following wording:

Plant X obtainable by the process comprising steps 1, 2, 3, ...

The case law has recently raised the question of whether the plant defined by such a product-by-process claim may be excluded from patentability when the recited process is an excluded “essentially biological process”. This question has been referred to the Enlarged Board of Appeal, and is discussed in more detail in the context of the term “essentially biological” in section D.VI.2.b above.

Examples of allowed product claims for natural plants are shown in the following:

EP – B1 – 2135504 – Claim 1:

A non-transgenic herbicide resistant plant, which plant expresses a mutant EPSPS gene product, which gene product has the same level of catalytic activity as compared to that of the wild type enzyme, wherein the EPSPS gene is mutated at the positions Thr₁₇₈ and Pro₁₈₂ in Arabidopsis or at an analogous amino acid residue in an EPSPS gene of another species, wherein Thr₁₇₈ is changed to Val or Leu and Pro₁₈₂ is changed to Leu or Ser.

This claim contains an explicit statement that the subject plant is not transgenic.

EP-B1 – 1973396 – Claim 1:

Lettuce plant having a reduced or absent wound-induced surface discolouration, obtainable by crossing a plant with the NCIMB accession number 41454 or 41441 with another plant of the same species and testing plants resulting from the cross by subjecting the plants or parts thereof to a screening method, which comprises

- a) creating a wound surface on the plants or plant parts to be screened and on the control plants or plant parts;
- b) incubating the wound surfaces to allow for discolouration to occur therein or thereon;
- c) observing the wound surface discolouration in or on the plants or plant parts;
- d) comparing the observed wound surface discolouration in or on the plants or plant parts to be screened with the discolouration that is observed on or in the control plant or plant part to identify the plants or plant parts that show no discolouration or a discolouration that is reduced as compared to the control plant or plant part.

EP-B1 – 1973396 – Claim 17:

Vegetable product, comprising a lettuce plant as claimed in any one of the claims 1–11 or part thereof.

The referenced claim 1 is shown directly above, and relates to the lettuce plant itself.

D.VI.2.e.b. Process claims for natural plants

When drafting process claims for preparing natural plants, the exclusion provision according to Art. 53(b) EPC is again a potential bar to the allowability of such a claim. Art. 53(b) EPC stipulates that a biological process for the production of plants is not patentable if it is “essentially biological”. This term is discussed above in section D.VI.1.a.b.

In decision **T 1360/08 (Annual medics/PRISTINE FORAGE TECHNOLOGIES PTY LTD)** the claims related to a plant and a method involving the treatment of a known cultivar with a mutagenic agent. The Board held that subjecting a known cultivar or a wild-type variety to treatment by a mutagenic agent cannot be regarded as a natural phenomenon such as crossing or selection. Rather, it is a step of a technical nature which by itself introduces a new trait into the genome of the plant produced. The Board therefore held that the method does not consist entirely of natural phenomena as described under Rule 26(5) EPC. The claimed method was therefore not an “essentially biological process” excluded from patentability under Art. 53(b) EPC.

As to the further patentability requirements, i.e. novelty, inventive step and industrial application, as well as the requirements of the application, i.e. sufficiency of disclosure and clarity and support of the claims, see C.I.3.

Claim drafting:

The general wording of a process claim for preparing natural plants could be as follows:

A process for preparing plant X comprising the following steps a, b, c, ...

In standing with the definition of “essentially biological” as discussed above, in order not to fall under the exclusion provision of Art. 53(b) EPC, either at least one individual step of said steps a, b, c, etc., should be an essential technical step changing a genetic trait (e.g. by radiation) or the method should be free of crossing and selection steps.

Apart from the above process for preparing a natural plant, wherein “preparing” means that a new plant genome is obtained, a process claim is also conceivable wherein the plant is cultivated under certain conditions –without affecting the plant’s genetic identity – in order to improve the productivity of the plant. Such a process must also comprise a technical step in order to escape exclusion under Art. 53(b) EPC. This requirement, however, should in most cases be ful-

filled, since usually the increase of productivity, etc., requires human intervention in a technical manner that is decisive for the result achieved.

Moreover, a process claim in which the plant is used as a source for the isolation of a product of interest is allowable. Such a claim is not affected by Art. 53(b) EPC since it is not directed to the preparation of a plant, but rather to the preparation of a plant-derived product.

Examples of granted process claims are shown in the following. These examples are of particular interest with regard to Art. 53(b) EPC, since they provide some guidance as to what kind of subject-matter was *not* excluded as an essentially biological process under the EPC. The following claims were also considered to fulfill the further requirements of the EPC, particularly the clarity requirement of Art. 84 EPC. The technical steps are underlined.

EP-B1 – 0257845 – Claim 1:

A method for producing variegated plants, characterized in that a plant is treated with chlorophyll inhibitors during the growing process of said plant, whereby destroying the chlorophyll in the body of said plant directly or indirectly or inhibiting biosynthesis of said chlorophyll.

In the above method the technical step can be seen in treating the plant with chlorophyll inhibitors during the growth process of the plant.

EP-B1 – 0361124 – Claim 1:

A method for generating diploid *Pelargonium peltatum* plants containing at least one of the anthocyanidins pelargonidin and paeonidin in the petals and/or a factor for male sterility, which plants are propagatable by seed, comprising:

- a) performing an initial cross wherein the genetic material of one parent is provided by *Pelargonium peltatum* and that of the other is provided by a plant selected from the group consisting of:
 - i) *P. x hortorum*
 - ii) *P. scandens*
 - iii) a cascade type pelargonium
- b) selecting the progeny of (a) and subjecting it to further crosses with genetic material provided by a member of the group consisting of:
 - i) *P. x hortorum*
 - ii) *P. scandens*
 - iii) a cascade type pelargonium
 - iv) a plant produced according to (a)
 - v) a plant produced in a breeding programme wherein the initial genetic material was provided by *Pelargonium peltatum* and one of *P. x hortorum*, *P. scandens* or a cascade type pelargonium,
 - vi) *P. peltatum*

wherein at any stage in the breeding programme a plant displaying the desired characteristics may be selected for self-pollination such that a uniform line is produced;

said method involving circumvention of spontaneous early abortion by removal of any fruit showing symptoms of such, and the in vitro cultivation of the embryo excised therefrom into differentiated plantlets.

The technical step in the above method can be seen in the removal of any fruit showing certain symptoms and the *in vitro* cultivation of the embryo into differentiated plantlets.

EP-B1 – 0374755 – Claim 1:

A method for producing double-haploid *Cucumis sativus* plants, which comprises isolating immature or unfertilized ovulae, or embryo sac cells, or immature or unfertilized ovulae or embryo sac cells contained in ovarial tissue, inducing the formation of embryos with the aid of a hormone-containing medium, which, in the case of parthenocarpous fruit, contains cytokinins, and in the case of non-parthenocarpous fruit, the medium contains auxins,

regenerating the embryos formed to give plants, and effecting duplication of the genome if this does not happen spontaneously.

The above method contains at least the technical steps of isolating the ovulae and applying a hormone containing medium.

EP-B1 – 2350290 – Claim 1:

A method for producing male sterile plants by expressing plant BECLIN 1 gene in the tapetum layer of anthers during early stages of pollen development.

EP-B1 – 2289310 – Claim 4:

A method of increasing the yield in crops of useful plants which are exposed to drought and/or heat stress, which comprises treating the useful plants by seed dressing, by foliar sprays or by soil application, with one or more compounds selected from the group consisting of mefenpyr-diethyl, isoxadifen-ethyl and 4-cyclopropylaminocarbonyl-N-(2-methoxybenzoyl)benzenesulfonamide.

EP-B1 – 2288253 – Claim 1:

A method for the production of somatic embryos from poinsettia plant tissue, characterized in that an embryo induction medium is used comprising between at least 0.1 and 1 mg/l α -naphthalene acetic acid and between at least 0.2 and 1 mg/l Thidiazuron, with the proviso that if the α -naphthalene acetic acid concentration is below 0.2 mg/l the Thidiazuron concentration is at least 0.4 mg/l.

EP-B1 – 2288253 – Claim 4:

A method for producing a non-chimeric poinsettia plant comprising the steps of:

- a) producing somatic embryos according to any of claims 1 to 3, and
- b) growing a mature non-chimeric poinsettia plant from a somatic embryo produced in step a), characterized in that the poinsettia plant used in step a) is a chimeric plant.

EP-B1 – 2198700 – Claim 2:

A method for producing a transgene-free plant with an altered methylation pattern in a target DNA sequence thereof, comprising the steps of,

- a) providing a polynucleotide suitable for the induction of RNA-directed DNA methylation in said plant, said polynucleotide comprising a sequence that is complementary to said target DNA sequence,
- b) introducing said polynucleotide into cells of a plant,
- c) expressing said polynucleotide in said transformed cells, thereby inducing RNA-directed DNA methylation,

- d) determining the methylation patten of said target DNA sequence in said transformed cells of the plant,
- e) selecting and self-crossing of a transformed plant that shows an altered methylation patten in said target DNA sequence, and
- f) selecting a plant from the progeny of the cross in e) which is characterized in that it is devoid of said polynucleotide as introduced according to step b).

EP-B1 – 2195438 – Claim 1:

A method of introducing a molecule of interest into a plant cell having a cell wall, the method comprising:

- i) sub-culturing a one-week-old plant suspension culture comprising a plant cell having a cell wall into fresh culture medium containing an effective amount of a microtubulin inhibitor for 4 to 7 days, thereby producing a plant sub-culture comprising the plant cell having a cell wall;
- ii) coating a nanoparticle having a diameter less than 100 nm with a molecule of interest;
- iii) placing the plant sub-culture and the coated nanoparticle in contact with each other; and
- iv) co-incubating the plant sub-culture and the coated nanoparticle for at least 20 minutes, so as to allow uptake of the nanoparticle and the molecule of interest into the plant cell comprising a cell wall.

EP-B1 – 1867728 – Claim 1:

A method for producing organically bound vitamin B, preferably selected from vitamin B1, B2, B3, B5, B6, B7, B9, B12, or mixtures thereof, in plants, wherein germinable plant seeds are at first soaked in a solution of a vitamin B and are sprinkled with vitamin B solutions during the germination process.

D.VI.2.e.c. Use claims/purpose-limited product claims for natural plants

When drafting use claims, one should consider that a use claim is interpreted as a process claim by the EPO, as outlined in C.I.3.e.a.

For example, a use claim of the following type:

Use of parental plant X for preparing the plant variety Y

will be read as a process claim of the following type:

Process for preparing the plant variety Y wherein plant X is used as parental plant.

It is evident that this claim can be interpreted as an “essentially biological” process for producing the plant variety Y, namely as a conventional breeding process, and thus falls under the exclusion provision of Art. 53(b) EPC.

However, use claims which, when interpreted as a process claim, comprise a technical step – as outlined under D.VI.2.a.b – should escape the exclusion of Art. 53(b) EPC.

As to the further patentability requirements, i.e. novelty, inventive step and industrial application, as well as the requirements of the application, i.e. sufficiency of disclosure and clarity and support of the claims, see C.I.3.

Claim drafting:

In order to avoid the exclusion provision of Art. 53(b) EPC, a use claim should be drafted as follows:

Use of plant X for (technical) purpose Y.

wherein the “technical” purpose Y can be any technical purpose. However, when the purpose resides in the use of plant X for preparing a further plant Y, such a purpose would be critical with regard to the exclusion provision of Art. 53(b) EPC. Of course, as discussed above, claims are allowable wherein the plant is used for example as a source for the isolation of a product of interest (or for any other technical purpose).

Examples of allowed use claims are shown in the following:

EP-B1 – 2350290 – Claim 7:

Use of the method as claimed in claim 1 for inducing male sterility in plants selected from the group of plants listed in claim 3.

The above claim is interestingly formulated as a “use of a method”.

EP-B1 – 2198700 – Claim 9:

Use of a plant produced according to a method according to any of claims 2 to 8 for the production of seeds, fruits, stems, roots and leaves or other plant derived products with reduced expression of a gene, preferably a gene encoding a product that is harmful for animals, humans or plants, preferably genes encoding allergens or genes influencing the level of poisonous biochemical substances in a plant, or a gene encoding an unwanted trait as for example a gene involved in the onset of over-ripeness.

EP-B1 – 1867728 – Claim 19:

Verwendung eines Verfahrens nach einem der Ansprüche 1 bis 18 zur Produktion von organisch gebundenem Vitamin B. (Use of a method according to one of claims 1 to 18 for the production of organically bound vitamin B – authors’ translation)

As above for EP 2350290, this claim is interestingly formulated as a “use of a method”.

D.VI.2.f. Hybrid plants

The meaning of the term “hybrid plants” as used herein is provided in the introduction of this chapter (4.5.1).

D.VI.2.f.a. Product claims for hybrid plants

As mentioned above in the context of natural plants (D.VI.2.e.a), Art. 53(b) EPC excludes plant varieties from patentability. This applies regardless of whether the plant in question may be classified as a natural or a hybrid plant. As decision **G 1/98 (Transgenic plants/NOVARTIS II)** makes clear, the question of whether or not a plant is considered an excluded plant variety de-

depends only on whether or not it meets the criteria set out in the definition of Rule 26(4) EPC. Rule 26(4) EPC makes clear the Legislator's intention that in order to be considered a plant variety, the plant in question must be both genetically homogenous as well as stable in its propagation. Rule 26(4)(c) EPC addresses the stability aspect required for classification as an excluded plant variety, when it specifies that the plant grouping in question can be "... considered as a unit with regard to its suitability for being propagated *unchanged*" (emphasis added).

The requirement of unchanged propagation becomes especially important when considering hybrid plants, because hybrid plants often exhibit high degrees of change, and therefore poor stability upon propagation. Poor stability was already an issue in decision **T 320/87 (Hybrid plants/LUBRIZOL)**, where the Board explicitly stated:

Hybrid seed and plants from such seed, lacking stability in some trait of the whole generation population, cannot be classified as plant varieties within the meaning of Article 53(b) EPC [...]. (headnote II)

Hybrid plants will be less likely to fall under the legal definition of a "plant variety", so product claims directed to hybrid plants which lack stability in some trait should be more likely to escape exclusion under Art. 53(b) EPC.

As to the further patentability requirements, i.e. novelty, inventive step and industrial application, as well as the requirements of the application, i.e. sufficiency of disclosure and clarity and support of the claims, see C.I.3.

Claim drafting:

Generally, a hybrid plant can be claimed in a product claim of the following type:

Hybrid plant X having characteristics a, b, c, ...

wherein a, b, c, etc., indicate structural features of the plant's phenotype or parameters which can be precisely defined.

However, it will often be difficult to describe a hybrid plant by its characteristics, e.g. its phenotype. In this case, a process for preparing the plant is more suitable to define the hybrid plant. Therefore, the appropriate claim type in most cases will be a product-by-process claim.

A generalized claim wording for a product-by-process claim could be:

Hybrid plant X obtainable by the process comprising steps 1, 2, 3, ...

wherein steps 1, 2, 3, etc., are the steps which are applied in order to obtain the desired plant. Note however the above discussion regarding the allowability of plant products which are defined as the product of an excluded "essentially biological" method. Although the EPC does not address this question – indeed, by the wording of Art. 53(b) EPC, a plant product should only be excluded from patentability when it is a "plant variety" – two Boards of Appeal have re-

ferred this question to the Enlarged Board of Appeal. As mentioned above in sections D.VI.2.a.b these decisions are currently pending as referrals **G 2/12 (Tomatoes II/STATE OF ISRAEL)** and **G 2/13 (Broccoli III/PLANT BIOSCIENCE)**.

The following example shows a claim directed to a hybrid plant which was granted by the EPO.

EP-B1 – 0044723 (underlying decision **T 320/87 – Hybrid plants/LUBRIZOL**) – Claim 21:

Phenotypically uniform hybrid plants produced from hybrid seed according to claim 20.

A product-by-process claim was allowed by the EPO because there was no information available in the application which could enable the Applicant to sufficiently define the product by its composition, structure or some other testable parameter. The plants could not be characterized by physiological or morphological features.

D.VI.2.f.b. Process claims for hybrid plants

When drafting process claims for the preparation of hybrid plants, the exclusion of an essentially biological process under Art. 53(b) EPC must again be considered. Therefore, such claims must comprise a technical step in order to be allowable (see discussion of “essentially biological process” above in section D.VI.2.b.b). Further information on the requirements for a process claim is given in connection with natural plants (D.VI.2.e.b).

In this context it should be emphasized that Art. 53(b) EPC excludes essentially biological processes for the production of any *plant*, regardless of whether or not the resulting plant is a plant variety. The consequence is that a process for the production of a hybrid plant could be excluded from patentability if it is essentially biological, whereas a product claim directed to the same hybrid plant could be allowable. This is an exception to the general practice as outlined in C.I.3.a.c, where for applications comprising an allowable product claim, a claim directed to the preparation of the product is usually allowed without substantive examination.

As to the further patentability requirements, i.e. novelty, inventive step and industrial application, as well as the requirements of the application, i.e. sufficiency of disclosure and clarity and support of the claims, see C.I.3.

Claim drafting:

Regarding the wording of a process claim for producing hybrid plants the same rules as outlined above in connection with process claims for producing natural plants apply (see D.VI.2.e.b).

Examples of granted process claims directed to the preparation of hybrid plants are shown below. The examples are of particular interest regarding the EPO’s interpretation of the provision of Art. 53(b) EPC, which excludes essen-

tially biological processes for the production of plants from patentability. Technical steps are underlined in the examples below.

EP-B1 – 0263017 – Claim 1:

A process for preparing a gramineous hybrid plant, said process comprising preparing a protoplast from a callus or suspension cell derived from *Oryza sativa*, preparing a protoplast from a callus or suspension cell derived from another gramineous plant, subjecting the protoplasts to cell fusion, characterized in that the fusion is effected by an electric treatment, said electric treatment comprising the application of direct current between successive alternating current applications and cultivating the resulting fused cells in a culture medium containing cultured cells of *Oryza sativa* as nurse cells, and further cultivating the formed colonies in a culture medium containing a plant hormone.

In the above process a technical step is for example the fusion of the protoplasts by an electrical treatment.

EP-B1 – 0385296 – Claim 1:

A method of producing a hybrid *Allium* plant comprising the steps of: preparing two different protoplast donors from two different *Allium* plants, isolating protoplasts from the donors, subjecting the protoplasts to cell fusion to provide hybrid cells, and thereafter culturing the hybrid cells, wherein, after the cell fusion, the hybrid cells are sorted out from the other cells and thereafter cultured separately therefrom, characterized in that: after the cell fusion and before the cell sorting, the hybrid cells together with the other cells are cultured at least to such an extent that cell membranes are regenerated.

In this method one technical step is the cell fusion of the protoplasts.

EP-B1 – 0044723 (underlying decision T 320/87 – Hybrid plants/LUBRIZOL) – Claim 1:

A process for rapidly developing hybrids and commercially producing hybrid seeds, comprising:

- (a) selecting a first heterozygous parent plant and selecting a second parent plant;
- (b) crossing said first parent plant with said second parent plant to obtain original-parent-derived hybrids that are phenotypically uniform;
- (c) cloning said first parent plant to produce a first cloned parental line;
- (d) crossing plants of said first cloned parental line with said second parent plant or with a second parental line produced therefrom to obtain hybrid seeds which yield hybrids that are phenotypically uniform provided that when said second parent plant is heterozygous and a second parental line produced therefrom is used in the crossing of step (d), said second parental line must be produced by cloning; and
- (e) repeating steps (c) and (d) as required to obtain hybrid seed that yields phenotypically uniform hybrid plants and, optionally, producing phenotypically uniform hybrid plants from the seed.

The combination of steps (a) to (e) rendered the process non-essentially biological at the time, although each single step is essentially biological. It is questionable whether such a claim would be allowable under the newer case law.

D.VI.2.f.c. Use claims/purpose limited product claims for hybrid plants

As already discussed in connection with natural plants, a use claim is interpreted as a process claim and, therefore, Art. 53(b) EPC represents a bar to the allowability of a use claim to the extent that the use claim relates to an essentially biological process for the production of a plant. For further details on this issue, see D.VI.2.b.

As to the further patentability requirements, i.e. novelty, inventive step and industrial application, as well as the requirements of the application, i.e. sufficiency of disclosure and clarity and support of the claims, see C.I.3.

Claim drafting:

The general wording of a use claim could be:

Use of hybrid plant X for (technical) purpose Y.

Regarding the “technical” purpose, see D.VI.2.e.c.

D.VI.2.g. Transgenic plants

The meaning of the term “transgenic plants” as used herein is provided in the introduction of this chapter (D.VI.1).

D.VI.2.g.a. Product claims for transgenic plants

As discussed in C.I.2.a, Art. 53(a) EPC excludes from patentability inventions the publication or exploitation of which would be contrary to “ordre public” or morality. The interpretation of the terms “ordre public” and “morality” as presently applied by the EPO is provided in C.I.2.a.a and D.VI.2.a.

Whether a claimed invention constitutes an exclusion from patentability within the meaning of Art. 53(a) EPC must be answered in each particular case. The decision **T 356/93 (Plant cells/PLANT GENETIC SYSTEMS)** examined the question of morality and “ordre public” in connection with a plant invention.

The patent underlying this decision, EP-B1 – 0242236, contained claims directed to transgenic plants which were made resistant to the herbicide bialaphos by incorporating into the plant genome a gene capable of protecting the plants against this herbicide. Further, the patent contained claims directed to seeds of such a plant and the following process claim 24:

Process for selectively protecting the culture of a plant species and selectively destroying weeds which comprises the steps of treating the field with a herbicide consisting of a glutamine synthetase inhibitor, wherein the cells of the plant species contain in the genome a foreign nucleotide sequence encoding a protein having an enzymatic activity capable of neutralizing or inactivating said glutamine synthetase inhibitor under the control of a promoter recognized by the polymerases of the cells of said plant.

The Opponent/Appellant argued that the exploitation of the claimed subject-matter would damage the environment and therefore contravene “ordre

public“ as well as morality in the meaning of Art. 53(a) EPC. The Board rejected this argument, first stating that

plant biotechnology per se cannot be regarded as being more contrary to morality than traditional selective breeding, (point 17.1)

and concluding that

the revocation of a European patent under Art. 53(a) EPC on the grounds that the exploitation of the invention for which the patent has been granted would seriously prejudice the environment presupposes that the threat to the environment be sufficiently substantiated at the time the decision to revoke the patent is taken by the EPO. (point 18.5)

The Board observed that the arguments against the allowability of the claims were mainly based on the *possibility* that the claimed subject-matter might result in undesirable, destructive events, including damage to the ecosystem. However, this mere possibility of some undesirable events resulting from the exploitation of the claimed invention was not sufficient for the Board to revoke the patent on the ground of Art. 53(a) EPC. The Board explicitly stated:

[T]he quoted documents do not lead to the definite conclusion that the exploitation of any of the claimed subject-matter would seriously prejudice the environment and is, therefore, contrary to “ordre public”. It would be unjustified to deny a patent under Art. 53(a) EPC merely on the basis of **possible, not yet conclusively – documented hazards**. (point 18.7)

In summary, a product claim directed to a transgenic plant should be allowable under Art. 53(a) EPC as long as there is no strong evidence that the exploitation of the invention will seriously prejudice the environment or breach public peace or social order which would contravene the “ordre public” requirement, or as long as the invention is not contrary to the conventionally accepted standards of conduct of European culture which would contravene the morality requirement of Art. 53(a) EPC. Decision **T 356/93 (Plant cells/PLANT GENETIC SYSTEMS)** also considered the “morality” requirement. In point 6 of that decision, the Board stated that “the concept of **morality** is related to the belief that some behavior is right and acceptable whereas other behavior is wrong, this belief being founded on the totality of the accepted norms which are deeply rooted in a particular culture”. For the purposes of the EPC, the culture in question is the culture inherent in European society and civilization. Accordingly, under Art. 53(a) EPC, “inventions the exploitation of which is **not** in conformity with the conventionally accepted standard of conduct pertaining to this culture are to be excluded from patentability as being contrary to morality”.

In an attempt to demonstrate that segments of the population found the claimed subject-matter objectionable, the Appellant in **T 356/93** relied on a survey conducted among Swedish farmers, according to which the large majority (82%) was against genetic engineering, in particular herbicide-resistant plants, as well as an opinion poll carried out in Switzerland regarding the patent-

ability of animals and plants, according to which the majority (69%) was opposed to patenting animals and plants. The Board however held that surveys and opinion polls are not decisive *per se* when assessing the patentability of subject matter with regard to the requirements of Art. 53(a) EPC. The Board's reasons for this included the fact that surveys and opinion polls may not reflect moral norms which are deeply rooted in European culture. Rather, the results of surveys and opinion polls can fluctuate as dependent on for example the types of questions posed or the sample size. Surveys of particular groups of people, for instance farmers, tend to reflect their specific interests and/or bias beliefs. Generally, the question as to whether Art. 53(a) EPC constitutes a bar to patentability has to be considered on a case-by-case basis, so relying on surveys or opinion polls is hardly feasible. The Board pointed out

that plant biotechnology is a technology which aims at accomplishing practical improvements or advances in the area of plants by using modern scientific knowledge. The development of this technology inevitably allows a better understanding and control of the natural phenomena linked to plants.

However, in the Board's view, this does not render activities in this technical field intrinsically wrong. Indeed, in the Board's judgment, plant biotechnology *per se* cannot be regarded as being more contrary to morality than traditional selective breeding because both traditional Breeders and molecular biologists are guided by the same motivation, namely to change the property of a plant by introducing novel genetic material into it in order to obtain a new and, possibly, improved plant. In the Board's view, the powerful potential of genetic engineering techniques is the origin of the concerns and apprehensions expressed by public opinion, and is responsible for the considerable disagreement and controversy in this field. In essence, the Appellant's objections are "... to the dominion gained by man over the natural world". The Board found such concerns understandable, because the power of science for good and evil has always troubled man's mind. Like any other tool, plant engineering techniques can be used for constructive or destructive purposes. The Board thought that it would undoubtedly be against "ordre public" or morality to propose a misuse or a destructive use of these techniques. With these thoughts in mind, the Board assessed whether the claimed subject-matter relates to a misuse or a destructive use of plant biotechnology. The Board found no such misuse, and therefore ruled that the claimed subject-matter, in addition to not contravening "ordre public" is also not contrary to morality. The claimed subject-matter thus was not excluded from patentability under Art. 53(a) EPC.

A later case, **T 475/01 (Phosphotrizene – Resistenzgen/BAYER)** picked up the same thoughts, explicitly relying on **T 356/93**. The claims in **T 475/01** related to transgenic plants, their parts as well as seeds, which were characterized by a resistance gene conferring resistance against certain herbicides. The Appellant's main argument against the morality of the claimed sub-

ject-matter in the sense of Art. 53(a) EPC was that certain groups of people in the field harbored significant ethical doubts against the patenting of living organisms and their genes. The Board did not agree, and could recognize no offense to “ordre public” or morality. The Board was well aware that the patenting of living organisms and their genes was objectionable to many people, but found that this objection in itself does not mean that such patenting is immoral in the sense of Art. 53(a) EPC. The Board pointed out that the member states of the European Union had participated in the drafting and ratification of Art. 4 of the Biotech Directive, stating that invention having as their subject matter plants can be patented as long as the technical feasibility of the invention is not confined with a particular plant variety. Art. 4 of the EU Directive sought to achieve an EU-wide consensus on this point. The Board found that it would be incongruent for the EU member states to ratify a provision saying that patenting plants was allowed, and at the same time support another provision contravening the first. The EU Directive was intended to be binding for all EU member states and it is indicative of their intention to codify the notion that plants are in principle patentable, including genetically altered plants. For all of these reasons, the Board did not accept the Appellant’s argument that the claimed subject-matter should be excluded under Art. 53(a) EPC simply because certain circles of people in the field found this subject matter objectionable. In reaching their opinion, the Board referred back to the earlier decision **T 356/93**, mentioned above.

Moreover, Art. 53(b) EPC excluding plant varieties from patentability, represents a bar to the allowability of a product claim directed to a transgenic plant to the extent that the transgenic plant fulfills the definitions of a “plant variety” in the sense of Rule 26(4) EPC.

The early practice of the EPO to allow transgenic plant claims – despite the provision of Art. 53(b) EPC – was based on the understanding that exclusion provisions should be narrowly construed and that consequently a claim not specifically directed to a plant variety but rather to a higher taxonomic order should be allowable. In practice this meant that product claims for transgenic plants were drafted such that they were not specifically directed to a certain plant variety, but used a more general wording such as “transgenic plant expressing characteristics X”.

As to the further patentability requirements, i.e. novelty, inventive step and industrial application, as well as the requirements of the application, i.e. sufficiency of disclosure and clarity and support of the claims, see C.I.3.

Claim drafting:

Generally, a product claim for transgenic plants can be drafted in a similar manner as outlined above for hybrid plants (D.VI.2.f.a).

The examples below refer to claims to transgenic plant products granted in the EPO.

EP-B1 – 0429458 – Claim 15:

A transformed plant which produces free L-lysine by a biosynthetic pathway employing dihydrodipicolinic acid synthase, (DHDPS), wherein said DHDPS is the product (a) of a foreign gene, and (b) is substantially resistant to feedback inhibition by endogenously produced free L-lysine.

EP-B1 – 0511979 – Claim 2:

A plant, seeds or propagation material, containing cells as claimed in claim 1.

Claim 1 of the patent was directed to a plant cell expressing a prokaryotic ammonium-specific asparagine synthetase.

EP-B1 – 0429478 – Claim 9:

A transgenic plant comprising transformed plant cells according to claim 8.

Claim 8 of the patent was directed to a transformed plant cell containing a specific expression cassette.

EP-B1 – 0412912 – Claim 26:

Transgenic phenotypically normal plants which belong to the species *Cucumis melo* and which can be obtained according to claim 11.

Claim 11 of the patent describes the process for preparing the transgenic *Cucumis melo*.

EP-B1 – 0369637 – Claim 11:

A transgenic plant which contains in its cells a chimaeric gene as defined in claim 8 such that the plant exhibits resistance to a herbicide which acts by inhibiting DHPS.

Claim 8 of the patent specifies the chimeric gene.

EP-B1 – 0269601 – Claim 7:

A differentiated tomato plant which exhibits toxicity towards Lipidopteran larvae comprising transformed tomato cells of claim 4.

Claim 4 of the patent was directed to a transformed tomato cell containing a certain chimeric gene.

EP-B1 – 0242246 – Claim 16:

Plants non-essentially biologically transformed, which possess, stably integrated in the genome of their cells, a heterologous DNA as defined in any of claims 1 to 3.

EP-B1 – 0186425 – Claim 25:

A transgenic, hygromycin-resistant plant comprising the plant cells of claim 23, and hygromycin-resistant progeny thereof.

Claim 23 of the patent was directed to a transformed plant cell which contained a specific chimeric gene.

EP-B1 – 2390339 – Claim 5:

A cell or an oilseed plant or a transgenic seed comprising in its genome the recombinant DNA construct of Claim 4.

EP-B1 – 2376635 – Claim 2:

A nematode-resistant transgenic plant comprising a recombinant expression vector comprising a root-specific promoter in operative association with a polynucleotide encoding a serine-arginine rich protein comprising amino acids 1 to 226 of SEQ ID NO: 38.

EP-B1 – 2356899 – Claim 4:

A transgenic plant provided with resistance to pathogens of anthracnose and bacterial leaf spot, comprising:

a combination of

- A) an RPS4 gene with the base sequence of [specified SEQ ID NOs]; or
 - i) a DNA encoding a protein having an amino acid sequence in which 1 to 30 amino acids are substituted, deleted, inserted and/or added in the amino acid sequence of [specified SEQ ID NOs]; or
 - ii) a DNA which hybridizes under stringent conditions to a DNA of SEQ ID [specified SEQ ID NOs]; or
 - iii) a DNA encoding a protein having an amino acid sequence having 90% or higher homology to the amino acid sequence of [specified SEQ ID NOs];

and

 - B) an RCH2 gene with the base sequence of [specified SEQ ID NOs]; or
 - i) a DNA encoding a protein having an amino acid sequence in which 1 to 30 amino acids are substituted, deleted, inserted and/or added in the amino acid sequence of [specified SEQ ID NOs]; or
 - ii) a DNA which hybridizes under stringent conditions to a DNA of [specified SEQ ID NOs]; or
 - iii) a DNA encoding a protein having an amino acid sequence having 90% or higher homology to the amino acid sequence of [specified SEQ ID NOs];
- introduced therein, wherein

A) and B) do not provide the plant with the resistance to the pathogens when each of A) and B) is introduced alone, but provide the plant with the resistance to the pathogens when introduced in the combination.

EP-B1 – 2301948 – Claim 11:

A transgenic plant comprising the transgenic plant cell of claim 10.

EP-B1 – 2298914 – Claim 1:

A transgenic plant having stably incorporated into its genome:

- (a) the polynucleotide sequence set forth in SEQ ID NO: 9;
- (b) a polynucleotide sequence at least 95% identical to SEQ ID NO: 9;
- (c) a polynucleotide encoding a polypeptide comprising an amino acid sequence set forth in SEQ ID NO: 7 or 8; or
- (d) a polynucleotide encoding a polypeptide comprising an amino acid sequence at least 95% identical to SEQ ID NO: 7 or 8.

EP-B1 – 2267136 – Claim 1:

A glyphosate tolerant alfalfa plant, or parts thereof, or seed thereof, or progeny thereof, the genome of said plant, parts, seed or progeny comprises

- (a) the transgene genetic elements shown in Fig. 1 and at least one of the junction sequences defining the insertion site thereof being selected from the SEQ ID NOs: 3 and 4; and
- (b) the transgene genetic elements shown in Fig. 1 and at least one of the junction sequences defining the insertion site thereof being selected from the SEQ ID NOs: 7 and 8,

wherein the transgene genetic elements shown in Fig. 1 are present in the alfalfa events J-101 and J-163 deposited with American Type Culture Collection (ATCC) with Accession Nos. PTA-4814 and 4815.

EP-B1 – 2230310 – Claim 14:

Transgenic plant having increased seed yield, relative to control plants, resulting from increased expression of a nucleic acid encoding a bHLH11-like polypeptide as defined in claim 1, wherein said nucleic acid is under the control of a medium strength constitutive promoter, or a transgenic plant cell derived from said transgenic plant.

The above examples only represent a small fraction of the patents relating to transgenic plants which have been granted by the EPO.

D.VI.2.g.b. Process claims for transgenic plants

Art. 53(a) EPC which excludes inventions from patentability which are contrary to morality or “ordre public”, represents a bar to the allowability of a process claim, as was stated in **T 356/93 (Plant cells/PLANT GENETIC SYSTEMS)**. This issue is addressed above in connection with product claims for transgenic plants (D.VI.2.g.a) and generally in D.VI.2.a.

The exclusion of essentially biological processes for the production of plants, which is discussed in connection with natural and hybrid plants (D.VI.2.e and D.VI.2.f.b), does not represent a major obstacle to the patentability of process claims directed to the preparation of transgenic plants, because a process for preparing a transgenic plant is in general *not* considered to be an “essentially biological” process within the meaning of Art. 53(b) EPC, as was concluded early on in **T 356/93 (Plant cells/PLANT GENETIC SYSTEMS)** and later confirmed and defined in **G 2/07 (Broccoli/PLANT BIOSCIENCE)**. See the detailed discussion of the latter decision above in D.VI.2.a.b.

More recently, in decision **T 1360/08 (Annual medics/PRISTINE FORAGE TECHNOLOGIES PTY LTD)** the Board considered a method claim directed to producing a plant, and involving subjecting a known cultivar or wild-type variety of a specified genus to a treatment by a mutagenic agent. The Board viewed the treatment by a mutagenic agent as a technical step which modified the plant genetics so as to obtain a new trait. The claimed process was therefore not excluded as an essentially biological method under Art. 53(b) EPC.

Since the generation of transgenic plants usually involves a step of genetically engineering a plant cell, and this step introduces or modifies a trait in the plant genome, processes for making transgenic plants essentially biological and, therefore, will normally not be excluded under Art. 53(b) EPC.

As to the further patentability requirements, i.e. novelty, inventive step and industrial application, as well as the requirements of the application, i.e. sufficiency of disclosure and clarity and support of the claims, see C.I.3.

Claim drafting:

A general claim wording for a process claim directed to the preparation of a transgenic plant could read:

A process for producing a transgenic plant comprising the step of introducing foreign DNA X into cells of said plant and regenerating the plant from said cells.

This claim would not be excluded from patentability under Art. 53(b) EPC as an essentially biological process for the production of plants, since it comprises a technical step, namely the introduction of foreign DNA into plant cells, and this foreign DNA introduces or modifies a trait in the plant genome.

Moreover, as outlined above for natural and hybrid plants, respectively, other process claims are possible, which are directed to the cultivation conditions for growing the plant or to the use of the plant in a process for the isolation of a product of interest.

The claims set forth below were allowed by the EPO. It is of particular interest that they were not considered as contravening Art. 53(b) EPC, which excludes from patentability essentially biological processes for producing plants. In each case, the technical steps which avoid exclusion as an “essentially biological process” under Art. 53(b) EPC are underlined.

EP-B1 – 0397687 – Claim 1:

A non-tissue culture process for producing a transgenic plant, which comprises:

- (a) germinating seed of a *Phaseolus vulgaris* or *Glycine max.* plant, for 24 to 48 hours;
- (b) inoculating the meristematic or mesocotyl cells produced during germination, prior to differentiation of the seed, with a virulent or non-virulent *Agrobacterium* strain containing a transferable gene in an *Agrobacterium*-derived vector; and
- (c) allowing the cells to differentiate into a mature plant.

EP-B1 – 0242246 – Claim 5:

Process for producing a plant or reproduction material of said plant including a heterologous genetic material stably integrated therein and capable of being expressed in said plants or reproduction material in the form of a protein capable of inactivating or neutralizing the activity of a glutamine synthetase inhibitor, which process comprises transforming cells or tissue of said plants with a DNA recombinant containing a heterologous DNA, as well as the regulatory elements selected among those which are capable of causing the stable integration of said heterologous DNA in said cells or tissue and of enabling the expression of said foreign nucleotide sequence in said plant cells or plant tissue, regenerating plants or reproduction material of said plants or both from the plants cells or tissue transformed with said heterologous DNA and, optionally, biologically replicating said last mentioned plants or reproduction material or both, characterized in that said heterologous DNA has the nucleotide sequence of the DNA fragment of any of claims 1 to 3 or of said part that codes for a protein having phosphinotricinacetyl transferase activity.

EP-B1 – 0186425 – Claims 17 and 18:

17. A method for selecting a hygromycin recombinant DNA-containing plant cell comprising

- (a) transforming the expression vector of claim 12 into an *Agrobacterium tumefaciens* strain,
- (b) inserting the chimeric gene of the expression vector into a hygromycin-sensitive plant cell and
- (c) selecting a cell expressing hygromycin resistance by growing the cell in the present of sufficient hygromycin to prevent growth should the hygromycin resistance gene be absent.

18. A method for regenerating mature plants from selected cells which comprises selecting a hygromycin resistant recombinant DNA-containing plant in accordance with the method of claim 17, culturing the selected cell under conditions suitable for regeneration of a mature plant, and regenerating a mature plant.

EP-B1 – 0290395 – Claim 8:

A method for producing transformed fertile plants which comprises transforming plant cell material [with a DNA] according to the method of claims 1 to 7 and culturing the thus transformed plant cells under culture conditions.

EP-B1 – 0316797 – Claim 4:

Process for the production of plants with a modified flower colour, characterized in that a DNA sequence which codes for a protein having the enzymatic activity of a dihydroflavonol-4 reductase with extended substrate specificity for dihydrokaempferol is introduced by gene technology into a plant which is not normally capable of reducing dihydrokaempferol.

EP-B1 – 0301749 – Claim 24:

A method of making a genetically transformed line of plants comprising the steps of:
 preparing copies of a foreign gene including a coding region and flanking regulatory sequences effective to express the coding region in cells of the plants;
 joining copies of the foreign gene to biologically carrier particles;
 placing a meristematic tissue of the plant on a target surface;
physically accelerating the particles carrying the foreign gene copies at the target surface in such a fashion that some particles lodge in the interior of at least some of the cells of the meristematic tissue;
 growing the meristematic tissue into a whole sexually mature plant;
 obtaining self-pollinated seed from the mature plant;
 growing out progeny plants from the seed and
 assaying the progeny plants for presence of the foreign gene.

EP-B1 – 0429478 – Claim 11:

A process for introducing a trait into a plant, comprising the steps of:
 (a) isolating a gene whose expression in a plant confers the trait;
 (b) constructing a DNA plant expression cassette according to any of claims 1 to 7 with the isolated gene;
 (c) transforming plant cells with the cassette; and
 (d) regenerating plants from the transformed plant cells.

EP-B1 – 0269601 – Claim 1:

A method of producing genetically transformed tomato plants which exhibit toxicity toward Lepidopteran larvae which comprises:

- (a) inserting into the genome of a tomato cell a chimeric gene which comprises

- (i) a promoter which functions in plants to cause the production of a mRNA transcript;
- (ii) a coding sequence that causes the production of mRNA encoding a toxin protein of *Bacillus thuringiensis* encoded by DNA sequence 1–3471 of Figure 1, and
- (iii) a 3' non-translated region which functions in tomato to cause the addition of polyadenylate nucleotides to the 3' end of the mRNA;
- (b) selecting transformed tomato cells; and
- (c) regenerating from the transformed tomato cells genetically transformed tomato plants which exhibit toxicity toward Lepidopteran larvae.

EP-B1 – 0221044 – Claim 35:

A method for producing genetically transformed plants able to produce a desired polypeptide in enhanced amounts, comprising the steps of:

- (a) inserting into the genome of a plant cell a plasmid DNA comprising:
 - (i) a first DNA segment containing a heterologous DNA sequence and a segment of the coat protein-encoding component of a binary geminivirus DNA which permits autonomous replication of the plasmid DNA in a plant cell and a second DNA segment comprising a directly repeating DNA sequence derived from a segment of the coat protein-encoding component of a binary geminivirus DNA, said second DNA segment flanking said first DNA segment and permitting release of a plant plasmid from said plant vector, and
 - (ii) a heterologous DNA sequence comprising a gene encoding desired polypeptide;
- (b) obtaining transformed plant cells; and
- (c) regenerating from the transformed plant cells genetically transformed plants able to produce the desired polypeptide in enhanced amounts.

EP-B1 – 2390339 – Claim 11:

A method for producing a transformed plant comprising transforming a plant cell with the polynucleotide of Claim 1 or Claim 2 and regenerating a plant from the transformed plant cell.

EP-B1 – 2376635 – Claim 1:

A method of making a nematode-resistant transgenic plant, the method comprising the steps of:

- a) providing a recombinant expression vector comprising a root-specific promoter in operative association with a polynucleotide encoding an AVR9-elicited_{111B}-like protein comprising amino acids 1 to 226 of SEQ ID NO:38;
- b) transforming a plant cell with the recombinant expression vector;
- c) regenerating transgenic plants from the transformed plant cell; and
- d) selecting transgenic plants which demonstrate increased resistance to plant parasitic nematode infection when compared to wild type plants which do not comprise the recombinant expression vector.

As above for claims directed to transgenic plant products, the above examples only represent a small fraction of the process patents relating to transgenic plants which have been granted by the EPO.

D.VI.2.g.c. Use claims/purpose-limited product claims for transgenic plants

The claim wording of use claims involving transgenic plants should be such that the claim cannot be interpreted as an essentially biological process for the production of plants (Art. 53(b) EPC), i.e. the plant should be used for a technical purpose consistent with the holding of **G 2/07 (Broccoli/PLANT BIOSCIENCE)**, discussed above in section D.VI.2.b and C.I.2.c.

As to the further patentability requirements, i.e. novelty, inventive step and industrial application, as well as the requirements of the application, i.e. sufficiency of disclosure and clarity and support of the claims, see C.I.3.

Claim drafting:

The general wording for a use claim could read as follows:

Use of transgenic plant X for (technical) purpose Y.

For further details on allowable “technical” purposes, see D.VI.2.b and C.I.2.c.

Examples of allowed use claims are shown in the following:

EP-B1 – 2045327 – Claim 20:

The use of a transgenic organism of any one of claims 10 to 12 or of cell cultures, parts of transgenic propagation material derived there from as claimed in claim 19 for the production of foodstuffs, animal feeds, seeds, pharmaceuticals or fine chemicals.

EP-B1 – 1961815 – Claim 4:

Use of a plant body as defined in any one of claims 1 to 3 for removing excess phosphorus in hydrosphere.

EP-B1 – 1881073 – Claim 10:

Use of a plant or seed of any of Claims 1 to 9 for the production of an agricultural product.

D.VI.2.h. Parts of plants

The meaning of the term “parts of plants” as used herein is provided in the introduction of this chapter (D.VI.1).

When directing claims to parts of plants, the provision of Art. 53(b) EPC relating to the exclusion of plant varieties from patentability must be considered. As outlined in C.I.2.b and D.VI.2.b.a., in early decision **T 49/83 (Propagating material/CIBA-GEIGY)** a Board interpreted the term “plant variety” broadly, as comprising the plant itself *as well as propagating material*. The Board explicitly stated:

The Legislator did not wish to afford patent protection under the European Patent Convention to plant varieties of this kind, whether in the form of propagating material or of the plant itself. (point 2, last sentence)

Therefore, the Board concluded:

However, Article 53(b) EPC prohibits only the patenting of plants *or their propagating material* in the genetically fixed form of the plant variety. (point 3, last sentence) (emphasis added)

This interpretation of the term “plant variety” which comprises propagating material, was developed further in the later decision **T 356/93 (Plant cells/PLANT GENETIC SYSTEMS)**.

However, it was not completely clear from **T 356/93 (Plant cells/PLANT GENETIC SYSTEMS)** whether the term “plant variety” should include propagating material which would therefore be excluded from protection under Art. 53(b) EPC. Despite its mention of “transformed plants or seeds” in the reasons, **T 356/93** did not finally decide on the allowability of claims directed to propagating material.

As mentioned above, the landmark decision **G 1/98 (Transgenic Plant/NOVARTIS II)** dealt with the term “plant variety”. The questions before the Enlarged Board in this case did not relate to whether or not propagating material such as seeds should be included within the term “plant” nor whether, in the event the plant in question is an excluded plant variety, this extension also extends to its seeds. However, the claims at issue in this case included a claim directed to “[a] transgenic plant and the seed thereof comprising recombinant DNA sequences ...”. It was therefore at least clear that plant and seed claims were considered together; where a plant was not excluded under Art. 53(b) EPC, then neither were its seeds, and the patent which eventually granted in that case included both plant and seed claims.

Later decision **T 1242/06 (Tomatoes/STATE OF ISRAEL)** did consider the question of whether the seeds of an excluded plant variety are also excluded as a “plant variety”. In that case, the Board considered claims which were directed to dehydrated tomato fruits rather than to whole tomato plants. The Board stated in this context:

The question thus arises whether for that reason alone the claimed subject-matter might escape the exclusion of plant varieties. However, a plant variety may be represented not only by whole plants but also by propagating material such as seeds and by parts of plants. [...]. The Board therefore concludes that claims which, as in the present case, are directed to plant fruits which contain seeds and which are therefore to be regarded as plant parts capable of producing entire plants may well in general fall under the patent exclusion of plant varieties contained in Article 53(b) EPC. (point 27 of decision; emphasis added).

From the above, it can be taken that the exclusion of “plant varieties” also extends to propagating material, for example seeds, as well as other parts of such excluded plants.

As long as it is not a “plant variety”, however, propagating material can be claimed if it can be distinguished from any other propagating material by a reliable parameter. Such a new parameter can be, for example, the treatment of propagating material with a chemical which confers new characteristics on the chemically treated propagating material. Such a claim was accepted by the EPO in EP-

A-0010588, the application underlying **T 49/83** mentioned above. Allowed claim 13 of this application is shown in the examples below. Another example is the mechanical treatment of propagating material to render the material non-viable, as in **T 542/04 (Soybean products/E.I. DU PONT DE NE-MOURS)**, relevant claim 1 of which is shown below.

Regarding plant cells, the Board clearly stated in **T 356/93**:

Plant cells as such ... cannot be considered to fall under the definition of a plant or of a plant variety. In this respect it is further noted that plant cells are considered to be “microbiological products” in the broad sense under the current practice of the EPO [...]. (point 23)

This was confirmed by the Enlarged Board of Appeal in later decision **G 1/98**, where the Board stated:

Microorganisms are different from the parts of living beings used for the genetic modification of plants. On the other hand, it is true that cells and parts thereof are treated like microorganisms under the current practice of the EPO [reference to decision T 356/93]. This appears justified since modern biotechnology has developed from traditional microbiology and cells are comparable to unicellular organisms. (point 5.2)

Therefore, plant cells are not “plants”, and therefore cannot be excluded as a “plant variety” under Art. 53(b) EPC.

D.VI.2.h.a. Highly differentiated parts of plants

The meaning of the term “highly differentiated parts of plants” as used herein is provided in the introduction of this chapter (D.VI.1).

D.VI.2.h.a.a. Product claims for highly differentiated parts of plants

Generally, any part of a plant can be the subject-matter of a product claim without contravening Art. 53(b) EPC. One exception might be propagating material in its genetically fixed form as discussed above.

As to the further patentability requirements, i.e. novelty, inventive step and industrial application, as well as the requirements of the application, i.e. sufficiency of disclosure and clarity and support of the claims, see C.I.3.

Claim drafting:

In general two possibilities exist for claiming parts of plants by means of a product claim.

A first possible claim version could read as follows:

Plant material X having characteristics a, b, c, ...

wherein characteristics a, b, c, etc. are structural features and/or parameters.

This type of claim will be appropriate if the material can be sufficiently defined by characteristics, such as the expression of a certain phenotype or a specific defined DNA contained in the plant material.

Often it is only possible to characterize the plant material by the process of its preparation, i.e. by means of a product-by-process claim.

A product-by-process claim directed to plant parts can have the general wording:

Plant material X obtainable by the process comprising steps 1, 2, 3, ...

Examples of allowed product claims are shown in the following:

EP-B1 – 0242246 – Claim 13:

Seeds, which possess, stably integrated in their genome, a DNA fragment as defined in any of claims 1 to 3.

In this claim the seeds are characterized by containing a specific DNA fragment in their genome.

EP-B1 – 0316797 – Claim 1:

Plant and plant parts which are not normally capable of reducing dihydrokaempferol, characterized by a DNA sequence which does not occur naturally in this plant, this sequence coding for a protein having the enzymatic activity of a dihydroflavonol-4 reductase (DFR) with extended substrate specificity for dihydrokaempferol.

The plant parts in the above claim are defined by the DNA sequence which does not naturally occur in the plant.

EP-A-10588 (underlying decision T 49/83 – Propagating material/ CIBA-GEIGY) – Claim 13:

Propagating material for cultivated plants treated with an oxime derivative according to formula I in claim 1.

The new feature in the above claim is the treatment of the propagating material with an oxime derivative. This feature is not a characteristic of a new variety which could be protected by a plant variety right and is not genetically fixed.

EP-B1 – 0511979 – Claim 2:

A plant, seeds or propagation material, containing cells as claimed in claim 1.

In the above claim the seeds and propagation material, respectively, are defined via the cells which form a part of the material and which express a specific prokaryotic gene.

EP-B1 – 0042912 – Claim 23:

Genetically transformed shoot buds which belong to the species *Cucumis melo* and which can be obtained in the course of the process according to any one of claims 8 to 14.

The shoot buds in the above claim are defined by the process of their preparation, which comprises the transformation of shoot buds with *Agrobacterium tumefaciens*. It is to be noted that the shoot buds *can* be obtained by the specific process indicated in claims 8 to 14; the shoot buds are not limited to the immediate product of the process of claims 8 to 14.

EP-B1 – 0369637 – Claim 13:

Seed obtained from a transgenic plant as claimed in claim 11 or 12.

In this case the seed is defined by the plant from which it is derived.

EP-B1 – 0362244 – Claim 1:

Mechanically exposed, mature embryos of useful plants having a water content of no more than about 20 weight percent as the receiving system for foreign genetic information in the form of DNA or RNA obtainable by breeding the seed coat and injuring the embryo.

The above claim is a combination of the first and second claim version proposed above, namely the product is defined by characteristics (the water content) and process steps (breeding the seed coat and injuring the embryo).

EP-B1 – 2390339 – Claim 5:

A cell or an oilseed plant or a transgenic seed comprising in its genome the recombinant DNA construct of Claim 4.

EP-B1 – 2390339 – Claim 15:

A transgenic seed obtained from the plant made by the method of Claim 11, wherein the seed contains the polynucleotide of Claim 1 or Claim 2.

EP-B1 – 2376635 – Claim 3:

A seed which is true breeding for a transgene comprising a recombinant expression vector comprising a root-specific promoter in operative association with a polynucleotide encoding an AVR9-elicited_{111B}-like protein comprising amino acids 1 to 226 of SEQ ID NO:38.

EP-B1 – 2356899 – Claim 6:

A portion or a propagation material of the transgenic plant according to any one of claims 4 or 5, wherein the portion or respectively the propagation material of the transgenic plant comprises the combination of A) and B) as described in claim 4.

EP-B1 – 2350290 – Claim 6:

A plant, cell, or tissue comprising a recombinant vector of claim 5.

EP-B1 – 2333088 – Claim 12:

A transformed seed of the plant of claim 10.

D.VI.2.h.a.b. Process claims for highly differentiated parts of plants

The Board's holding in **T 1242/06 (Tomatoes/STATE OF ISRAEL)** that a plant variety may be represented not only by whole plants but also by propagating material such as seeds, and by parts of plants, means that protection for propagation material can – even if a plant variety – at least be obtained via a process claim, since such a claim also protects the product directly obtained by such a process (see C.I.3.e.a). This was confirmed in **G 1/98 (Transgenic Plant/NOVARTIS II)**, in which the Enlarged Board stated that

the protection conferred by a process patent is extended to the products obtained directly by the process, even if the products are not patentable per se.

The Enlarged Board concluded by stating:

When a claim to a process for the production of a plant variety is examined. Art. 64(2) EPC is not to be taken into account.

Art. 64(2) EPC specifies that if the subject-matter of the European patent is a process, the protection conferred by the patent extends to the products directly obtained by such process. The same must apply to processes for the production of highly differentiated parts of plants; as long as the claimed process is not “essentially biological” in the sense of Art. 53(b) EPC, then the process should not be excluded from patentability, even if the direct products of the process are.

As to the further patentability requirements, i.e. novelty, inventive step and industrial application, as well as the requirements of the application, i.e. sufficiency of disclosure and clarity and support of the claims, see C.I.3.

Claim drafting:

A process claim for the preparation of a part of a plant could have the following generalized wording:

A process for preparing part X of a plant comprising the steps a, b, c, ...

In addition to the above process claim, wherein “preparing” means that a new genome of a plant part is prepared, process claims are also possible, which are directed to the conditions for culturing a plant part, wherein the genetic identity of the treated plant part remains unchanged.

Further, process claims can be drafted wherein a plant part is used as a source for the isolation of a product of interest.

Examples of granted process claims are shown in the following:

EP-B1 – 0242236 (underlying decision T 356/93 – Plant cells/PLANT GENETIC SYSTEMS) – Claim 7:

Process for producing a plant or reproduction material of said plant including a heterologous genetic material stably integrated therein and capable of being expressed in the said plants or reproduction material in the form of a protein capable of inactivating or neutralizing the activity of a glutamine synthetase inhibitor, which process comprises transforming cells or tissue of said plants with a DNA recombinant containing a heterologous DNA including a foreign nucleotide sequence encoding said protein as well as the regulatory elements selected among those which are capable of causing the stable integration of said heterologous DNA in said plant cells or tissue and of enabling the expression of said foreign nucleotide sequence in said plant cells or plant tissue, regenerating plants or reproduction material of said plants or both from the plant cells or tissue transformed with said heterologous DNA and, optionally, biologically replicating said last mentioned plants or reproduction material or both.

The above process is directed, among other things, to the production of propagation material, wherein the essential step is the transformation of cells

or tissue of the plant with a DNA recombinant containing a heterologous DNA. This claim was allowed in the appeal proceedings underlying decision **T 356/93 (Plant cells/PLANT GENETIC SYSTEMS)**.

EP-B1 – 0290395 – Claim 6:

The method of claims 1 to 5 wherein the plant material is plant tissue, plant embryo, meristematic tissue, auxiliary buds, stem strips or callus.

Claim 1 of the patent was directed to a process for transforming plant material.

EP-B1 – 0362244 – Claim 5:

A process for preparing embryos according to claim 1, wherein the coat of the embryo-containing seed is so abraded in the area of the embryo which has a water content of no more than 20 weight percent, that the embryo is accessible to foreign genetic information in the form of DNA or RNA, but is not substantially impaired in its germinative abilities.

EP-B1 – 0242246 – Claim 5:

Process for producing a plant or reproduction material of said plant including a heterologous genetic material stably integrated therein and capable of being expressed in said plants or reproduction material in the form of a protein capable of inactivating or neutralizing the activity of a glutamine synthetase inhibitor, which process comprises transforming cells or tissue of said plants with a DNA recombinant containing a heterologous DNA, as well as the regulatory elements selected among those which are capable of causing the stable integration of said heterologous DNA in said plant cells or tissue and of enabling the expression of said foreign nucleotide sequence in said plant cells or plant tissue, regenerating plants or reproduction material of said plants or both from the plants cells or tissue transformed with said heterologous DNA and, optionally, biologically replicating said last mentioned plants or reproduction material or both, characterized in that said heterologous DNA has the nucleotide sequence of the DNA fragment of any of claims 1 to 3 or of said part that codes for a protein having phosphinotricinacetyl transferase activity.

EP-B1 – 1865053 – Claim 1:

A method of increasing seed size or weight which comprises increasing the level or activity of a cytokinin oxidase in seeds in a plant.

While not directed to a process of preparing a plant, the above claim is interesting because the product of increasing seed size or weight is the altered seed itself.

D.VI.2.h.a.c. Use claims/purpose limited product claims for highly differentiated parts of plants

As mentioned in D.VI.2.e.c, a use claim is a form of process claim. As such, when drafting a use claim one must keep in mind that the claim may not cover an essentially biological process for the production of plants (excluded by Art. 53(b) EPC) as defined in decision **G 2/07 (Broccoli/PLANT BIO-SCIENCE)**. This means that, for example, a claim with the following wording:

Use of plant part X for preparing plant Y.

might not be allowable because it could be interpreted as an essentially biological process for preparing a plant as follows:

A process for producing plant Y by growing plant part X to a complete plant.

The regeneration of a plant from a part of a plant could be interpreted as merely comprising biological steps. Such a process is at least not regarded as a microbiological process – which is patentable under Art. 53(b) EPC – but rather as a process comprising a series of agrotechnical and biological steps (point 40.9 of **T 356/93 (Plant cells/PLANT GENETIC SYSTEMS)**). That agrotechnical steps are not necessarily sufficient to render a process as a whole essentially non-biological was clarified in **G 2/07**.

The use of plant parts for a technical purpose should be allowable under Art. 53(b) EPC (see D.VI.2.e.c).

As to the further patentability requirements, i.e. novelty, inventive step and industrial application, as well as the requirements of the application, i.e. sufficiency of disclosure and clarity and support of the claims, see C.I.3.

Claim drafting:

The wording of a use claim could be as follows:

Use of plant part X for (technical) purpose Y.

The “technical” purpose Y could be, for example, the isolation of a product from the plant part.

An example of an allowed use claim is shown in the following:

EP-B1 – 2247736 – Claim 7:

Use of the corn seed of claim 5 to prepare a processed food or feed commodity, wherein said processed food or feed commodity comprises a detectable amount of a polynucleotide comprising a nucleotide sequence of SEQ ID NO: 1, SEQ ID NO: 2, or a complement thereof.

D.VI.2.h.b. Undifferentiated or poorly differentiated parts of plants

The meaning of the term “undifferentiated or poorly differentiated parts of plants” as used herein is provided in the introduction of this chapter (D.VI.1).

D.VI.2.h.b.a. Product claims for undifferentiated or poorly differentiated parts of plants

The protection of plant cells, cell cultures and plant tissue is not affected by the exclusion of plant varieties under Art. 53(b) EPC, mainly for the following reasons:

- plant cells as such are not regarded as a “plant” or “plant variety” (**T 356/93 (Plant cells/PLANT GENETIC SYSTEMS)**, point 40.2) and, hence, are not excluded from patentability under Art. 53(b) EPC;
- according to EPO practice plant cells are comprised by the term microorganisms (e.g. **T 356/93 (Plant cells/PLANT GENETIC SYSTEMS)**, point 34; confirmed by Enlarged Board of Appeal decision **G 1/98 (Transgenic plant/NOVARTIS II)**, point 5.2) which are patentable in accordance with Art. 53(b);
- plant cells which were genetically modified as well as cultures thereof are regarded as “microbiological products” (**T 356/93 (Plant cells/PLANT GENETIC SYSTEMS)**, point 35) and, hence, are patentable under Art. 53(b) EPC.

As to the further patentability requirements, i.e. novelty, inventive step and industrial application, as well as the requirements of the application, i.e. sufficiency of disclosure and clarity and support of the claims, see C.I.3.

Further information on the patentability of microbiological products is provided in D.V.

Claim drafting:

There are several possible ways to define cells, cell cultures, etc., in a product claim. For example, these inventions can be defined by their characteristics, by their process of preparation, or by making reference to a deposit accession number, when cells have been deposited with a recognized depositary institution. Particulars regarding such a deposit are discussed in more detail in D.V.

Generally, a claim describing the product by its characteristics could have the following wording:

A plant cell (or plant cell culture or plant tissue culture) having characteristics a, b, c, ...

In the most common cases where transformed cells are claimed, the cells can be appropriately defined by indicating the foreign gene introduced into the cells (i.e. by genotype) or by the foreign gene product expressed by the cells (i.e. by phenotype).

As an alternative to the above type of claim, one may consider drafting a product-by-process claim, if the plant cell to be claimed cannot be sufficiently defined by its expressed characteristics. In the case of transgenic plant cells a product-by-process claim should normally not be necessary since, as shown above, plant cells can usually be sufficiently characterized by the foreign DNA introduced therein. However, if the plant cell is obtained by a complex process, for example by cell fusions, etc., it will be difficult to describe the obtained fusion product by its characteristics. In this case a product-by-process claim is more suitable to define the product.

A product-by-process claim could have the following general wording:

A plant cell (or plant cell culture or plant tissue culture) obtainable by the process comprising the following steps 1, 2, 3, ...

As discussed above, the question of whether or not a product-by-process claim to a plant should be allowable when the referenced method is excluded as “essentially biological” is currently outstanding under referrals **G 2/12 (Tomatoes II/STATE OF ISRAEL)** and **G 2/13 (Broccoli II/PLANT BIOSCIENCE)** to the Enlarged Board of Appeal, and opinions have not yet issued. However, the Enlarged Board’s future holding in these cases should not affect the allowability of a product-by-process claim directed to a plant cell. The reason for this is as given above: various decisions have held that a plant cell should be classified as a microorganism rather than a plant. In the absence of “plant” subject-matter, the exclusion of Art. 53(b) EPC cannot apply.

Examples of granted product claims are shown below. Characterizing features are underlined in each case.

EP-B1 – 0270615 – Claim 1:

Transgenic *Brassica* species cells and progeny thereof comprising an expression cassette wherein said cells are characterised as oncogene-free and capable of regeneration to morphologically normal whole plants and wherein said expression cassette comprises in the 5’ to 3’ direction of transcription

- (1) a transcription initiation region functional in said *Brassica*;
- (2) a DNA sequence comprising an open reading frame having an initiation codon at its 5’ terminus or a nucleic acid sequence complementary to an endogenous transcription product;
- (3) a transcription termination region functional in *Brassica* species cells; and
- (4) a structural gene capable of expression in said *Brassica* providing for selection of transgenic *Brassica* species cells;

wherein said expression cassette is capable of altering the phenotype of said *Brassica* species cells when said cells are grown under conditions whereby said DNA sequence of said nucleic acid sequence is expressed.

The same patent contained as claim 14 a claim directed to a cell culture reading as follows:

A cell culture of cells according to any one of claims 1 to 4.

EP-B1 – 0154204 – Claim 6:

A plant tissue culture, the growth of which is resistant to inhibition by a 2-(2-imidazolin-2-yl)-pyridine or -quinoline herbicide or a sulfonamide herbicide at levels which normally inhibit the growth of said tissue culture wherein said resistance is conferred by an altered acetohydroxyacid synthase resistant to inhibition by said herbicide at levels which normally inhibit the activity of an unaltered acetohydroxyacid synthase.

EP-B1 – 0369637 – Claim 10:

A plant cell which has been transformed with a chimaeric gene as defined in claim 8.

EP-B1 – 0429458 – Claim 10:

A transformed plant cell comprising a foreign gene which expresses dihydrodipicolinic acid synthase (DHDPS) which is substantially resistant to feedback inhibition by endogenously-produced free L-lysine.

EP-B1 – 0511979 – Claim 1:

A plant cell expressing a prokaryotic ammonium-specific asparagine synthetase (ASN-A).

EP-B1 – 0301749 – Claim 22:

A regenerable soybean tissue including soybean cells which comprise in their genome an exogenous gene characterized in that at least some of the soybean cells carry small particles of biologically inert material which were used to carry the foreign gene into the cells.

EP-B1 – 1973396 – Claim 12:

Part of a plant as claimed in any one of the claims 1–11, wherein the plant part shows a reduced wound-induced surface discolouration or can be grown into a plant that shows a reduced wound-induced surface discolouration.

EP-B1 – 1785481 – Claim 9:

A plant embryo containing a DNA sequence comprising at least one *Wuschel* coding sequence under the control of a promoter selected from the group consisting of a nucellus-specific promoter and a promoter that is both nucellus-specific and inducible.

D.VI.2.h.b.b. Process claims for undifferentiated or poorly differentiated parts of plants

As outlined in connection with product claims, plant cells and cultures thereof are not regarded as plants within the meaning of Art. 53(b) EPC. Therefore, a process for preparing plant cells, cultures thereof, etc. is not excluded from patentability under Art. 53(b) EPC. Moreover, the most important process – namely a process for preparing a transgenic plant cell which includes the step of genetically engineering a plant cell – is regarded as a “microbiological process” (**T 356/93 (Plant cells/PLANT GENETIC SYSTEMS)**, point 35) and, therefore, allowable under Art. 53(b) EPC.

As to the further patentability requirements, i.e. novelty, inventive step and industrial application, as well as the requirements of the application, i.e. sufficiency of disclosure and clarity and support of the claims, see C.I.3.

Claim drafting:

A process claim for preparing a plant cell or a cell culture derived therefrom could have the following wording:

A process for preparing a plant cell (or plant cell culture or plant tissue culture) comprising the following steps 1, 2, 3, ...

Besides the above process claims for preparing a plant cell, etc. – wherein “preparing” means that the genetic identity of a plant cell is changed by the process – claims directed to certain conditions for culturing the cells are allowable, wherein the genetic identity of the cells is not changed by the process. Moreover, process claims directed to the preparation of a product of interest are allowable, wherein a plant cell is used as the source of said product.

Examples of allowed process claims include the following:

EP-B1 – 0200746 – Claim 10:

A method of conferring herbicidal GS-inhibitors resistance to a plant cell which comprises transforming said cell with the DNA sequence combination of claim 5.

EP-B1 – 0186425 – Claim 19:

A method for conferring hygromycin resistance on a plant cell which comprises integrating the chimeric gene of any of claims 1 to 10 into the genome of a hygromycin-sensitive plant cell as a functional element of a chromosome or plasmid.

D.VI.2.h.b.c. Use claims/purpose limited product claims for undifferentiated or poorly differentiated parts of plants

As outlined earlier in D.VI.2.e.c, a use claim is interpreted as a type of process claim. Art. 53(b) EPC must therefore be considered when drafting a use claim directed to the use of a plant cell for a particular purpose. The use claim should be drafted such that it does not read as an essentially biological process for the production of plants (as defined by decision **G 2/07 (Broccoli/PLANT BIOSCIENCE)**) which is excluded from patentability under Art. 53(b) EPC. (D.VI.2.b.b.)

As to the further patentability requirements, i.e. novelty, inventive step and industrial application, as well as the requirements of the application, i.e. sufficiency of disclosure and clarity and support of the claims, see C.I.3.

Claim drafting:

As outlined above, the claimed use should be of a technical nature, meaning that it should recite at least one “technical”, non-biological feature or step. A generalized claim could have the following wording:

Use of plant X for (technical) purpose Y.

The technical purpose can be any purpose except the production of a new plant. For example, the purpose could be the preparation of a product of interest, etc.

D.VI.2.i. Summary

In summary, a claim to a plant product will avoid exclusion from patentability under Art. 53(b) EPC as long as the claim is not directed to individual plant varieties. This holds even if the claim embraces plant varieties in a broader-claimed genus. A claim directed to one or more individual plant varieties will be excluded from patentability under Art. 53(b) EPC, regardless of the type of plant claimed (e.g. natural, hybrid, transgenic, etc.). EPO case law views seeds as equivalent to the plants from which the seeds originated, and into which the seeds are capable of growing, with the result that the above criteria for exclusion from patentability also apply for claims directed to seed products.

A natural plant is likely to be seen either as a “discovery”, which is not considered an invention available for patent protection under Art. 52(2)(a) EPC, or as a “plant variety”, which is excluded under Art. 53(b) EPC.

A claim to undifferentiated or poorly differentiated plant material such as e.g. cells or cell tissue culture should not be excluded from patentability under Art. 53(b) EPC, because such products are not considered “plants”, and therefore cannot be considered an excluded “plant variety” under Art. 53(b) EPC.

Claims to processes for the production or use of plants (including seeds) avoid exclusion from patentability as long as they are not “essentially biological” in the sense of Art. 53(b) EPC. A process is “essentially biological” in character, and therefore excluded from patentability, if it contains or consists of sexually crossing the whole genomes of plants and subsequently selecting progeny plants. But if the method includes a step of a technical nature which introduces or modifies a genomic trait of the plant produced, so that the plant product is not the result of merely mixing the genes of plants chosen for sexual crossing, then the process is not “essentially biological” and is not excluded from patentability under Art. 53(b) EPC. This holds even in the event that the resulting plant product (or seed) itself might be excluded as a “plant variety” *per se*. This is because the provision of the EPC stipulating that the direct products of a claim to a preparation method fall under such a claim, (Art. 64(2) EPC) is not to be taken into account when in examining a claim to a process for the production of a plant variety.

The fact that a plant is not excluded from patentability as a “plant variety” or as contrary to “ordre public”, or that a process for producing a plant is not excluded from patentability as “essentially biological” in character, does not mean that the claim reciting the plant or process is necessarily allowable. As for any other invention, subject-matter not excluded from patentability must still satisfy the normal patentability requirements in order to be allowed.

D.VII. Animals

D.VII.1. Introduction

This chapter discusses the possibilities for protecting animals and parts of animals.

As used herein:

The term “animals” includes natural animals and transgenic animals.

The term “natural animals” includes naturally occurring animals and animals which are the result of an animal breeding process.

The term “transgenic animals” means animals which contain a foreign DNA sequence that is normally not observed in a respective wild-type animal. Usually the foreign DNA is introduced into an animal by genetically engineering an appropriate animal cell which is then grown to the complete transgenic animal.

The foreign DNA can for example be a regulatory sequence controlling the expression of another gene or a protein-coding sequence *per se*.

The term “parts of animals” includes animal organs, e.g., liver, heart, skin, blood, etc.; propagating material, e.g., semen and eggs; and animal tissue. Animal components such as animal cells, genes, proteins, etc. are separately discussed in D.II, D.III and D.IV.

The relevant types of protection will be explained for each of the above subjects considering the presently common practice of the EPO and referring to relevant case law.

When comparing the possibilities for protecting animals with the possibilities for protecting plants as previously discussed in Chapter D.VI, one difference is that animals can only be protected via a patent. There exists no parallel protection right for animals analogous to plant variety rights.

D.VII.2. Protecting animals under the EPC

General patentability requirements for animals apply as for any other kind of invention. As above, this applies for the basic patentability requirements of novelty, inventive step and industrial application, as well as the requirements for the application, for example, sufficiency of disclosure (Art. 83 EPC) and clarity (Art. 84 EPC). Because of the particular importance of sufficiency of disclosure (Art. 83 EPC) for applications relating to certain types of animal inventions, subchapter D.VII.2.a addresses this topic in greater detail below.

As mentioned earlier in B.I. and C.I.2.b, Art. 53(b) EPC in its English wording excludes animal varieties (German wording: “Tierrassen” (animal breeds); French wording: “races animales” (animal breeds)) from patentability. The EPC mentions animal varieties in the context of patentable biotechnological inventions. Rule 27(b) EPC and (c) EPC stipulates that

Biotechnological inventions shall also be patentable if they concern:

[...]

- (b) plants or animals if the technical feasibility is not confined to a particular plant or animal variety;
- (c) a microbiological or other technical process, or a product obtained by means of such a process other than a plant or animal variety.

Unlike the term “plant variety” which is explicitly defined in Rule 26(4) EPC, the term “animal variety” is not formally defined in either the EPC or case law of the EPO Boards of Appeal. However, decision **T 315/03 (Transgenic animals/HARVARD)** held in its headnote 7.2 that

a definition [of the term “animal variety”] by reference to taxonomical rank would be both consistent with the position in relation to plant varieties and in the interest of legal certainty. With such a definition, an assessment could be made as to whether the claimed subject-matter is excluded from patentability under Article 53(b) EPC as interpreted by Rule [27](b) EPC – i.e. whether, in a case concerning animals, the technical feasibility of the invention is not confined to a particular animal variety.

Unfortunately, the Board was not more specific as to the level of “taxonomical rank” which is sufficient to meet the threshold of “animal variety”. In doubt, this will likely be the taxonomical rank which specifies a particular animal species meeting the requirements of Rule 26(4) EPC for plants, i.e. any animal grouping within a single animal taxonom which can be (a) defined by the expression of the characteristics that results from a given genotype or combination of genotypes; (b) distinguished from any other animal grouping by the expression of at least one of said characteristics; and (c) considered as a unit with regard to its suitability for being propagated unchanged.

The reader will note that the above corresponds to the definition of Rule 26(4) EPC, simply applied to animals rather than plants. However, given multiple Boards’ statements that the EPO’s stances for the exclusion provision of Art. 53(b) EPC regarding plants should also apply for animals, such an extension seems justified.

Much of the relevant European case law in connection with animals focuses on the exclusion provisions of the EPC (Art. 53 EPC). For this reason, the exclusion provisions are a major topic in the following subchapters. Many of the patent applications in the EPO relating to animals pertain to transgenic animals. Due to this prevalence, the patentability exclusions established under Art. 53(a) EPC and Art. 53(b) EPC are discussed in greatest detail below within the broader chapter relating to transgenic animals.

D.VII.2.a. Sufficiency of disclosure in animal inventions

The requirement of sufficiency of disclosure was examined by a Board of Appeal in decision **T 19/90 (Onco-mouse/HARVARD)**. The product claim underlying this decision – claim 19 – was directed to a “non-human mammalian animal”. The patent specification contained examples wherein the representative non-human mammalian animal was a mouse. The Board concluded that the claimed invention was sufficiently disclosed in the specification, explicitly stating:

However, the mere fact that a claim is broad is not in itself a ground for considering the application as not complying with the requirement for sufficient disclosure under Article 83 EPC. Only if there are serious doubts, substantiated by verifiable facts, an application may be objected to for a lack of sufficient disclosure. (point 3.3)

The Board then further explained:

The invention clearly indicates how the skilled person can achieve chromosomal incorporation of an activated oncogene sequence into the genome of a non-human mammal, disclosing as it does an activated mouse myc gene introduced into a suitable plasmid and then micro-injected into mouse eggs at a given stage of cellular development. Firstly, this ensures that the invention can be reproduced on mice. Secondly, it may be assumed that the skilled person is aware [...] of other suitable mammals on which the invention can likewise be successfully performed. There is thus no reason why the application should be refused on the ground that it involves an extrapolation from mice – as particularly featured in the application – to mammals in general. (point 3.8)

In the subsequent related decision **T 315/03 (Transgenic animals/HARVARD)**, the Board assessed sufficiency of disclosure for auxiliary request 1 (reproduced below in D.VII.2.c.a.a). The Opponents had alleged difficulties in obtaining oncomice, but had provided no evidence other than referring to the Patentee's own arguments. The Board referred to the previous decision **T 19/90** which held that a patent may only be objected to for lack of sufficient disclosure if there are serious doubts, substantiated by verifiable facts, that the claimed subject matter could be reproduced. The Board saw these as lacking and held that the subject matter of auxiliary request 1 was sufficiently disclosed.

D.VII.2.b. Natural animals

The meaning of the term “natural animals” as used herein is provided in the introduction of this chapter (D.VII.1).

D.VII.2.b.a. Product claims for natural animals

The attempt to obtain patent protection for a natural animal by means of a product claim encounters several obstacles.

First, without further characterization representing a new technical teaching, a naturally occurring animal which is merely found in nature is not regarded as an invention but rather as a discovery. Since European patents are only granted for inventions and not for discoveries (Art. 52(2)a EPC), a product claim directed to such an uncharacterized natural animal as such is not allowable. A discussion of the exclusion of discoveries from patentability is provided in C.I.1.a.

Second, Art. 53(a) EPC, excluding inventions from patentability which would be contrary to “ordre public” or morality, presents a bar to the allowability of a product claim directed to a natural animal. Probably the most important decisions relating to the relevance of Art. 53(a) EPC for the patenting of an animal are **T 19/90 (Onco-mouse/HARVARD)** and the later related decision **T 315/03 (Transgenic animals/HARVARD)**. Because those decisions, however, concerned a transgenic animal and the questions of morality and “ordre public” were closely linked to the transgenic nature of the animal, they will be discussed below in D.VII.2.c.a.

Third, Art. 53(b) EPC, relating to the exclusion of “animal varieties” from patentability, can represent a bar to the allowability of a product claim. The exclusion provision of Art. 53(b) EPC is discussed in more detail below in connection with the patenting of transgenic animals (D.VII.2.c.a).

If an animal invention does not fall under the above exclusion provisions, it must fulfil the further requirements for patentability, namely, the invention must be novel (Art. 54 EPC), it must involve an inventive step (Art. 56 EPC) and it must also be susceptible to industrial application (Art. 57 EPC). The same principles applied to any conventional subject-matter are equally applicable to animal inventions. This was demonstrated for example in decision **T 315/03**, in which the Board stated that the EPC contains a *prima facie* presumption in favor

of patentability. This is clear, said the Board, in Arts. 52(1) and 54–57 EPC, according to which inventions “shall” be patentable if they fulfill the three criteria of novelty, inventive step and industrial applications. In that decision, the Board’s subsequent assessment of inventive step followed the standard approach taken for other non-animal inventions, including a consideration of whether or not the skilled person would have expected success based on the prior art available on the relevant date of the patent in question.

Similar considerations regarding inventive step can be drawn from decision **T 606/03 (Gene trap/ARTEMIS)**, in which the Board applied a standard assessment of inventive step to claims which included a claim directed to a transgenic mouse.

All of the above indicates that the EPO applies the same standards for the patentability requirements of i.a. novelty and inventive step when considering animal inventions as when considering non-animal inventions.

In addition to the above patentability requirements, the requirements of the application must also be fulfilled. In particular, the application must disclose the invention in such a manner as to enable the skilled person to carry out the invention (Art. 83 EPC), and the claims must be sufficiently clear for the skilled person and also be supported by the description (Art. 84 EPC). General information on these requirements of the application is provided in C.I.3.b, C.I.3.e.b and C.I.3.e.c.

An early seminal decision of an Appeal Board examined the requirement of sufficiency of disclosure according to Art. 83 EPC in connection with an animal invention (**T 19/90 (Onco-mouse/HARVARD)**). The application underlying this decision disclosed a transgenic *mouse* in the examples, but the product claim was directed to a transgenic *non-human mammalian animal*. The Board considered the invention as claimed to be sufficiently disclosed in view of the description. Since the question of sufficiency of disclosure was closely linked to the claimed transgenic animal, this question is considered in more detail in the discussion relating to transgenic animals in D.VII.2.c.a.

In connection with the disclosure of animal inventions in accordance with Art. 83 EPC, the question arises whether propagating material of an animal can be deposited in accordance with Rule 31 EPC (see Annex 4 and C.I.3.b.b). This should be possible because Rule 31 EPC allows the deposit of “biological material”, and Rule 26(3) EPC defines this term as any material containing genetic information and capable of reproducing itself or being reproduced in a biological system. Animal propagating material would appear to fall within this definition.

Claim drafting:

In general, an animal can be described in the same way as any other product, namely by its characteristics, e.g. intrinsic/extrinsic features or parameters, or alternatively by a product-by-process claim. A claim wording for the first alternative could be:

Animal X having characteristics a, b, c, ...

In case the animal is the result of a breeding process, a product-by-process claim might be the best way to define the claimed animal. Generally, such a claim could have the following wording:

Animal X obtainable by a process comprising steps 1, 2, 3, ...

Examples of allowed product claims are shown in the following:

EP-B1 – 1982587 – Claim 1:

An animal model for evaluating hyperpigmentations, wherein dark skin from a person of African descent is grafted onto an immunodeficient non-human animal.

EP-B1 – 1757186 – Claim 3:

A model rodent of Restless Legs Syndrome (RLS) and Periodic Limb Movement Disorder (PLMD), produced by a method according to claim 1 or 2.

EP-B1 – 1645183 – Claim 1:

A newborn NOD/SCID/IL2rg-null mouse into which human hematopoietic precursor cells or human mature hematopoietic cells have been transplanted.

EP-B1 – 1645183 – Claim 11:

A disease-model mouse produced by administering any one of bacteria, viruses, tumor cells and tumor antigen to a mouse as defined in claim 1.

EP-B1 – 1640454 – Claim 1:

A CD9/CD81 double-deficient non-human animal, wherein functions of a gene coding for CD9 and a gene coding for CD81 are deficient at least in the somatic cells.

EP-B1 – 1321032 – Claim 9:

An animal model of heart failure obtainable by the method according to claim 1.

D.VII.2.b.b. Process claims for natural animals

When drafting process claims, Art. 53(c) EPC must be considered. According to this provision, methods of treatment of the animal body by surgery or therapy and diagnostic methods practiced on the animal body are excluded from patentability. Therefore, method of treatment claims are not allowable. This subject is discussed in C.I.2.d.

However, methods wherein an animal is used for preparing a product of interest, e.g. a therapeutically active product – also known as drug farming – are not excluded by Art. 53(c) EPC. The same reasoning applies to methods for increasing the productivity of animals, e.g. increasing the wool production of sheep or the quality of meat, etc. Such methods are neither therapeutic nor diagnostic in nature and are thus not excluded by Art. 53(c) EPC.

Moreover, the exclusion provision of Art. 53(b) EPC, according to which an essentially biological process for the production of animals is not patentable, bars the allowability of a claim relating to a process for preparing natural animals.

In the field of plants, early decision **T 320/87 (Hybrid plants/LUBRIZOL)** considered the question of when a process is “essentially biological” within the meaning of Art. 53(b) EPC. In this decision the Board held that this question has to be judged on the basis of the essence of the invention, taking into account the totality of human intervention and its impact on the result achieved. Although in that decision the Board had to decide the allowability of a process for preparing hybrid plants, the Board’s holding should also be applicable to an animal invention and in particular to the question whether a process for preparing an animal is essentially biological. According to this early decision, a process claim should be allowable under Art. 53(b) EPC if it comprises at least one technical step having a decisive impact on the final result.

This holding was further specified with regard to the nature of the technical steps in the later (consolidated) decisions of the Enlarged Board of Appeal **G 2/07 (Broccoli/PLANT BIOSCIENCE)** and **G 1/08 (Tomatoes/STATE OF ISRAEL)**, the headnotes of which are identical and read as follows:

1. A non-microbiological process for the production of plants which contains or consists of the steps of sexually crossing the whole genomes of plants and of subsequently selecting plants is in principle excluded from patentability as being “essentially biological” within the meaning of Article 53(b) EPC.
2. Such a process does not escape the exclusion of Article 53(b) EPC merely because it contains, as a further step, or as part of any of the steps of crossing and selecting, a step of a technical nature which serves to enable or assist the performance of the steps of sexually crossing the whole genomes of plants or of subsequently selecting plants.
3. If, however, such a process contains within the steps of sexually crossing and selection an additional step of a technical nature, which step in itself introduces a trait into the genome or modifies a trait in the genome of the plant produced, so that the introduction or modification of that trait is not the result of the mixing of the genes of the plants chosen for sexual crossing, then the process is not excluded from patentability under Article 53(b) EPC.
4. In the context of examining whether such a process is excluded from patentability as being “essentially biological” within the meaning of Article 53(b) EPC, it is not relevant whether a step of a technical nature is a new or a known measure, whether it is trivial or a fundamental alteration of a known process, whether it does or could occur in nature or whether the essence of the invention lies in it.

The EPO Guidelines state that the same standard should be applied to inventions relating to animals:

A process for the production of plants or animals which is based on the sexual crossing of whole genomes and on the subsequent selection of plants or animals is excluded from patentability as being essentially biological, even if other technical steps relating to the preparation of the plant or animal or its further treatment are present in the claim before or after the crossing and selection steps (see G 1/08 and G 2/07). To take some examples, a method of crossing, inter-breeding, or selectively breeding, say, horses involving merely selecting for breeding and bringing together those animals (or their gametes) having certain characteristics would be essentially biological and therefore unpatentable. This method remains essentially biological and unpatentable even if it contains an additional feature of a technical nature, for example the use of genetic molecular markers to select either parent or progeny. (EPO Guidelines at section G-II, 5.4.2; emphasis added)

As to the further patentability requirements, i.e. novelty, inventive step and industrial application, as well as the requirements of the application, i.e. sufficiency of disclosure and clarity and support of the claims, see C.I.3.

Claim drafting:

A general wording for a claim directed to the preparation of natural animals could be as follows:

A process for preparing animal X comprising the following steps a, b, c, ...

In this context “preparing” means that a new animal genome is prepared so that an animal is obtained, the genome of which is different from the starting animal.

In order to avoid falling under the exclusion provision of Art. 53(b) EPC at least one of the steps a, b, c, etc., should be an essential technical step which is decisive for the characteristics of the animal obtained, in standing with the holding of the above decisions **G 2/07** and **G 1/08**, discussed under plants above.

In addition to the above process claim for preparing an animal, process claims are also conceivable wherein an animal is used as a source for the isolation of a product of interest. Such a claim could for example read:

A process for preparing product X from animal Y comprising steps a, b, c, ...

It is also possible to obtain process claims directed to a certain treatment of an animal in order to achieve a desired effect, as long as the treatment does not include a therapeutic or diagnostic method or is of a surgical nature. For example, process claims relating to the cultivating conditions of an animal in order to increase its productivity should be allowable.

Examples of allowed process claims include the following:

EP-B1 – 0213405 – Claim 1:

Process for the bulk production of an entomophagous insect, in a multiplication cage in which adult insects, originating from a previously formed inoculum composed of parasitized first host eggs are arranged on a first support, are brought into contact with second host eggs to be parasitized, arranged on a second support, from which a portion is withdrawn to form the said inoculum, which process is characterized in that a constant population of adult insects from the said inoculum which has been subjected to a prior incubation is maintained at constant temperature, in that the said inoculum is activated in the cage for a period corresponding to the time needed for emergence of the adult at the said temperature, in that the said first and second supports are passed in continuous fashion through the said cage at the same speed, the said speed enabling the second host eggs, which are to be parasitized by the insect which has emerged from the said inoculum, to be presented in a continuous and regular manner for a specified presentation time while the said insect is fed, and in that the second host eggs thus parasitized are then collected in continuous fashion, from which second host eggs the fraction forming the inoculum is withdrawn in the form of the said first support after the prior incubation.

The above process contains several technical steps, for example, the step of passing the first and second support in continuous fashion through the

cage at the same speed, which step renders the process, as a whole, non-essentially biological.

EP-B1 – 0348543 – Claim 1:

A method of signalling birth for animals, in particular dogs, characterized in that the atmospheric humidity which is abruptly increased by the amniotic fluid which is released at birth is detected and immediately thereafter an acoustic and/or optical signal is triggered off.

The above method is neither a method wherein the animal body is treated by surgery or therapy, nor a diagnostic method, and is therefore allowable under Art. 53(c) EPC. Moreover, no animal is prepared, so Art. 53(b) EPC does not exclude the claim from patentability.

EP-B1 – 0186833 – Claim 19:

A process for preparing monoclonal antibodies against a cytotoxin having M.W. of $17,000 \pm 500$ D as determined by polyacrylamide SDS gel electrophoresis, which comprises immunizing mice with either pure or impure preparations of such protein, detecting hybridomas which produce such antibodies by means of the immunoassay of any of claims 15 to 18, cultivating such hybridomas and obtaining the desired antibodies.

Although the above process comprises the step of immunizing mice, it was considered allowable under Art. 53(c) EPC because it is directed to the preparation of a product and not to the treatment of an animal body.

EP-B1 – 0193585 – Claim 19:

A method of preparing antibodies to a circumsporozoite protein of a member of the genus plasmodium, said method comprising the immunisation of a non human host using the peptide of claim 1.

The above claim was allowed under Art. 53(c) EPC, because the method was directed to the preparation of a protein and not to the treatment of the non-human host for a therapeutic purpose.

EP-B1 – 0187858 – Claim 16:

A method of preparing antibodies to CS antigen of *P. falciparum* Sporozoites, said method comprising the immunisation of a host using the peptide of any of claims 1 to 4, said host being used only as a source for obtaining the antibodies.

Compared to the first two claim examples, this claim contains the limitation that the host is only used as a source for obtaining the antibodies. This makes clear that the claimed method is not directed to the treatment of the host for a therapeutic purpose.

EP-B1 – 1982587 – Claim 5:

A method of preparing an animal model for evaluating hyperpigmentations, which comprises grafting dark skin from a person of African descent onto an immunodeficient non-human animal, and raising the animal for at least 6 months after the grafting.

EP-B1 – 1887859 – Claim 1:

Method for preparing an animal model for the human immune system in a non-human mammal, comprising the steps of:

- a) transplantation of human hematopoietic stem cells into a NOD/SCID mouse, and
- b) conditioning the mouse with cell culture supernatant of a culture of a human cell line, selected from 358/8, which has been derived from NCI-H358, and sub clones thereof, as well as A-549, wherein the culture supernatant contains 20 pg/ml to 10 ng/ml of each of the human factors interleukin-8, interleukin-6, vascular endothelial growth factor (VEGF), interferon- γ -induced Protein 10, monocyte chemoattractant protein-1, angiogenin und tissue-type plasminogen activator.

EP-B1 – 1769677 – Claim 10:

A method for producing a non-human animal carrying human herpesviruses, comprising the steps of

- a) crossbreeding a first non-human animal carrying human herpesviruses obtained according to the method of claim 9 with a second non-human animal belonging to the same species as said first animal but of a different sex, and
- b) selecting the descendants carrying human herpesviruses.

With its emphasis on crossbreeding features, the above claim might be considered an “essentially biological” process in the sense of Art. 53(b) EPC under newer case law (e.g. **G1/08 (Tomatoes/STATE OF ISRAEL)**), and therefore excluded from patentability.

D.VII.2.b.c. Use claims/purpose limited product claims for natural animals

When drafting use claims, one should consider that a use claim is interpreted as a process claim, as explained in C.I.3.e.a. Therefore, the exclusion of essentially biological processes for preparing animals under Art. 53(b) EPC also presents a bar to the allowability of a use claim, if the claim does not include a technical step.

For example, a claim having the wording:

Use of animal X for breeding animal Y

will be read as a claim of the following type:

Process for breeding animal Y wherein animal X is used as one parent.

Such a claim would be excluded under Art. 53(b) EPC as “essentially biological process”. However, a use claim which comprises a technical step according to **G 2/07 (Broccoli/PLANT BIOSCIENCE)** and **G 1/08 (Tomatoes/STATE OF ISRAEL)** should not be excluded by Art. 53(b) EPC since it would not be “essentially biological”.

As to the further patentability requirements, i.e. novelty, inventive step and industrial application, as well as the requirements of the application, i.e. sufficiency of disclosure and clarity and support of the claims, see C.I.3.

Claim drafting:

In order to avoid falling under the exclusion provision of Art. 53(b) EPC, a use claim should be drafted as follows:

Use of animal X for (technical) purpose Y

wherein the “technical” purpose can be any purpose. However, as soon as the purpose resides in the use of animal X for breeding a further animal, such a purpose becomes critical, as it may fall under the exclusion provision of Art. 53(b) EPC. In particular, uses of animals for test purposes in industry, e.g., for testing industrial products (for example, for ascertaining the absence of pyrogenic or allergic effects) or phenomena (for example, for determining water or air pollution) are patentable (EPO Guidelines, G-III, 2).

Examples of allowed use claims involving animals are shown in the following:

EP-B1 – 2327299 – Claim 1:

Use of a rodent to which reserpine was administered for inducement of chronic muscle pain and/or chronic tactile allodynia as a disease animal model for chronic pain.

EP-B1 – 1982587 – Claim 7:

A method of evaluating or screening a hyperpigmentation formation suppressant or a hyperpigmentation remover, wherein the animal model of claim 1 is used.

EP-B1 – 1645183 – Claim 19:

Use of the mouse of claim 1 or 2 or of a mouse produced by the method of any one of claims 3 to 6 for producing immunocompetent cells and/or physiologically active substances derived from said immunocompetent cells.

EP-B1 – 1640454 – Claim 11:

Use of the CD9/CDB1 double-deficient non-human animal of any one of claims 1 to 7 as a chronic obstructive pulmonary disease model animal, comprising a step of measuring the degree of a phenotype similar to chronic obstructive pulmonary disease of the CD9/CD81 double-deficient non-human animal.

EP-B1 – 1545195 – Claim 1:

Use of a female mouse having a complete depletion of ovarian primordial follicles, increased circulating levels of FSH, depletion of antral follicles, undetectable levels of plasma 17 β -estradiol, disrupted estrous cyclicity and reduced ovarian weight which have been induced by administration of 4-vinylcyclohexene diepoxide at a dosage of 160 mg/kg/day for 15 days, as a model for human perimenopause and/or menopause.

EP-B1 – 1321032 – Claim 8:

Use of the animal model of heart failure according to claim 1 for screening of a substance to be used for prevention or treatment of heart failure.

EP-B1 – 2246434 – Claim 1:

Use of a GNMT $^{-/-}$ mouse whose genome is disrupted by recombination at the Glycine N-Methyltransferase (GNMT) gene locus for studying depression, schizophrenia or Alzheimer's disease.

EP-B1 – 1644733 – Claims 7, 10, 24–29, 32–36:

Use of the existence of and time of formation of a blood brain barrier in a zebrafish in the design of a screening assay for a substance with biological activity ...

... in the central nervous system (CNS), brain or eye. (Claim 7)

... and which does not cross the blood brain barrier. (Claim 10)

Use of zebrafish to determine whether a test substance ...

... is actively transported across the blood brain barrier. (claim 24)

... is actively transported into the brain. (claim 25)

... is actively transported out of the brain. (claim 26)

... is transported across the blood brain barrier by p-glycoprotein. (claim 27)

... interferes with p-glycoprotein function. (claim 28)

... alters p-glycoprotein expression. (claim 29)

... is metabolised by the blood brain barrier. (claim 36)

Use of zebrafish ...

... to determine whether a combination of test substances have altered BBB penetration in comparison to a test substance given in isolation. (claim 32)

... to determine body:brain drug concentration gradients. (claim 33)

... to compare relative efficacies of test substances with desired CNS activity in the presence of a blood brain barrier. (claim 34)

... To determine penetration of a test substance across the blood-retinal barrier. (claim 35)

D.VII.2.c. Transgenic animals

The meaning of the term “transgenic animals” as used herein is provided in the introduction of this chapter (D.VII.1).

*D.VII.2.c.a. Product claims for transgenic animals**D.VII.2.c.a.a. Morality and “ordre public”*

As discussed in C.I.2.a, Art. 53(a) EPC excludes from patentability inventions the publication or commercial exploitation of which would be contrary to “ordre public” or morality. These terms were interpreted in decision **T 356/93 (Plant cells/PLANT GENETIC SYSTEMS)** and later confirmed in decision **T 315/03 (Transgenic animals/HARVARD)**. Essentially, the “ordre public” in the sense of Art. 53(a) EPC is interpreted as meaning the protection of physical security and the physical integrity of individuals as part of society, including protection of the environment. The concept of “morality” in the sense of Art. 53(a) EPC is interpreted as related to the belief that some behavior is right while other behavior is wrong. This belief is founded on the totality of the accepted norms deeply rooted in, for the purposes of the EPC, European society and civilization. Inventions which are not in conformity with the conventionally accepted standards of conduct pertaining to this culture are excluded from patentability under the “morality” aspect of Art. 53(a) EPC.

In the field of animal inventions, the above provision was examined by an Appeal Board in the well-known oncomouse decision (**T 19/90 (Oncomouse/HARVARD)**).

In that case, claim 19 of the main request was directed to a transgenic non-human mammal and had the following wording:

A transgenic non-human mammalian animal whose germ cells and somatic cells contain an activated oncogene sequence introduced as a result of chromosomal incorporation into the animal genome, or into the genome of an ancestor of said animal, said oncogene optionally being further defined according to any one of claims 3 to 10.

The Board did not decide whether Art. 53(a) EPC constitutes a bar to the allowability of the above claim, but rather remitted the case to the Examining Division to decide this question by carefully weighing the suffering of the animals and possible risks to the environment on the one hand, and the invention's usefulness to mankind on the other hand (**T 19/90 (Oncomouse/HARVARD)**, point 5).

The Examining Division then considered three different interests to be relevant in the specific case, namely, the interest of mankind to remedy widespread and dangerous diseases, the protection of the environment against an uncontrolled dissemination of unwanted genes, and the avoidance of cruelty to animals. Taking into account the above interests, the Examining Division concluded that the invention in question was not considered contrary to morality or "ordre public". The Examining Division, however, stressed that the weighing of all interests involved is necessary from case to case and that in a different case a different conclusion might be reached in applying Art. 53(a) EPC.

Following grant of a patent in **T 19/90**, the patent was vigorously opposed by a number of parties, and eventually went to appeal containing the following product claim:

19. A transgenic rodent whose germ cells and somatic cells contain an activated oncogene sequence as a result of chromosomal incorporation into the animal genome, or into the genome of an ancestor of said animal, said oncogene optionally being further defined according to any one of claims 3 to 10. (emphasis added)

In the course of its voluminous decision, an Appeal Board considered, among other things, how the patentability exclusion of Art. 53(a) EPC should be applied. The Board noted that Rule 28 EPC (see Annex 2) sets out several cases which are in any event excluded from patentability under Art. 53(a).

These cases listed in Rule 28 EPC are however not exhaustive but rather exemplary. A claim falling under one of the cases and set out in Rule 28 EPC is automatically excluded from patentability under Art. 53(a) EPC without requiring any further consideration. However, a claim which does not fall under any of the specific cases set out in Rule 28 EPC may still fall under the more general exclusion as contrary to "ordre public" or morality as specified in Art. 53(a) EPC, which is controlling. In view of this thinking, the Board defined two dif-

ferent types of exclusions under Art. 53(a) EPC: a “Rule 28-type” Art. 53(a) EPC exclusion and a “real” Art. 53(a) EPC exclusion.

In **T 315/03**, the Board considered the case set out in Rule 28(d) EPC particularly carefully in view of the claimed subject-matter. Rule 28(d) EPC specifies a likelihood of animal suffering (no matter how minor), which must likely correlate to a “substantial medical benefit” to man or animal, in order to escape exclusion under this provision. The Board held that the test of Rule 28(d) EPC entails three questions:

- 1) Is the animal suffering likely?
- 2) Has substantial medical benefit been established?
- 3) If yes to (1) and (2), do the suffering and medical benefit exist in relation to the same animal?

In evaluating this balance, the Board spoke of a “necessary correlation between suffering and benefit”, and stated that the patent should extend to only those animals whose suffering is balanced by a medical benefit. Further, the Board held that the establishment of likelihood for animal suffering and substantial medical benefit is a matter of evidence, and that the same level of proof for demonstrating should apply for each criterion.

As mentioned above, even in the event that a claim is not excluded under Rule 28(d) EPC (i.e. a “Rule 28 EPC-type” exclusion under Art. 53(a) EPC), it may still be excluded under the broader, and controlling Art. 53(a) EPC. In **T 315/03**, the Board held that the standard to be applied for such a “real” Art. 53(a) EPC exclusion should be as developed in the previous decision **T 19/90 (Onco-mouse/HARVARD)**. In that decision, the Board balanced “usefulness to mankind” against animal suffering, thus applying a broader standard than the “substantial medical benefit” mentioned in Rule 28(d) EPC.

In **T 315/03** the Board held that claim 19 as reproduced above was excluded from patentability under Rule 28(d) EPC because, though the claim was directed to the broad class of “a transgenic rodent”, no evidence existed that any benefit, let alone a substantial medical benefit is likely to be derived from applying the claimed process to all rodents, or indeed any rodents other than mice. The “necessary correlation between suffering and benefit” mentioned above was therefore absent for a claim directed to a transgenic rodent. For this reason, the case set out in Rule 28 EPC applied, and the claim was excluded under a “Rule 28-type” Art. 53(a) EPC exclusion for this reason alone.

Notably, however, claim 1 of the first auxiliary request read as follows:

19. A transgenic mouse whose germ cells and somatic cells contain an activated oncogene sequence as a result of chromosomal incorporation into the animal genome, or into the genome of an ancestor of said animal, said oncogene optionally being further defined according to any one of claims 3 to 10. (emphasis added)

This claim was no longer directed to any rodent, but was restricted to a mouse. The Board confirmed that for this claim, there did exist a necessary

correlation between suffering and substantial medical benefit for all subject-matter of the claim, i.e. for the mouse. The Board concluded that the claimed subject-matter was not excluded under Rule 28(d) EPC (i.e. it was not excluded as a “Rule 28(d)-type” case). In standing with the above standard, this meant that the Board then had to consider whether the claim may still be excluded under the broader provision of Art. 53(a) EPC, i.e. whether it may nevertheless constitute a “real” Art. 53(a) EPC exclusion. The Board reached the same conclusion applying the broader standard of the test under **T 19/90**, stating that “... no suffering is envisaged to any animals without a corresponding prospect of benefit”. Nor could the subsidiary arguments of the Opponents, relating to the degree of suffering and possible environmental threats (neither of which were substantiated) convince the Board that the broader standard of Art. 53(a) EPC as interpreted under the **T 19/90** test should exclude the claim of the first auxiliary request from patentability as contrary to morality or *ordre public*.

The detailed and nuanced discussion in **T 315/03** is perhaps the most complete examination of the patentability exclusion of Art. 53(a) EPC as applied to animals available in EPO jurisprudence.

Examples of allowed product claims are shown in the following:

EP-B1 – 2421357 – Claim 1:

A non-human mammal whose genome comprises:

- a) a plurality of human IgH V regions, one or more human D regions and one or more human J regions upstream of a host non-human mammal constant region; and
- b) optionally one or more human Ig light chain kappa V regions and one or more human Ig light chain kappa J regions upstream of the host non-human mammal kappa constant region and/or one or more human Ig light chain lambda V regions and one or more human Ig light chain lambda J regions upstream of the host non-human mammal lambda constant region

wherein the non-human mammal is able to produce a repertoire of chimaeric antibodies, or chimaeric heavy chains and optionally chimaeric light chains, having a non-human mammal constant region and a human variable region;

wherein the non-human mammal genome into which DNA is inserted comprises endogenous V(D)J regions which have not been deleted,

wherein the non-human mammal is a rodent,

and wherein the Insertion of the human heavy chain DNA is made between the non-human mammal constant region and the last, 3', non-human mammal J region. or a non-human mammal whose genome comprises:

- (a) a plurality of human Ig light chain kappa V regions and one or more human Ig light chain kappa J regions upstream of the host non-human mammal kappa constant region and/or a plurality of human Ig light chain lambda V regions and one or more human Ig light chain lambda J regions upstream of the host non-human mammal lambda constant region; and
- (b) optionally one or more human IgH V regions, one or more human D regions and one or more human J regions upstream of a host non-human mammal constant; wherein the non-human mammal is able to produce a repertoire of chimaeric antibodies, or chimaeric light chains, and optionally chimaeric heavy chains, having a non-human mammal constant region and a human variable region

wherein the non-human mammal genome into which DNA is inserted comprises endogenous V(D)J regions which have not been deleted
 wherein the non-human mammal is a rodent,
 and wherein the insertion of the human kappa or lambda chain DNA is made between the non-human mammal constant region and the last, 3', non-human mammal J region.

EP-B1 – 2392657 – Claim 27:

A genetically recombined non-human animal generated by using either a non-human ontogenetic transformed cell expressing a foreign gene in which a modified transposon vector as defined in claim 1 is incorporated, or a nonhuman ontogenetic transformed cell expressing a foreign gene in which a modified transposon vector as defined in claim 1 is incorporated, and in which an expression cassette of a foreign gene with addition of the Lox or Frt sequence at either both ends or at any one thereof is further incorporated.

EP-B1 – 2218786 – Claim 9:

A non-human mammalian animal, which retains the mammalian artificial chromosome vector according to any one of claims 1 to 4 and enables expression of human cytochrome P450 genes.

EP-B1 – 2218786 – Claim 13:

The non-human mammalian animal according to any one of claims 9 to 12, which is a mouse.

EP-B1 – 2218786 – Claim 14:

The non-human mammalian animal according to claim 13, wherein the mouse is a progeny mouse.

D.VII.2.c.a.b. Animal varieties and essentially biological processes

Moreover, Art. 53(b) EPC, which excludes animal varieties from patentability, presents a bar to the allowability of a product claim directed to a transgenic animal.

In **T 19/90 (Onco-mouse/HARVARD)**, the Board further examined whether Art. 53(b) EPC is relevant to the following claim:

A transgenic non-human mammalian animal whose germ cells and somatic cells contain an activated oncogene sequence introduced as a result of chromosomal incorporation into the animal genome, or into the genome of an ancestor of said animal, said oncogene optionally being further defined according to any one of claims 3 to 10.

In the past, this provision caused particular problems of interpretation because the group of animals to be excluded from protection was defined by different, non-equivalent terms in the three official languages of the EPC. The previous German term “Tierarten” (animal species) related to a higher taxonomic unit than the French term “races animales” (animal breeds) or English term “animal varieties”.

These differences in the meaning of Art. 53(b) EPC in the three official languages were alleviated in the new version of Art. 53(b) EPC under the EPC-2000, in which “Tierarten” (animal species) in the German version was

amended to “Tierrassen” (animal races). This is congruent with the French “ races animals” (animal races), and at least more congruent with the English “animal varieties”, since both animal races and animal varieties represent smaller subgroupings of animals within a species.

Decision **T 19/90 (Onco-mouse/HARVARD)** did not provide a definition of the group of animals to be excluded from patent protection, but merely stated:

The exception to patentability under Article 53(b) EPC applies to certain categories of animals but not to animals as such. (headnote I)

The Board left it to the discretion of the Examining Division – to which the case was remitted for further examination – to examine whether Art. 53(b) EPC constitutes a bar to the allowability of the above product claim.

The Examining Division concluded that the above product claim was allowable under Art. 53(b) EPC essentially for the following reason:

Mammals and rodents constitute a taxonomic classification unit higher than “animal variety”, “race animale”, “Tierart” in Article 53(b) EPC and are therefore not excluded under this provision from patentability. (Headnote I in the decision of the Examining Division (Onco-mouse/Harvard)).

As mentioned above, the patent as granted by the Examining Division went to opposition, and product claim 19 was maintained in opposition, and went into subsequent appeal with the following language:

19. A transgenic rodent whose germ cells and somatic cells contain an activated oncogene sequence as a result of chromosomal incorporation into the animal genome, or into the genome of an ancestor of said animal, said oncogene optionally being further defined according to any one of claims 3 to 10.

Decision **T 315/03 (Transgenic animals/HARVARD)** decided on this appeal. Certain Opponents had argued on appeal that with Art. 53(b) EPC, it had been the Legislator’s intention to exclude all animals falling within any species. The Board did not agree, stating that the way Art. 53(b) EPC was worded made clear that the Legislator’s intention was to exclude only a limited category of animals and not all animals.

But which animals were to be specifically excluded? The Board further addressed this question in **T 315/03**, stating in point 11.8 of this decision that:

The definition of animal variety (or species or race) by reference to taxonomical rank would be consistent with the position in relation to plant varieties and in the interest of legal certainty, allowing assessment under Article 53(b) EPC as interpreted by Rule 23c(b) EPC [corresponding to present Rule 27(b) EPC] to be made by considering whether, in a case concerning animals, the technical feasibility of the invention is not confined to a particular animal variety (or species or race).

The Board in **T 315/03** therefore made clear that the same standard should be applied in defining both plant and animal varieties, and went on to explicitly state that the holding of **G 1/98 (Transgenic plant/NOVARTIS II)**

should apply to animal varieties as well: A patent should not be granted for a single animal variety (or species or race, depending on which language text of the EPC is used) but can be granted if varieties may fall within the scope of its claims.

The language of Art. 53(b) EPC indicates that a transgenic animal would not fall under the exclusion provision of Art. 53(b) EPC if it is the product of a microbiological process. According to Art. 53(b) EPC microbiological processes or the products thereof are patentable.

The EPO has not yet decided whether a transgenic animal can be regarded as a product of a microbiological process in the sense of Art. 53(b) EPC. In decision **T 19/90** this question was not examined, and in the related subsequent decision **T 315/03**, the Board stated that the proviso of Art. 53(b) EPC relating to microbiological processes or the products thereof was irrelevant for the claims under consideration.

However, when considering the case law in the field of transgenic plants, in particular **T 356/93 (Plant cells/PLANT GENETIC SYSTEMS)**, wherein the EPO did not consider a transgenic plant to be a microbiological product (discussed in D.VI.2.g.a), one could similarly conclude that a transgenic animal cannot be regarded as a microbiological product, even if it is admitted that the process for preparing a transgenic animal comprises a microbiological step, namely the step of transforming animal cells with a recombinant DNA. The process for preparing the complete transgenic animal, however, comprises further steps in addition to the initial cell transformation step, so that the whole process as such probably would not be regarded as a microbiological process and, hence, the product thereof would not be a microbiological product.

As to the further patentability requirements, i.e. novelty, inventive step and industrial application, as well as the requirements of the application, i.e. sufficiency of disclosure and clarity and support of the claims, see C.I.3.

Claim drafting:

In general, transgenic animals can be defined in a product claim by means of their characteristics, e.g. intrinsic or extrinsic features and/or parameters, which can be unambiguously defined or alternatively by a product-by-process claim, wherein the animal is characterized by its process of preparation.

A claim wherein the animal is described by its characteristics could have the following general wording:

A transgenic animal characterized in that it contains foreign DNA X.

A product-by-process claim could have the general wording:

A transgenic animal obtainable by the process comprising steps a, b, c, ...

Steps a, b, c, etc. are the essential measures which are necessary to prepare the claimed animal.

EP-B1 – 0169672 (underlying the decision of the Examining Division (*Onco-mouse/HARVARD*) – Claim 19:

A transgenic non-human mammalian animal whose germ cells and somatic cells contain an activated oncogene sequence as a result of chromosomal incorporation into the animal genome, or into the genome of an ancestor of said animal, said oncogene optionally being further defined according to any one of claims 3 to 10.

D.VII.2.c.b. Process claims for transgenic animals

The exclusion of method of treatment claims from patent protection has been discussed above in connection with process claims for natural animals in D.VII.2.b.b. The same considerations apply to a transgenic animal invention. For a more detailed discussion of the relevance of Art. 53(c) EPC, see C.I.2.d.

Moreover, Art. 53(a) EPC, excluding inventions from patentability which are contrary to “ordre public” or morality, must be considered. In both **T 19/90 (*Onco-mouse/HARVARD*)** and **T 315/03 (*Transgenic animal/HARVARD*)** the Board did not differentiate between the process claim and the product claim of either the underlying application (in **T 19/90**) or the resulting patent (in **T 315/03**) with regard to the relevance of Art. 53(a) EPC. The same criteria as discussed in D.VII.2.c.a.a therefore apply to a process claim.

The exclusion of essentially biological processes for the production of animals according to Art. 53 (b) EPC (discussed in D.VII.2.c.a.b) does not appear to be a major bar to the patentability of process claims directed to the preparation of transgenic animals, since exclusion provisions, in principle, are construed narrowly. Therefore, a process for preparing a transgenic animal, in general, is not considered to be an essentially biological process as defined in decisions **G 2/07** and **G 1/08** (discussed in D.VI.2.b) as long as the transgene is not merely incorporated for e.g. marker selection during breeding. For example, claim 1 of the main request underlying **T 19/90 (*Onco-mouse/HARVARD*)** was directed to the following method:

A method for producing a transgenic non-human mammalian animal having an increased probability of developing neoplasms, said method comprising chromosomally incorporating an activated oncogene sequence into the genome of a non-human mammalian animal.

The Board found this claim allowable under Art. 53(b) EPC, and explicitly stated:

The present invention contains process claims for the production of transgenic, non-human mammals with an increased propensity to develop neoplasms through chromosomal incorporation of an activated oncogene sequence into the genome of the non-human mammal. The oncogene is inserted by technical means into a vector (e.g., a plasmid), which is then micro-injected at an early embryonic stage. In the Board’s view, [...] this is not an “essentially biological process” within the meaning of Article 53(b) EPC. (point 4.9.1)

In decision **T 19/90**, the Board left undecided whether the claimed process could be regarded as a microbiological process within the meaning of Art. 53(b)

EPC, and in the subsequent subsequent related decision **T 315/03** in the same matter, the Board stated that the proviso of Art. 53(b) EPC relating to microbiological processes or the products thereof was irrelevant. The question whether a process for preparing a transgenic animal is considered as a microbiological process is, however, of importance for the allowability of such a process claim since in most cases it should not be regarded as essentially biological as long as the transgene is not incorporated for the simple purpose of selective marking during breeding. It should not therefore be excluded under Art. 53(b) EPC.

The recent decision **T 15/10 (Fishy taint/LOHMANN)** considered whether a claimed method constituted an essentially biological process for the production of an animal. The claim in question related to a method of selecting an avian involving the step of genetically testing for a fishy taint (i.e. taste) in the avian's eggs, selecting an avian based on the testing information, and (optionally) using the information for further breeding considerations. The Opponent had alleged that the claimed method constituted an essentially biological process for the production of animals within the meaning of Art. 53(b) EPC, which was excluded from patentability. Applying the standards set in **G 2/07** and **G 1/08** (discussed in D.VI.2.b), the Board did not agree. The Board stated that the claim was not directed to a method of producing an animal at all, let alone a method comprising the step of crossing whole genomes of animals. Rather, the method provides information of potential use for further breeding considerations. The Board therefore held that the claim was not excluded as an "essentially biological process for the production of animals" under Art. 53(b) EPC.

As to the further patentability requirements, i.e. novelty, inventive step and industrial application, as well as the requirements of the application, i.e. sufficiency of disclosure and clarity and support of the claims, see C.I.3.

Claim drafting:

A general wording for a process claim could read:

A process for producing a transgenic animal comprising the step of introducing foreign DNA x into cells of said animal.

In addition to process claims directed to the preparation of an animal, one may also imagine process claims in which an animal is used as a source for the isolation of a product. In the case of transgenic animals this type of claim is of particular relevance in connection with processes known as "drug farming" wherein, for example, a transgenic cow secretes the product encoded by the transgene as a component of the milk from which the product is purified. Such a process claim could read:

A process for preparing product X comprising the step of isolating from transgenic animal Y said compound X.

Examples of allowed process claims include the following:

EP-B1 – 0169672 (underlying the decision of the Examining Division (*Onco-mouse/HARVARD*) – Claim 1:

A method for producing a transgenic non-human mammalian animal having an increased probability of developing neoplasms, said method comprising chromosomally incorporating an activated oncogene sequence into the genome of a non-human mammalian animal.

The step of chromosomally incorporating an activated oncogene sequence into the genome of the animal is of a technical nature which renders the process, as a whole, non-essentially biological and, therefore, allowable under Art. 53(b) EPC.

EP-B1 – 2421357 – Claim 15:

A method for producing a fully humanised antibody or antibody chain comprising immunizing a non-human mammal according to any of claims 1,3–5,8–10 and 14, and then replacing the non-human mammal constant region of an antibody or chimaeric antibody chain specifically reactive with the antigen with a human constant region, optionally by engineering of the nucleic acid encoding the antibody or chimaeric antibody chain.

EP-B1 – 2218786 – Claim 17:

A method for preparing biologically active human cytochrome P450, comprising expressing human cytochrome P450 genes in the non-human mammalian animal according to any one of claims 9 to 14, the mouse or progeny thereof according to claim 15, or the cell, organ, or tissue according to claim 16 to produce the biologically active human cytochrome P450, and recovering the produced human cytochrome P450.

EP-B1 – 2218786 – Claim 18:

A method for testing pharmacological effects and/or metabolism of drug or food products, comprising administering drugs or food products to the non-human mammalian animal according to any one of claims 9 to 14, the mouse or progeny thereof according to claim 15, or the cell, organ, or tissue according to claim 16, and measuring pharmacological effects and/or metabolism of the drugs or food products.

EP-B1 – 2147594 – Claim 19:

A method for producing a desired antibody comprising exposing a murine mammal according to any one of claims 1–18 to an antigen such that an antibody response is induced and isolating the antibodies specific for the antigen

EP-B1 – 2147594 – Claim 20:

A method for producing a desired antibody comprising exposing a murine mammal according to any one of claims 1–18 to an antigen such that an antibody response is induced and isolating cells producing such antibodies, culturing and harvesting said antibodies.

EP-B1 – 2147594 – Claim 21:

A method for producing a desired antibody comprising exposing a murine mammal according to anyone of claims 1–18 to an antigen such that an antibody response is induced and isolating a nucleic acid molecule encoding at least part of such an antibody, inserting said nucleic acid molecule or a copy or a derivative thereof in an expression cassette and expressing said antibody in a host cell.

D.VII.2.c.c. Use claims/purpose limited product claims for transgenic animals

The problems in drafting use claims resulting from the exclusion of an essentially biological process for producing animals under Art. 53(b) EPC, have been discussed in connection with use claims for natural animals (D.VII.2.b.c). Again, the claim wording should be such that the claim cannot be interpreted as an essentially biological process for the production of an animal. The allowability of a use claim under Art. 53(b) EPC should generally not be precluded if the animal is used for a technical purpose such as testing drugs, etc. Moreover, Art. 53(c) EPC should be kept in mind when drafting such claims so that the claim would be interpreted as a method of treatment claim.

As to the further patentability requirements, i.e. novelty, inventive step and industrial application, as well as the requirements of the application, i.e. sufficiency of disclosure and clarity and support of the claims, see C.I.3.

Claim drafting:

The general wording for a use claim could read as follows:

Use of transgenic animal X for (technical) purpose Y

wherein the “technical” purpose can be any purpose. However, when the purpose is the use of an animal for breeding another animal, such a purpose is critical with regard to the exclusion provision of Art. 53(b) EPC. Of course, claims are allowable wherein a transgenic animal is used as a source for the isolation of a product of interest, e.g., the product encoded by the transgene. In this case, a use claim of the following type could be drafted:

Use of transgenic animal X for preparing compound Y.

Moreover, Art. 53(c) EPC should be kept in mind when drafting such claims so that the claim is not interpreted as an excluded method of treatment claim.

Examples of allowed use claims are shown in the following:

EP-B1 – 2207885 – Claim 8:

Use of the quadruple transgenic mouse according to any one of claims 1 to 7 as model for treatment of Alzheimer’s disease.

EP-B1 – 2207885 – Claim 9:

Use of the quadruple transgenic mouse according to any one of claims 1 to 7 as model for preventing Alzheimer’s disease.

EP-B1 – 2154250 – Claim 10:

Use of a non-human animal according to any one of claims 1 to 9 in a method of screening a compound for xenobiotic induction of CYP3A4 expresston in a cell, the method including exposing the non-human animal to a compound and measuring the induction or the potential for expression of the gene encoding the reporter molecule.

EP-B1 – 2114130 – Claim 1:

The use of a NK1–/– rodent or a rodent having a functional substance P receptor to which an antagonist of the substance P receptor has been administered as an animal model

for ADHD, wherein the rodent shows reduced locomotor activity in response to methylphenidate or d-amphetamine.

EP-B1 – 2093280 – Claim 22:

Use of a non-human model animal according to any one of claims 1 to 10 for the identification of mast cells as effector-, regulator-, or target cells in a physiological or pathological context.

EP-B1 – 2093280 – Claim 23:

Use of a non-human model animal according to any one of claims 1 to 10 for testing the influence of mast cells on exogenously administered compounds in a physiological or pathological context.

D.VII.2.d. Parts of animals

The meaning of the term “parts of animals” as used herein is provided in the introduction of this chapter (D.VII.1).

D.VII.2.d.a. Product claims for parts of animals

Generally, any part of an animal can be the subject-matter of a product claim.

Art. 53(a) EPC, excluding inventions from patentability which contravene “ordre public” or morality, should not present a severe bar to the allowability of a product claim directed to an animal organ, etc. The same principles as discussed above in connection with product claims directed to natural or transgenic animals (D.VII.2.b.a and D.VII.2.c.a) should also apply to the allowability of a product claim directed to parts of an animal, the morality aspect being less relevant as compared to claiming living animals.

In section D.VI.2.h above, relating to the patentability of parts of plants, it was mentioned that recent case law has considered that seeds of plant varieties should also be considered as “plant varieties” within the meaning of Art. 53(b) EPC, and therefore excluded from patentability. However, it seems that a corresponding view would not be justified for parts of animals. The seed of a plant is capable of independent reproduction, leading to the fully developed plant variety. A corresponding potential for independent propagation does not exist for any one part of an animal body alone, except totipotent stem cells. These aspects of stem cell technology are discussed in D-VIII. Since exclusion provisions in general are construed narrowly, Art. 53(b) EPC should not be interpreted to comprise parts of animals.

As to the further patentability requirements, i.e. novelty, inventive step and industrial application, as well as the requirements of the application, i.e. sufficiency of disclosure and clarity and support of the claims, see C.I.3.

Claim drafting:

In general, two possibilities exist for claiming parts of animals by means of a product claim: a) by a claim wherein the product is defined by its characteristics, e.g. intrinsic or extrinsic features and/or parameters which can be unambigu-

ously defined, or b) by a product-by-process claim wherein the claimed matter is characterized by the step of its preparation.

Generally, the parts of animals to be claimed will not be parts of animals as they are contained in the animal body, but naturally occurring parts of animals, such as organs, that have been treated in a specific manner to provide the part with new characteristics. For example, the treatment could render an animal organ better suited for transplantation or storage. In many cases, a product-by-process claim will be the appropriate claim type, wherein the claimed part is characterized by the essential treatment steps.

Such a claim type could have the following general wording:

Part X of an animal treated by a process comprising steps a, b, c, ...

Of course, if the claimed part of an animal which was treated in a certain manner can be fully defined by its new characteristics which were achieved by the treatment, a product claim of the following type is possible:

Part X of an animal having characteristics a, b, c, ...

wherein characteristics a, b, c, etc., are the structural features and/or parameters.

In the case of parts of a *transgenic* animal, the claimed part can usually be defined by the new genetic information contained therein. A wording for such a claim could be as follows:

Part X of an animal characterized in that it contains DNA Y.

DNA Y is the transgene introduced into an animal, which normally does not contain this DNA.

Examples of claims directed to parts of animals which have been allowed by the EPO are shown below:

EP-B1 – 0105290 – Claim 7:

Cardiac valvula obtained by utilizing the process according to any one of claims 1 to 9.

In the above claim, the product is characterized by its process of preparation. Claims 1 to 9 of the patent disclose a process for preserving a biological tissue intended to be grafted upon a human or animal subject.

EP-B1 – 0296475 – Claim 13:

A frozen, cultured, stratified epithelial sheet obtainable by the method of claims 1 to 9 which, when thawed, is useful as a skin wound dressing, exhibits conserved intercellular structure, and comprises mitotically and metabolically competent epithelial cells.

In the above claim, the product is defined by its characteristics and by its process of preparation. Claims 1 to 9 are directed to a method for preserving epithelial sheets.

EP-B1 – 0065827 – Claim 10:

A porcine heart valve suitable for implantation in a living body, characterized in that a piece of cusp tissue excised from said valve remains substantially free of calcification for at least 4 weeks when implanted in the abdominal wall muscle of a male Sprague-Dawley rat.

EP-B1 – 0116579 – Claim 1:

Natural tissue implant for carrying out an anti-wrinkle treatment, characterized in that it consists of a cartilage collagen having been taken in a fetus of a ruminant and having only undergone a maceration and malaxage treatment, the maceration comprising an immersion of the cartilage tissues in a mixture of equal volumes of 9% physiological classical serum and 90% ethanol for 25 to 35 days, the cartilage tissues having been rinsed in 9% physiological serum and malaxed in a mill to a homogeneous injectable mixture.

The above implant is characterized by its method of preparation.

EP-B1 – 2218786 – Claim 16:

A cell or an organ or tissue containing the cell derivable from the non-human mammalian animal according to any one of claims 9 to 14 or the mouse or progeny thereof according to claim 15, characterized in that it retains the mammalian artificial chromosome vector according to claims 1 to 4 and that it enables expression of human cytochrome P450 genes.

EP-B1 – 1680959 – Claim 5:

An immunocyte derived from the transgenic mouse wherein a part or a whole of TRIF-related adaptor molecule (TRAM) genes on its chromosome is homozygously deleted according to claim 1 or 2.

EP-B1 – 1340424 – Claim 14:

An organotypic brain slice culture derived from a transgenic non-human mammal or its descendants according to claims 5 to 12.

D.VII.2.d.b. Process claims for parts of animals

The exclusion of methods of treatment under Art. 53(c) EPC represents a bar to the allowability of a process claim, e.g. in the case that a part of an animal is taken from an animal body (e.g. blood), treated in a certain manner outside of the body and then returned to the same body. However, a process wherein a part of an animal (e.g. blood) is taken from the animal and then treated outside of the animal body without being returned to the donor body, but rather, to a different body, is a process allowable under Art. 53(c) EPC (EPO Guidelines, G-II, 4.2.1), provided that taking the material from the animal does not require a surgical step. Moreover, any process which is directed to the preparation of a part of an animal, for example, artificial skin, is allowable under Art. 53(c) EPC. Further discussion of this issue is provided in C.I.2.d.

The provision according to Art. 53(b) EPC, which excludes an essentially biological process for the production of *animals* from patentability, should not represent a bar to the patentability of a process for the preparation of *parts of animals*

since exclusion provisions are construed narrowly; the term “animals” in Art. 53(b) EPC cannot be interpreted to include “parts of animals”, except in the case of totipotent stem cells.

As to the further patentability requirements, i.e. novelty, inventive step and industrial application, as well as the requirements of the application, i.e. sufficiency of disclosure and clarity and support of the claims, see C.I.3.

Claim drafting:

In most cases a process claim will be directed to a certain treatment of a naturally occurring part of an animal, such as an organ, rather than to a process for preparing such an organ. Therefore, a process claim could have the following generalized wording:

A process for treating a part of an animal, comprising steps a, b, c, ...

However, in the case of an invention relating to transgenic animals, one may also imagine a claim for preparing a part of an animal of the following type:

A process for preparing a part X of an animal comprising the step of introducing foreign DNA Y into cells of said animal and regenerating part X therefrom.

In addition to the above types of process claims, further process claims are possible wherein a part of an animal is used as a source for the isolation of a product of interest.

Examples of granted process claims are shown below:

EP-B1 – 0116579 – Claim 4:

Process for producing a natural tissue implant for carrying out an anti-wrinkle treatment, characterized in that the cartilage tissues are taken in a fetus of a ruminant, mascerated for 25 to 35 days by immersion in a mixture of equal volumes of a 9% classical physiological solution and 90% ethanol, rinsed exhaustively in 9% classical physiological serum, then malaxed in a mill to a homogeneous injectable mixture and introduced into a sterile and sealed package, these different operations being carried out in an ozone atmosphere at room temperature.

The above process is conducted outside the animal body and does not comprise the introduction of the tissue to the donor animal. Therefore, it is not a method of treatment within the meaning of Art. 53(c) EPC.

EP-B1 – 0296475 – Claim 1:

A method for preserving epithelial sheets comprising the steps of:

- a) incubating the epithelial sheets at room temperature in media containing a cryopreservant for a period of time from 2 minutes to 15 minutes;
- b) freezing said epithelial sheets using a cooling rate of no more than $-2^{\circ}\text{C}/\text{min}$ through the range of temperature immediately above and immediately below 0°C .

The above claim is also directed to a method of treatment of an organ outside of the animal body without returning the organ to the same donor animal. Therefore, the claim is allowable under Art. 53(c) EPC.

EP-B1 – 0105290 – Claim 1:

Process for treating and preserving a biological tissue intended to be grafted upon a human or animal subject and the reduction or extended attenuation of calcification after the grafting operation, characterized in that it consists in putting into contact the said tissue with an effective hypophosphated isotonic solution in order to reduce calcification of the tissue, the said isotonic solution comprising at least one physiologically acceptable salt or buffer having a pH comprised between 7.0 and 7.6 and more than 0.003% by weight of a divalent cation other than calcium entering into competition with respect to the fixation sites of the calcium, and in preserving the said tissue in the said solution until its utilization.

In the above process the tissue is treated outside of the animal body and not returned to the same donor body. Therefore, the process is allowable under Art. 53(c) EPC.

EP-B1 – 0096997 – Claim 1:

A method of cooling and preserving an excised organ which comprises:

- (a) perfusing the organ with a liquid blood substitute having a freezing point of less than 2°C, the temperature of the substitute being reduced during perfusion from body temperature (37°C) to 2°C,
- (b) perfusing the organ with a liquid cryoprotective agent having a freezing point of less than -4°C, the temperature of the agent being reduced during perfusion from 2°C to -4°C,
- (c) perfusing the organ with an inert liquid having a freezing point of not higher than -60°C, the temperature of the liquid being reduced during perfusion from -4°C to from -60°C to -80°C, the lower temperature being at or above the freezing point of the liquid, and
- (d) preserving the organ at a temperature at or below that achieved in step (c) until such time as the organ is required for transplantation.

In the above method the organ is treated outside the body without being returned to the same body. Therefore, the claim is allowable under Art. 53(c) EPC.

EP-B1 – 0080518 – Claim 1:

A method of extraction of therapeutically effective hormones from the thymus glands of freshly slaughtered calves by extraction by water, characterized in that the thymus glands of calves of about 12–16 weeks old are removed under sterile precautions, the substance removed is cooled down to low temperatures of at least -30°C, after thawing is homogenized with the addition of distilled water, the homogenized liquid is set aside for a few days at about +4°C and subsequently centrifuged rapidly and filtered, that the supernatant above the sediment from the filtrate is decanted, is set aside for a few days at about +4°C and again centrifuged rapidly and filtered, and the supernatant from the second filtrate is processed into an applicable preparation.

EP-B1 – 1118268 – Claim 1:

1. Method for cryoconservation of Zebrafish sperm comprising

- (a) removing the testis from the body cavity of a male Zebrafish;
- (b) rinsing the testis isolated in step (a) with a cryoprotectant to yield a sperm suspension; and
- (c) freezing said sperm suspension,

wherein the amount of cryoprotectant used in step (b) is such that the volume of the resulting sperm suspension is less than 30 µl.

In the above method the organ “thymus glands” is used as the starting material for isolating a product of interest. This type of claim is not affected by Art. 53(c) EPC.

D.VII.2.d.c. Use claims/purpose-limited product claims for parts of animals

As discussed in D.VI.2.e.c, use claims are interpreted as process claims. Therefore, the exclusion of methods of treatment under Art. 53(c) EPC, as well as the exclusion of essentially biological processes for preparing animals under Art. 53(b) EPC, present a bar to the allowability of a use claim. For example, a claim of the following type:

Use of part X of an animal for treating disease Y

is not allowable under Art. 53(c) EPC.

Moreover, with regard to Art. 53(b) EPC, a claim of the following type:

Use of part X of an animal for preparing animal Y

might not be allowable. This claim could be interpreted as a claim directed to an essentially biological process for preparing animals.

However, a claim to a technical application of a part of an animal should not be objectionable under Art. 53(c) EPC or under Art. 53(b) EPC. The allowability of so-called “second medical use claims” under Art. 53(c) EPC is discussed in C.I.3.e.d.

As to the further patentability requirements, i.e. novelty, inventive step and industrial application, as well as the requirements of the application, i.e. sufficiency of disclosure and clarity and support of the claims, see C.I.3.

Claim drafting:

The wording of a use claim could be as follows:

Use of part X of an animal Y for (technical) purpose Y.

The “technical” purpose Y could be, for example, the isolation of a product from the animal part, the testing of the activity of products, or the preparation of a medicament.

Examples of use claims directed to parts of animals which were allowed by the EPO are shown below:

EP-B1 – 0357958 – Claim 1:

The use of a mammalian liver composition for the manufacture of a medicament for the treatment of mammals suffering from any non-dermatological viral infection other than a hepatitis virus infection such as infection caused by a retrovirus, by HIV-1 virus, by Epstein-Barr virus or suffering from chronic fatigue syndrome comprising as active

principle a mammalian liver extract, which is heat stable, insoluble in acetone and soluble in water.

The above claim is a second medical use claim in traditional “Swiss-type” format.

EP-B1 – 0200214 – Claim 1:

Use of a calf thymus extract, which extract shows, upon electrophoresis on polyacrylamide gel at pH 8.6, two main characteristic bands with an Rf of about 0.25 and about 0.44 compared with bromophenol blue used as a tracer for the preparation of a pharmaceutical composition for the treatment of a parasitic infection in a mammal.

The above claim is also a second medical use claim in “Swiss-type” format.

EP-B1 – 1716752 – Claim 4:

The use of a macrophage or splenocyte cell derived from a non-human animal as defined in any of claims 1 to 3 as a model cell unresponsive to bacterial cell wall components.

EP-B1 – 1932544 – Claim 1:

A modified mammalian chondrocyte for use in an *in vivo* method of treating a cartilage defect, wherein the chondrocyte has been modified *in vitro* by the introduction of a heterologous polynucleotide encoding a heterologous polypeptide, operably linked to a promoter, and wherein said modified chondrocyte produces said polypeptide when introduced into a joint of a mammal.

The above claim is a medical use claim in purpose-limited product format as allowed under Art. 54(5) EPC.

D.VII.2.e. Summary

In summary, a claim to an animal will avoid exclusion from patentability under Art. 53(a) EPC as long as it is not contrary to “ordre public”. EPO case law has developed several tests for determining whether this is the case.

A claim to an animal will avoid exclusion from patentability under Art. 53(b) EPC as long as the claim is not directed to individual animal varieties. This holds even if the claim embraces animal varieties in a broader-claimed genus. A claim directed to one or more individual animal varieties will be excluded from patentability under Art. 53(b) EPC, regardless of the type of animal claimed (e.g. natural or transgenic).

A natural animal is likely to be seen as a “discovery”, which is not considered an invention available for patent protection under Art. 52(2)(a) EPC, or as an “animal variety”, which is excluded under Art. 53(b) EPC.

Claims directed to animal parts such as organs or tissue cultures should not be excluded from patentability unless such parts may be considered an “animal variety”. This should not normally be the case.

Claims to processes for the production or use of animals avoid exclusion from patentability as long as they are not “essentially biological” in the sense of Art. 53(b) EPC. The EPO Guidelines suggest that the criteria developed for evaluating this question in respect of plants should also be applied for animals. Following this, a process is “essentially biological” in character, and therefore excluded from patentability if it contains or consists of sexually crossing the whole animal genomes and subsequently selecting progeny animals. But if the method includes a step of a technical nature which introduces or modifies a genomic trait of the animal produced, so that the animal product is not the result of merely mixing the genes of animals chosen for sexual crossing, then the process is not “essentially biological” and is not excluded from patentability under Art. 53(b) EPC.

The fact that an animal is not excluded from patentability as an “animal variety” or as contrary to “ordre public”, or that a process for producing an animal is not excluded from patentability as “essentially biological” in character does not mean that the claim reciting the animal or process is necessarily allowable. As for any other invention, subject-matter not excluded from patentability must still satisfy the normal patentability requirements in order to be allowed.

D.VIII. Human Body

D.VIII.1. Introduction

This chapter discusses the possibilities for protecting the human body and parts thereof, considering the present common practice of the EPO and also referring to important case law.

As used herein:

The term “human body” means the living human body, if not otherwise described.

The term “parts of the human body” includes human organs, such as liver, heart, skin, blood, etc. and propagating materials, such as germ cells and human tissue. Other components of the human body, such as cells, genes, proteins, etc. are discussed separately in D.II., D.III. and D.IV.

D.VIII.2. Protecting the human body under the EPC

The relevant European case law in connection with the human body focuses on the exclusion provisions of the EPC, in particular on Art. 52(4) 1973 (now Art. 53(c)) and Art. 53(a) EPC. For this reason the exclusion provisions are a major aspect of the following sub-chapters.

It is to be noted that Art. 53(b) EPC is not relevant for inventions relating to the human body, since it is directed to plant and animal varieties and not human

beings. Most importantly, accordingly to Rule 29(2) EPC, an isolated part of the human body constitutes patentable matter, even if the part in question is identical in its composition to the naturally occurring part, see also the Guidelines G-II, 5.2.

D.VIII.2.a. Human body

The meaning of the term “human body” as used herein is provided in the introduction of this chapter (D.VIII.1).

D.VIII.2.a.a. Product claims for the human body

The main bar to obtaining patent protection for a human body is represented by Art. 53(a) EPC which, in particular, excludes inventions from patentability which would be contrary to morality. Although to date exists no case law which clearly states that the patenting of the human body contravenes Art. 53(a) EPC, the common understanding is that patents directed to the living human body shall not be allowed. The cloning of human beings is one of the explicit exceptions to patentability under R 28(a) EPC.

Similarly, claims directed to human embryos should not be allowable under Art. 53(a) EPC and Rule 29(1) EPC (see Guidelines G-II, 5.3).

Art. 53(b) EPC is not an obstacle to the allowability of a product claim directed to the human body since it only excludes from patentability inventions which relate to plants and animals. It can hardly be argued that the exclusion of certain animal inventions from patentability extends to inventions relating to the *human* body because the EPC clearly distinguishes between the animal and human body in Art. 53(c) EPC, wherein methods of treatment of the *human* or *animal* body are separately mentioned.

Since product claims to the human body as such are not patentable, it is not necessary to discuss the further patentability requirements such as novelty and inventive step, or any possible claim wording for product claims directed to the human body.

D.VIII.2.a.b. Process claims for the human body

Concerning process claims in an application directed to the human body, Art. 53(a) and (c) EPC must be considered. According to Art. 53(a), Rule 28 (a) and Rule 28 (c) EPC, processes for the cloning of human beings and processes for modifying the germline genetic identity of human beings are exempted from patent protection. Art. 53(c) EPC excludes from patent protection methods of treatment of the human body by surgery or therapy or diagnostic methods practiced on the human body. Therefore, such method of treatment claims are not allowable, as discussed in C.I.2.d.

Art. 53(c) EPC may also constitute a bar to the allowability of claims directed to a “somatic gene therapy” process, wherein cells of the human body are ge-

netically engineered outside the human body – e.g. by replacing a non-functional gene by a functional gene – and then returned to the donor body. Although the decisive technical step in such a method, namely the genetic engineering of the cell, is performed outside the human body, the process as a whole will probably be regarded as an excluded method of treatment of the human body in the sense of Art. 53(c) EPC. The Guidelines mention a similar process as falling under Art. 53(c) EPC, namely a process wherein an endoprosthesis is produced outside the body but requires that a further surgical step is included. Also, a process of blood analysis is excluded from patent protection when the treated blood is returned to the donor (Guidelines, G-II, 4.2). Further discussion of the exclusion of methods of treatment of the human body from patentability is provided in C.I.2.d.

Moreover, Art. 53(a) EPC can present a bar to the allowability of a process claim directed to the preparation of a human body, since such a process may be considered a human breeding process. Additionally, this provision will be of particular importance for inventions concerning so-called “germline gene therapy”, which comprises the genetic engineering of germ cells in order to cure hereditary diseases. Such processes are not allowable under Art. 53(a) EPC, Rule 28(b) EPC.

Concerning process claims wherein the human body is used as a “factory” for preparing a product of interest – e.g. for preparing human antibodies, or as the source for the isolation of products of interest, e.g. proteins having valuable pharmaceutical activities – the question of morality has not yet been addressed by an Appeal Board.

If a process claim does not fall within the above exclusion provisions, it must fulfill the further requirements for patentability, namely the invention must be novel (Art. 54 EPC), it must involve an inventive step (Art. 56 EPC) and it must be susceptible to industrial application (Art. 57 EPC).

Since the case law in connection with the allowability of process claims directed to the preparation of products from the human body mainly relates to body components such as cells, proteins, etc. this case law is discussed in the separate chapters D.II., D.III., D.IV. and D.V.

In addition to the above patentability requirements, the requirements of the application must also be fulfilled. In particular, the application must disclose the invention in such a manner as to enable the skilled person to carry out the invention (Art. 83 EPC), and the claims must be sufficiently clear for the skilled person and must be supported by the description (Art. 84 EPC). General discussion of these requirements of the application is provided in C.I.3.b., C.I.3.e.b. and C.I.3.e.c.

Claim drafting:

As is evident from the above comments, a process claim for preparing a human being will not overcome the bar presented by the exclusion of inventions

contravening morality according to Art. 53(a) EPC and Rule 28(a) EPC. Therefore, a process of the type:

Process for preparing human beings comprising the following steps a, b, c, ...

will not be allowable. Similarly, a process for changing the genetic identity of humans will be exempted by Rule 28(b) EPC.

Moreover, a claim directed to a diagnostic, therapeutic or surgical method practiced on the human body will not be allowable under Art. 53(c) EPC. However, process claims which involve the treatment of the human body and which are not surgical, therapeutic or diagnostic in nature, are allowable under Art. 53(c) EPC. This means that, for example, cosmetic methods are not excluded. Further examples of allowable and non-allowable matters can be found in the Guidelines under G-II,4.2. Therefore, a process claim which is allowable under Art. 53(c) EPC could have the following wording:

A cosmetic method comprising steps a, b, c, ...

wherein “cosmetic” means that the claimed method does not serve a therapeutic purpose.

Regarding the distinguishing features between cosmetic methods and therapeutic methods, further discussion is provided in C.I.2.d.

In addition to the above claim directed to a cosmetic method, a claim directed to a process in which the human body is used as a source for the isolation of a product of interest, is allowable under Art. 53(c) EPC, as well as under Art. 53(a) EPC, although according to the Guidelines, using the human body as a “test animal” for screening purposes will conflict with Art. 53(a) EPC (see Guidelines, G-II, 4.2.2). Such a process claim could have the following wording:

A process for preparing product X comprising treating the human body by steps a, b, c, ...

It must be clear from the application that the above process does not comprise a therapeutic method. Optionally, a therapeutic process must be disclaimed.

An example of an allowed process claim is shown in the following:

EP-B1 – 0187858 – Claim 16:

A method of preparing antibodies to CS antigen of *P. falciparum* sporozoites, said method comprising the immunization of a host using the peptide of any of Claims 1 to 4, said host being used only as a source for obtaining the antibodies.

In this method, the underlined phrase clarifies that a therapeutic treatment is not intended.

D.VIII.2.a.c. Use claims/purpose-limited product claims for the human body

When drafting use claims, one should consider that a use claim is generally interpreted as a process claim, as outlined in C.I.3.e.a. Therefore, the above

problems regarding the exclusion of certain processes from patentability under Art. 53(a) EPC and 53(c) EPC should also be considered in connection with use claims.

A conceivable use claim could be directed to the use of the human body for obtaining a product of interest.

As to the further patentability requirements, i.e. novelty, inventive step and industrial application, as well as the requirements of the application, i.e. sufficiency of disclosure and clarity and support of the claims, see C.I.3. and D.VIII.2.a.

Claim drafting:

In principle, a use claim could have the following general wording:

Use of the human body for the preparation of product X.

D.VIII.2.b. Parts of the human body

The meaning of the term “parts of the human body” as used herein is provided in the introduction of this chapter D.VIII.1.

D.VIII.2.b.a. Product claims for parts of the human body

In principle, any part of the human body can be made the subject-matter of a product claim.

Whether Art. 53(a) EPC, which excludes inventions contravening morality or “ordre public” from patentability, represents a bar to the allowability of a product claim directed to a part of a human body, such as an organ or tissue, has so far not been decided by the EPO. According to legal literature, patents for human organs and transplants should not be granted. In particular, major concerns exist regarding the patenting of human germ cells. This will be discussed separately in D.VIII.2.b.d.

As to the further patentability requirements, i.e. novelty, inventive step and industrial application, as well as the requirements of the application, i.e. sufficiency of disclosure and clarity and support of the claims, see C.I.3 and D.VIII.2.a.e.

Claim drafting:

In general, two possibilities exist to claim parts of the human body by a product claim: a claim defining the product by its characteristics, e.g. its intrinsic or extrinsic features and/or parameters which can be unambiguously defined, or a product-by-process claim characterizing the product by the steps of its preparation.

Generally, the parts of the human body to be claimed will not be parts of the human being as contained in the body, but naturally occurring parts of the body, such as tissue, that have been treated in a specific manner to provide such parts with new characteristics. For example, the treatment could render the part bet-

ter suited for transplantation or storage. In many cases a product-by-process claim will be the appropriate claim type wherein the claimed part of the body is characterized by the essential treatment steps. Such a claim type could have the following general wording:

Part X of the human body obtained by a process comprising steps a, b, c, ...

If the claimed part of the human body, which was treated in a certain manner, can be fully defined by its new characteristics which were achieved by the treatment, a product claim of the following type is possible:

Part X of the human body having characteristics a, b, c, ...

wherein characteristics a, b, c, etc., are the structural features and/or parameters.

Examples of claims directed to parts of the human body – underlined in the claims below – which have been allowed by the EPO are shown in the following:

EP-B1 – 0108588 – Claim 1:

A storage-stable substantially plasma-free platelet concentrate comprising blood platelets in a balanced salt solution for use for administration to a human or an animal.

In claim 9, the platelets are defined as human platelets. The concentrate is characterized in that it is storage stable. The process for rendering the concentrate storage stable is defined in claims 10 to 16.

EP-B1 – 0020753 – Claim 6:

A skin-equivalent characterized by a contracted hydrated collagen lattice containing fibroblast cells therein, and keratinocyte cells supported upon said contracted hydrogen collagen lattice.

According to Example 9 of the specification, the fibroblasts can be human foreskin fibroblasts, which were obtained in a biopsy.

EP-B1 – 0105290 – Claim 11:

Cardiac valve obtained by utilizing the process according to any one of claims 1 to 9.

Claims 1 to 9 of the patent describe the process for treating and preserving the biological tissue intended to be grafted on a human or animal subject.

EP – B1 – 1305410 – Claim 1:

A human pancreatic cell line produced by electrofusion of normal human islet cells with cells from at least one immortal human cell line wherein the human pancreatic cell-line is capable of secreting insulin.

EP-B1 – 0795008 – Claim 1:

A human hypertrophic chondrocyte cell-line.

D.VIII.2.b.b. Process claims for parts of the human body

The exclusion of methods of treatment under Art. 53(c) EPC presents a bar to the allowability of a process claim reciting that a part of the human body (e.g. blood) is taken from the human body, treated in a certain manner outside of the body, and then returned to the same donor body such as e.g. a dialysis process (see Guidelines G-II, 4.2). However, a part of the human body (e.g. blood) which is taken from the human body and then treated outside of the human body and e.g. stored in a blood bank is an allowable process under Art. 53(c) EPC (Guidelines G-II, 4.2.1).

Moreover, claims in which a part of the human body, e.g. an organ, is used as a starting material for the isolation of a product of interest are allowable under Art. 53(c) EPC.

Whether or not such a process contravenes Art. 53(a) EPC has so far not been decided by an Appeal Board.

As to the further patentability requirements, i.e. novelty, inventive step and industrial application, as well as the requirements of the application, i.e. sufficiency of disclosure and clarity and support of the claims, see C.I.3. and D.VIII.2.a.a.

Claim drafting:

In most cases, a process claim will be directed to a certain treatment of a naturally occurring part of the human body, such as an organ or tissue, rather than to a process for preparing such an organ. Such a claim could have the following generalized wording:

A process for treating a part of the human body comprising steps a, b, c, ...

In addition to the above type of claim, one may imagine further process claims in which the part of the human body is used as a source for the isolation of a product of interest. Such a claim may read:

A process of isolating X from human body part Z comprising steps a, b, c.

Prepared parts of the human body are underlined in the following examples of granted process claims:

EP-B1 – 0020753 – Claim 1:

A method of producing living tissue characterized by:

- a) forming a hydrated collagen lattice;
- b) bringing fibroblast cells into contact with the said collagen lattice; and
- c) maintaining said lattice and said cells under conditions sufficient for said cells to attach to said collagen lattice and to contract said collagen lattice thereby forming living tissue.

EP-B1 – 0108588 – Claim 10:

A method for making a storage stable blood platelet concentrate according to claim 1 comprising centrifuging plasma containing platelets to obtain a platelet pellet and re-

suspending the pellet characterized in that substantially all the supernatant plasma is removed from the platelet pellet and the pellet is then resuspended in a balanced salt solution which is substantially free of plasma.

In claim 11 of the above patent the plasma was defined as human plasma derived from freshly collected whole blood or by apheresis.

EP-B1 – 0341245 – Claim 1:

A method of cryopreserving a heart valve comprising the steps of:

- a. dissecting a heart valve from a heart;
 - b. placing the dissected heart valve into an isotonic medium with antibiotics and a cryopreservative;
 - c. freezing the heart valve according to a freezing schedule that will maintain acceptable levels of cell viability;
 - d. storing the heart valve at a temperature below -132°C ;
- characterized by the freezing schedule comprising:
- (1) placing the dissected heart valve in a freezing chamber;
 - (2) lowering the temperature of said freezing chamber at a rate of approximately $0.01^{\circ}\text{C}/\text{minute}$ to a sample temperature of approximately $+4^{\circ}\text{C}$;
 - (3) lowering the temperature of said freezing chamber at a rate of approximately $1.5^{\circ}\text{C}/\text{minute}$ to a sample temperature of approximately -3°C ;
 - (4) lowering the temperature of said freezing chamber at a rate of approximately $95^{\circ}\text{C}/\text{minute}$ to a chamber temperature of approximately -140°C ;
 - (5) holding the temperature of said freezing chamber at approximately -140°C for approximately 1 minute;
 - (6) raising the temperature of said freezing chamber to approximately -100°C at a rate of approximately $20^{\circ}\text{C}/\text{minute}$;
 - (7) holding the temperature of said freezing chamber at approximately -100°C for approximately 6 minutes;
 - (8) raising the temperature of said freezing chamber to approximately -70°C at a rate of approximately $10^{\circ}\text{C}/\text{minute}$;
 - (9) raising the temperature of said freezing chamber to approximately -26°C at a rate of approximately $20^{\circ}\text{C}/\text{minute}$;
 - (10) holding the temperature of said freezing chamber at approximately -26°C for approximately 2 minutes;
 - (11) lowering the temperature of said freezing chamber at a rate of $1^{\circ}\text{C}/\text{minute}$ until the temperature of the freezing chamber is approximately -80°C .

EP-B1 – 0033402 – Claim 18:

A process for preserving an organ to be transplanted comprising perfusing the organ with a perfusion liquid containing a saturated perfluorocarbon compound under oxygenation, the perfusion liquid being a mixture of albumin, a Ringer's solution and a stable emulsion of a perfluorocarbon compound, and the concentration of albumin being 1 to 8% (weight/volume) and that of the perfluorocarbon compound being 7.5 to 12.5% (weight/volume) based on the perfusion liquid, which process is characterized in that the Ringer's solution is modified in the amount of potassium ion by increasing the amount to 8 to 20meq/ltr.

EP-B1 – 0105290 – Claim 1:

Process for treating and preserving a biological tissue intended to be grafted upon a human or animal subject and the reduction or extended attenuation of calcification after the grafting operation, characterized in that it consists in putting into contact the said

tissue with an effective hypophosphated isotonic solution in order to reduce calcification of the tissue, the said isotonic solution comprising at least one physiological acceptable salt or buffer having a pH comprised between 7.0 and 7.6 and more than 0.003% by weight of a divalent cation other than calcium entering into competition with respect to the fixation sites of the calcium, and in preserving the said tissue in said solution until its utilization.

D.VIII.2.b.c. Use claims/purpose-limited product claims for parts of the human body

As outlined in C.I.3.e.a, use claims are generally interpreted as process claims, except for the so called purpose-limited product claims in the field of medical applications. Therefore, the exclusion of methods of treatment under Art. 53(c) EPC presents a bar to the allowability of a use claim. For example, a claim of the following type:

Use of part X of the human body for treating disease Y

is not allowable under Art. 53(c) EPC, but in the form of “Part X for use in treating disease Y” should be admissible under Art. 53(c) EPC.

Also, a use claim in which the part of a human body is used for a technical purpose, for example, for the isolation of a product of interest, is not prohibited by Art. 53(c) EPC.

So far, the question of whether the use of a part of a human body, like an organ, for a technical purpose contravenes Art. 53(a) EPC, has not been decided by an Appeal Board.

As to the further patentability requirements, i.e. novelty, inventive step and industrial application, as well as the requirements of the application, i.e. sufficiency of disclosure and clarity and support of the claims, see C.I.3 and D.VIII.2.a.e.

Claim drafting:

The wording for a use claim could be as follows:

Use of part X of the human body for (technical) purpose Y.

The “technical” purpose Y could for example be the isolation of a product from the part of the body.

D.VIII.2.b.d. Human stem cells

D.VIII.2.b.d.a. Introduction

Human stem cells harbor a vast, largely untapped potential for the future development of new avenues of disease treatment. Estimated value is in the billion dollar range. Due to this potential, stem cells are being accorded their own separate chapter under human body-based inventions. Although not too many cases have been filed, the field has nevertheless been under intense scrutiny in view of

morality considerations. These have resulted in an Enlarged Board of Appeal decision in the EPO, **G 2/06 (Use of embryos/WARF)** and the decision by the CJEU in the so-called **Brüstle Case (CJEU case C 34/10)**. Although the considerations underlying these two cases were slightly different, each case required a decision whether and under which circumstances the use of human embryos for providing stem cells would be a bar to the patenting of stem cells and stem cell-derived inventions. Although the CJEU decision is not binding for the EPO, EPO Examiners may nevertheless use it as a further reference for their own decisions on stem cell inventions. Of particular relevance for the patentability of human stem cell inventions are Art. 53(a) EPC and Rules 28(a) and (c), and 29(1) and (2) EPC. Moreover, the Guidelines contain further information on the EPO's practice when examining the compliance of stem cell inventions with Article 53(a) and Rule 28(c) EPC (G-II,5.3). According to the Guidelines, Rule 28(c) EPC poses a problem for allowing a product claim directed to human stem cells if at the filing date of the application, the stem cells could only be obtained by a method necessarily involving the destruction of human embryos. This means it is advisable when drafting stem cell applications to indicate in the patent specification alternative means for obtaining the stem cells such as the publication by Chung Y et al. (2008) *Cell Stem Cell*, pages 113–117.

This publication by Chung et al. is important for patent applications relating to methods and products using human embryonic stem cell lines. A further article Yamanaka et al. (2007) *Cell*, volume 135, pages 861–872 is important for patent applications claiming methods and products that encompass human induced pluripotent stem cells. Applications filed after the above mentioned dates might experience fewer problems during examination under Rule 28(c) EPC, which certainly constitutes a bar to the patenting of an invention if it makes use of a human embryo in particular if it requires its destruction to obtain the stem cells. Very recent case law still also takes a restrictive position on patenting inventions relating to human embryonic stem cells.

In a recent case, **T 2221/10 (Culturing stem cells/TECHNION)**, an Appeal Board stated, by way of *obiter dictum*, that inventions which make use of human embryonic stem cell lines without a *de novo* destruction of embryos, but which were initially derived by destroying human embryos, are excluded from patentability under Art. 53(a) and Rule 28(c) EPC.

In a further case, **T 1836/10 (Obtaining embryonic stem cells/WÜRFEL)**, an Appeal Board decided that an invention may contravene Art. 53(a) and Rule 28(c) EPC whenever a human embryo is used as a starting material in a process for preparing embryonic stem cells, even if the embryo is not destroyed in the course of such process. Rule 28(c) EPC broadly excludes any use of human embryos for industrial or commercial purposes, so a process which makes direct use of embryos as a starting material and which has commercial applicability is to be interpreted as the use of embryos “for industrial or commercial purposes” which violates Rule 28(c) EPC, and is therefore excluded from patentability.

Legal flux still exists, as can be seen from a recent referral to the CJEU **C 364/13** asking whether “embryos” produced by parthenogenesis (parthenotes) would also be regarded as an “embryo” according to Rule 28(c) EPC. The Advocate General has now issued his opinion on this referral. He recommends to the CJEU that parthenotes should not be regarded as embryos in the sense of Rule 28(c) EPC since parthenotes are not able to develop into a human being.

The following discusses which type of stem cells and methods of using them might face problems under any of the existing exclusion provisions and the currently established practice.

D.VIII.2.b.d.b. Totipotent human stem cells

Totipotent human stem cells are capable of developing into the complete human body. They cannot be patented because they violate Rule 29(1) EPC, and because they are not in line with the practice established in either **G 2/06** or **C 34/10** of the CJEU.

Method and use claims will face problems under Rule 28(a) and (c) EPC in that a process using totipotent stem cells would be regarded as a process for cloning human beings and also as the use of human embryos (i.e. the totipotent cells) for industrial or commercial purposes.

D.VIII.2.b.d.c. Pluripotent human stem cells

Here, one may distinguish between pluripotent human embryonic stem cells derived from an embryo and pluripotent stem cells obtained by inducing human differentiated cells to become pluripotent stem cells (so called iPSC). In the former case (pluripotent embryonic stem cells), patentability could be a problem under Rule 28(c) EPC in view of **G 2/06** and the very recent decision **T 1836/10**, discussed above, according to which any invention which makes use of a human embryo might encounter problems under Rule 28(c) EPC. In the case of iPSCs, this technology became available upon publication of the Yamanaka work in the journal *Cell* on November 30, 2007, and a patent filed after that date and relating to induced pluripotent cells should no longer face a problem under Rule 28(c) EPC. Similarly, processes and uses of such cells should in principle be allowable under Rule 28 EPC.

D.VIII.2.b.d.d. Cells obtained by a somatic cellular nuclear transfer (SCNT) cells

Establishing such cells in order to have a source for stem cells would involve the production of cells resembling a fertilized oocyte, which could be regarded as an embryo in line with both **G 2/06** of the EPO and **C 34/10** of the CJEU. Therefore, obtaining stem cells by way of somatic nuclear cell transfer could also face problems under Rule 28(a) and (b) EPC and in view of **T 1836/10** under

Rule 28(c) EPC. Consequently, methods and uses directed to such cells also would not be allowable under these rules.

D.VIII.2.b.d.e. Stem cells obtained by parthenogenesis

From reading the decision **C 34/10** of the CJEU, one might conclude that parthenogenesis also leads to a developmental stage that could be regarded as an embryo and, thus possibly facing problems under Rule 28 EPC. However, a recent referral to the CJEU (**C 364/13**) addresses whether production of an embryo by parthenogenesis would lead to an “embryo” in the sense of **C 34/10**. At present, it therefore remains open as to whether such a route could be an option for Applicants to obtain stem cells without conflicting with the provisions of Rule 28 EPC. There is hope that parthenotes could be a source of stem cells. This would allow patents to such cells or processes for obtaining them in view of the Advocate General’s favorable opinion regarding these (discussed above).

D.VIII.2.b.d.f. Adult stem cells

Adult stem cells will most likely not be regarded as embryos in the sense of Rule 28 EPC and therefore would not face any problems under Rule 28 EPC. Consequently, the same should apply to processes and uses based on adult stem cells.

D.VIII.2.b.d.g. Examples of allowed claims in the field of human stem cells

The type of cell and/or the form in which the cell is claimed is marked by underlining in the claims below. As one may take from the claims below, several options are available to avoid a claim reading on cells derived from human embryos, which claims could be problematic under Rule 28(c) EPC.

EP-B1 – 2139989 – Claim 1:

An isolated homogeneous population of cells comprising more than 95% of human ectodermal progenitor cells having a detectable expression of K8 and K18, as determined by RT-PCR, and being sustainable in a proliferative state for at least 15 passages.

EP-B1 – 2137300 – Claim 1:

An isolated pluripotent or multipotent stem cell derived from the mucosa of the gastrointestinal tract.

EP-B1 – 2078073 – Claim 1:

An isolated or purified human kidney-derived cell population, said cell population capable of self-renewal and expansion in culture, wherein the cell population is positive for expression of cell surface markers HLA I and CD44 and at least one of Oct-4, Red-1, Pax-2, Cadherin-11, FoxD1, WT1, Eyal, HNF3B, CXC-R4, Sox-17, EpoR, BMP2, BMP7, or GDF5 and negative for the expression of cell surface markers CD133, E-cadherin, and Wnt-4 and at least one of Sox2, FGF4, hTert, SIX2 or GATA-4.

EP-B1 – 2019861 – Claim 1:

Kidney stem cells **characterized in that** they coexpress CD133 and CD24.

EP-B1 – 1896571 – Claim 1:

An isolated multipotent cell population produced by:

- (a) providing adult pancreatic duct tissue comprising whole ducts;
- (b) mincing said duct tissue;
- (c) culturing said minced tissue; and
- (d) harvesting an emergent cell population monolayer from the culture of step (c)

EP-B1 – 1711597 – Claim 1:

An isolated cell population consisting of cells derived from liver tissue of a human which are

- (a) CD117+, CD34+, CD45- and Lin-;
- (b) capable of proliferating in a culture; and
- (c) capable of differentiating in vivo into a hepatocyte, a cholangiocyte and a sinusoidal cell.

EP-B1 – 1619244 – Claim 1:

Size-sieved stem cells derived from human bone marrow that have been treated with

- (a) a neurotrophic factor comprising glial cell linederived neurotrophic factor (GDNF) or
- (b) a neurotrophic factor comprising pituitary adenylate cyclase-activating polypeptide (PACAP) for use in the treatment of neurological diseases.

EP-B1 – 1979470 – Claim 1:

A method of retarding differentiation of a biological cell other than a human embryonic stem cell, the method comprising culturing the cell in the presence of an inhibitor of E-cadherin activity, and expanding a population of the biological cells in vitro, while retarding differentiation of the proliferating cultured cells.

EP-B1 – 1698639 – Claim 1:

An in vitro method of maintaining a pluripotent cell population other than a cell population derived from a human embryo comprising administering to that population a factor which acts intracellularly and maintains or confers pluripotency on a cell in the absence of gp130 activation, whereas the factor has at least 50% sequence identity to the polypeptide of SEQ ID NO: 2.

EP-B1 – 0701608 – Claim 1:

A method for making a chimeric ungulate comprising:

- (a) introducing an ungulate embryonic stem cell that has a first genetic complement into a recipient embryo of the same species as the embryonic stem cell, said recipient having a second genetic complement, to form a chimeric ungulate embryo; and
- (b) placing the chimeric ungulate embryo in an environment suitable for the completion of development to form a chimeric ungulate.

EP-B1 – 1435787 – Claim 1:

A method to isolate hair follicle stem cells, which method comprises:

isolating nestin-expressing cells from the bulge area of the hair follicle right below the sebaceous gland during the telogen or early anagen phase, wherein the isolation is based on the expression of the marker nestin.

D.VIII.2.c Summary

The table below summarizes the patentability of human body-derived material under the EPC.

Patentability of human body-derived material under the EPC

Human body derived material	Allowability of product, process and use claim and relevant provision
– Human body as such	
Product	(–) Art. 53(a) EPC
Process	(+) if not contravening Art. 53(a) and Art. 53(c) EPC
Use	(+) if not contravening Art. 53(a) and Art. 53(c) EPC
– Parts of the human body	
a) parts, e.g. organs, tissue culture, etc.	
Product	(+) if not contravening Art. 53(a) EPC
Process	(+) if not contravening Art. 53(a) and Art. 53(c) EPC
Use	(+) if not contravening Art. 53(a) and Art. 53(c) EPC
b) stem cells/human embryos	
b1) embryonic stem cells	(?) Rule 28(c) EPC; very critical in view of T 2221/10 and T 1836/104 , depending on filing date
b2) iPSCs	(+)
b3) adult stem cells	(+)
c) human genes, proteins, etc.*	
Product	(+)
Process	(+)
Use	(+)

Explanation of the symbols:

(–): non-allowable

(+): allowable

(?): very difficult in view of established case law

*: details in chapter D.II and D.III

E. Patent Infringement

E.I. Introduction

As regards patent litigation, the EU still lacks uniformity. This is true not only for patents granted by the national Patent and Trademark Offices of the EU member states, but also with respect to European patents: Despite the fact that European patent applications are examined centrally at the EPO in Munich and The Hague, and even though a European patent takes effect in (potentially) all EPC countries, the owner of a European patent must enforce it in the various member states separately; so far, there exists no single or unified action that would cover all EU or EPC Countries. To some extent, this will change with the introduction of the Unitary Patent and the Unified Patent Court, which will likely enter into effect in 2016.

For the time being, however, and until the new “Unitary System” has entered into effect, one must still contemplate traditional enforcement on a country-by-country basis. After all, even after introduction of the Unitary Patent, litigation based on national patents and “opted-out” European patents (more on these below) will still be handled as before. For this reason we begin with an overview of patent litigation in the European market as has been practiced for decades, before turning to the new Unitary System.

E.I.1. Pre-Suit Considerations

With the exception of the UK, all countries of the EU have a civil law system. The UK has a common law system. Patent infringement suits in the various EU countries are fundamentally different in structure from those in the US. The following highlights various issues relevant for the practitioner.

First, a Plaintiff/Patentee will try to enforce its patent in the venue it deems most favourable to its case.

In most cases a Plaintiff/Patentee may choose a venue within the EU rather freely, assuming that the attacked product is distributed EU-wide. According to applicable EU law, a company may be sued not only in the country where it is domiciled, but also where it manufactures, distributes or advertises infringing products. In most cases, however, a Plaintiff/Patentee will try to stop the infringing Defendant effectively, which is usually by suing where the Defendant is manufacturing. If the lawsuit is successful and the Plaintiff/Patentee obtains injunctive relief, manufacturing – and subsequent sale – can be enjoined most effectively.

In some cases, however, a Plaintiff/Patentee is confronted with an Infringer manufacturing in an EU country where either no patent protection exists or

where, for other reasons, it does not want to lodge a complaint. Moreover, there are cases in which the Defendant is domiciled and manufactures in a non-EU country but sells in several or even all EU countries. In such cases, the Plaintiff/Patentee must make a choice, because it certainly does not want to sue the Defendant in all 28 EU member states. In most cases, only one infringement case is initiated. It is only in rare cases that parallel infringement suits are lodged in various EU countries.

Financial considerations play an important role when choosing the court and, thus, the country in which to enforce the patent. Among them is certainly the expectation of prevailing in the suit.

A review of cases handled each year by the various infringement courts within the EU reveals that the majority of patent infringement cases are heard in only a few countries. In 2011 about 2000 new patent infringement cases were filed in the EU, the breakdown of which, per country, was as follows¹:

Member States	Cases in 2011
Germany	1250
France	280
Italy	260
Great Britain	53
The Netherlands	50
remaining countries	< 10

This is not to say that courts in other countries than those above have no experience or reputation, but handling a large number of patent infringement cases speaks for itself in a way. A Patentee who can freely choose will file the infringement case in the country that is regarded to be the best choice – and which is known to have high Patentee win rates. An analysis done for the District Court Düsseldorf (with 475 new cases in 2011 by far the most frequented court in the whole EU), reveals a Patentee win rate for 2006–2009 of about 63%, as compared to only 23% in the Netherlands². If a jurisdiction is seen as patent-friendly, it attracts Patentees to bring their case there.

Costs also affect the choice of venue. As compared to the US, patent enforcement in the various EU countries tends to be very cost-efficient. Costs will vary depending on the complexity of the technology, the number of patents involved, the number of witnesses and experts and the duration of the trial. In most cases, costs (for the most part fees for a party's attorney and patent attorney) will range from EUR 40,000 (for less complex cases) to EUR 200,000 (for more complex

¹ Source: Kühnen/Claessen, GRUR 2013, 592, 593.

² Source: Elmer/Lewis, in: Managing Intellectual Property, September 2010, p. 5, 6.

cases). Leaving minor differences aside, this cost range is probably realistic for all EU countries. The only exception is the UK, where costs are rather in the range of EUR 150,000³ up to EUR 1.5 million.

A further factor influencing the choice of venue is the expected duration of the proceedings. Litigation proceedings in Europe tend to be rather speedy. This also explains why costs are rather low. There are a number of reasons for this, most importantly the absence of time-consuming discovery or separate “Mark-man hearings”. Moreover, proceedings in Europe tend to be in writing; with the exception of the UK, multi-day infringement hearings are unknown in the EU countries.

E.I.2. Cross-Border Issues

In many EU cases, cross-border issues arise, simply because a product is distributed EU-wide, and the Patentee holds (parallel) patents in more than one EU member state.

E.I.2.a. General Principles – limited territorial reach

The general rule is that a patent which is infringed in, say, the UK but not in Germany, does not allow the Patentee to sue for patent infringement in Germany. Any given patent has a territorial limitation.

However, many fact patterns are not clear-cut in that they entail certain cross-border elements. One must analyze in detail whether such trans-border actions infringe a domestic patent.

For example, exporting from Germany is regarded as a domestic act, i.e. it may infringe a domestic (German) patent⁴. A device patent may be infringed by manufacturing all parts of a patented device domestically and exporting them to another country where they are assembled⁵.

With respect to process patents, a number of highly complex fact patterns have evolved over the past few years, in particular with respect to client-server systems, where client, database and user are located in various countries. Again, even though the general rule is that every step of a process needs to be performed domestically in order to establish domestic jurisdiction, a more practical approach may be followed by courts in Europe – they may ask for where the “core” of the patented process is performed, or whether domestic actions are indispensable for performing the process⁶.

If the process is performed abroad (e.g. in a country where no patent protection exists), but the resulting product is imported into an EU member state, the

³ For streamlined High Court procedures.

⁴ German Federal Supreme Court, GRUR 1957, 231 – *Täeschner v. Pertussin I*.

⁵ District Court Düsseldorf, InstGE 6, 130 f. – *Diffusor* – this shall be limited to cases where the different parts are exclusively suited to be assembled for the patented device.

⁶ Court of Appeals Düsseldorf, BeckRS 2010, 12415 – *Prepaid-Karten II*.

Patentee can enjoin importation of such product based on Article 5^{quarter} Paris Convention⁷. In practice, this allows the owner of a European patent to enjoin importation of products that are directly obtained by a process which is performed in a country where no patent protection exists (e.g. in China).

However, in some cases it is not immediately clear what constitutes such “product directly obtained” by the patented process. For example, in the area of life sciences one often deals with screening processes. If a screening process is performed in a country where no patent protection exists, the Patentee cannot prevent it. However, cases have evolved where test results generated in a patent-free country are sent to a country where a valid process patent exists. The question then arises whether such test results qualify as a “product directly obtained” by the patented process. This is highly debatable. The District Court Düsseldorf⁸ held that the owner of a patent to a screening process has no right to prohibit importation of such test results from a country where no protection exists⁹.

Highly relevant in practice is determining whether a particular advertisement on an internet page may constitute domestic infringement. The fact alone that an internet page is in a foreign language does not necessarily help a Defendant. In France, offering a product on the internet without disclosing prices and sales conditions was not regarded to constitute a domestic offering¹⁰.

Whether domestic execution of a sales contract for distribution of a device that is manufactured and distributed abroad may constitute infringement, is in dispute among different courts: Italian courts regard this to be an infringing act¹¹ whereas German courts¹² and Dutch courts¹³ do not.

E.I.2.b. Cross-Border Injunction

In theory, and under limited conditions, courts in one country may also hear infringement actions in relation to foreign patents and grant injunctions in respect of those patents. Since these injunctions take effect outside these courts’ national jurisdictions, they are called “cross-border injunctions”. However, these cases are rare.

⁷ More precisely, one must say that all member states of the European Union are also signatories of the EPC and the Paris Convention. The EPC provides in Article 64 (2) for protection of products directly obtained by the patented process; this provision is transposed into the national patent laws of the EU/EPC member states.

⁸ District Court Düsseldorf, docket no. 4b O 247/09 of February 16, 2010 (www.duesseldorfer-archiv.de/?=node/3079).

⁹ For the US, cf. US Court of Appeals for the Federal Circuit, GRUR Int. 2003, 1040, 1043 – *Bayer AG v. Housey Pharmaceuticals, Inc.* regarding the comparable Section 271 (g) US Patent Code.

¹⁰ TGI Paris, PIBD N° 840 – III – 50 (abbreviated version in GRUR Int. 2007, 442).

¹¹ CCass Rom, GRUR Int. 2004, 876 – *Omeprazol*.

¹² RGZ 75, 128, 131 = JW 1911, 227 – *Hartgußarbeitsbacken*.

¹³ RB Den Haag, BIE 1995, 365, 367.

For instance, Dutch and German courts have acknowledged that in some cases courts may grant cross-border injunctions that take effect outside the territory of the court. Dutch courts, in particular, developed the “spider in the web” doctrine in 1998¹⁴. This doctrine allowed a Plaintiff to sue a number of Defendants that were domiciled in countries other than the Netherlands if the main Defendant (the “spider in the web”) was domiciled in the Netherlands. This far-reaching Dutch interpretation of the relevant EU Regulation¹⁵ was however vacated by the *Primus v. Roche* decision of the CJEU in 2006¹⁶.

Also in 2006, another cut-back for cross-border injunctions came with the *GAT v. LuK* decision of the CJEU¹⁷. Basically, leaving all unnecessary details of the case aside, the court held that once the validity of a patent was under scrutiny of a foreign court (which is usually the case), this foreign court had exclusive jurisdiction, with the effect that a domestic court needed to dismiss or at least suspend the infringement action, based on this foreign patent.

However, *GAT v. LuK* bars cross-border decisions in cases on the merits only. In 2012, regarding cross-border preliminary injunction proceedings, the CJEU held in its eagerly awaited *Solvay v. Honeywell* decision¹⁸ that it is permissible to grant a claim for a provisional cross-border injunction based on a foreign part of an European Patent even if its invalidity is asserted. This is at least how Dutch courts¹⁹ interpret the ruling, which means a revival of (preliminary) cross-border injunctions for the Netherlands.

E.I.2.c. Torpedo Actions

In the past, “torpedo” actions were filed in countries known to process infringement actions very slowly. Such torpedo actions were often pursued by a potential Defendant seeking a negative declaratory judgment in relation to multiple foreign patents (in most cases parts of a European patent) by a court likely to be slow²⁰, thus preventing the Plaintiff/Patentee from filing an infringement action relating to all such foreign patents before any other court for a long time. This was based on Article 21 of the Brussels Convention²¹, stipulating that once the same dispute is brought before courts of different EU countries, any court other than the court first seized shall stay its proceedings until the court first seized has established jurisdiction. The court used for the torpedo action would ultimately refuse to assume jurisdiction for any foreign part of a European patent

¹⁴ *EGP v. Boston Scientific* (Gerechtshof Den Haag, 23.04.1998), [1999] FSR 352.

¹⁵ Article 6 No. 1 of Regulation 44/2001.

¹⁶ *Primus v. Roche*, CJEU, C-539/03.

¹⁷ *GAT v. LuK*, CJEU, C-4/03.

¹⁸ *Solvay v. Honeywell*, CJEU, C-616/10.

¹⁹ Rechtsbank Utrecht, GRUR-Prax 2012, 498 – *Boehringer v. Teva*.

²⁰ Italian and Belgian courts were often (ab)used for this purpose.

²¹ Convention of 27 September 1968 on jurisdiction and the enforcement of judgments in civil and commercial matters.

held by a foreign Patentee, but as the court first seized could, in practice, take years to refuse assumption of jurisdiction, the effect was to block a foreign infringement action for years. One of the reasons why this “torpedo”-practice could develop at all was a considerable difference among EU countries as regards the point in time at which a court is considered “seized”. But in 2001, the law was harmonized by EU Regulation 44/2001. Art. 30 (*lis pendens* rule) of this Regulation provides that in all EU member states a court is regarded as “seized” with a matter once the complaint is filed with it. Moreover, courts clearly realized “torpedo tactics” of an Infringer – and German courts even considered refusing to stay in view of an apparent abuse of EU law²², while UK courts²³ did not acknowledge a potential abuse. Finally, the most prominent courts to hear such actions (those in Italy and Belgium) are now reported to act more quickly in rendering a decision than in years past, with the effect that any delay may be minimized. Be that as it may, any “torpedo” action filed certainly remains a nuisance for the Plaintiff/Patentee.

These days, “torpedo” actions no longer play any important role in the EU. However, one still needs to follow the relevant case law closely. For instance, rather recently, on June 10, 2013, the Italian Supreme Court panel sitting in Unified Session (SCUS) decided in *General Hospital v. Asclepion*²⁴ that Italian courts may also have jurisdiction for foreign parts of European patents, even though the Patentee is also a foreign entity. Before this decision, it was pretty clear that Italian courts would ultimately refuse to assume jurisdiction in such a case. This could represent a problematic departure from prior case law.

E.II. Scope of Protection

E.II.1. Claim Construction and Literal Infringement

Patent infringement is assessed by comparing the allegedly infringing product or process with the asserted patent claim(s). When such a comparison reveals that the accused product or process fulfills every feature of an asserted claim, the court shall find for infringement. If each element is literally found, literal infringement is established.

In all European jurisdictions, European patents must be construed in accordance with Art. 69 EPC and its Protocol. This means that the scope of a European patent is determined by the claims, as interpreted by the description and drawings. Such work is always necessary when the meaning of a patent claim is under dispute. According to Art. 1 of the Protocol on the interpretation of

²² District Court Düsseldorf, InstGE 3, 8 – *Cholesterin-Test*.

²³ Court of Appeal, *Research in Motion UK Ltd v. Visto Corporation*, [2008] EWCA Civ 153.

²⁴ Unpublished decision.

Art. 69 EPC, the EPC should not be interpreted to mean that the scope of protection is limited to the strict, literal meaning of the wording used in the claim, and that the description and drawings are only to be taken into consideration for resolving any ambiguity found in the claims. On the other hand, the claims shall not serve as a general guideline only. Rather, a court needs to balance fair protection for the Patentee with a reasonable degree of certainty for third parties which might wish to avoid infringement.

Almost needless to say, every patent is different, and accordingly the decisions across Europe may vary even when considering a single given patent and the same infringing device. Years ago, the *Epilady* patents were enforced in various countries, with a remarkable number of different views of the courts as regards claim construction²⁵. But *Epilady* is just one of many examples that can be experienced by patent litigators in Europe. Whenever the alleged Infringer disputes infringement, it is far from clear that different EU courts will construe the meaning of a patent claim in the same way.

The court will take into account the understanding of the person skilled in the art and ask how this person would have understood the language of the claims when reading them in context²⁶.

German courts tend to emphasize that a patent is its own dictionary, meaning that the understanding of terms used in the claims is determined by the words as they are used in the description²⁷. However, German courts also acknowledge the ordinary meaning of words used in the claims and/or the meaning generally ascribed to them²⁸. In a recent decision, the German Federal Supreme Court emphasized that the scope of protection is limited by the claims²⁹, meaning that alternatives which are described in the specification, but not claimed, do not fall within the scope of protection.

²⁵ See, e.g. Germany: Court of Appeals Düsseldorf, decision of November 21, 1991, GRUR Int. 1993, 242; Italy: Tribunale di Milano, decision of May 4, 1992, GRUR Int. 1993, 243; The Netherlands: Gerechtshof Den Haag, decision of February 20, 1992, GRUR Int. 1993, 242.

²⁶ House of Lords in *Kirin-Amgen v. Hoechst Marion Roussel*, [2004] UKHL 46; German Federal Supreme Court, docket no. X ZR 163/03, GRUR 2006, 311 – *Baumscheibenabdeckung*.

²⁷ German Federal Supreme Court, docket no. X ZR 85/96, GRUR 1999, 909/IIC 1992, 932 – *Tension Screw*.

²⁸ German Federal Supreme Court, docket no. X ZR 255/01, GRUR 2004, 1023/IIC 2005, 971 – *Bottom Separating Mechanism*.

²⁹ German Federal Supreme Court, docket no. X ZR 16/09, GRUR 2011, 701, IIC 2011, 851 – *Occlusion Device* – this decision is not too spectacular, but is a recent example for a patent that is a borderline case in that when emphasizing the wording of the claim, one comes to a different result than when emphasizing the description and the meaning of the technical teaching of the patent.

E.II.2. Equivalent Infringement and Purposive Construction

Even if one or more features of the claim are not literally infringed, the accused product or process may still infringe. In most countries, this is determined by applying the “doctrine of equivalents”, which examines whether there exist only insubstantial (immaterial) differences between the feature of a claim and the attacked product/process – and whether the variant solves the problem underlying the invention by means which have the same technical effect.

In Germany, the Federal Supreme Court summarized in a “quintet” of decisions³⁰ three criteria, which became known as the *Cutting blade* or *Custodiol* questions (from the names of the decisions):

In order for an embodiment which deviates from the literal meaning of the patent claim to fall within the scope of this claim, it is [...] not enough that

- (1) it solves the problem underlying the invention with means which, although modified, still objectively have the same effect;
- (2) the skilled person’s specialist knowledge allows him to arrive at the modified means with the same effect.

In the same manner as the sameness of effect cannot be determined without reference to the patented claim [...],

- (3) the things which the skilled person must consider must additionally be guided by the meaning of the technical teaching protected by the patent claim in such a manner that the skilled person considers the deviating embodiment with this modified means as an equally valuable solution.

The third criterion is somewhat vague and is especially complicated to answer in practice.

In its decision *Thermostable DNA-Polymerase*³¹ the Court of Appeals Düsseldorf dealt with a patent directed to a thermostable DNA-polymerase having a molecular weight of 86.000–90.000 Da as determined by SDS-PAGE. However, the DNA-polymerase in the attacked embodiment had a molecular weight of only 85.000 Da. The court found for non-infringement under the doctrine of equivalents because the skilled expert would assume that it was essential and decisive for the protected teaching of the patent to be within the limits of the claims.

In its decision *Murine Monoclonal Antibody*³², the Court of Appeals Düsseldorf again had the opportunity to apply the *Custodiol* questions. The patent was directed to a murine monoclonal antibody, whereas the attacked product was a re-

³⁰ German Federal Supreme Court, GRUR 2002, 511 et. seq.; IIC 2003, 302 – *Plastic Pipe*; GRUR 2002, 515 et. seq.; IIC 2002, 873 – *Cutting blade I*; GRUR 2002, 519 et seq. – *Cutting blade II*; GRUR 2002, 523 et. seq. – *Custodiol I*; GRUR 2002, 527 et. seq.; IIC 2003, 197 – *Custodiol II*.

³¹ Court of Appeals Düsseldorf, decision of January 14, 2010, docket no. I-2 U 69/08, BeckRS 2010, 15821 – *Thermostable DNA-Polymerase*.

³² Court of Appeals Düsseldorf, decision of February 10, 2012, docket no. I-2 U 80/02, InstGE 5, 91 – *Murine Monoclonal Antibody*.

combinant humanized monoclonal antibody with hypervariable regions derived from a murine antibody.

The Court held that the attacked product did not make use of the patent: A literal infringement needed to be ruled out because the term “murine antibody” could not be extended to also comprise a “humanized antibody”. The Court then discussed whether the attacked product was covered by the doctrine of equivalents, but decided against it: Even though the skilled expert working on the priority date could have possibly thought about using animals other than mice when producing antibodies, he would not have considered changing the antibodies of cells from one species by introducing human sequences in order to obtain a humanized antibody. Interestingly, the Court acknowledged that the skilled person working on the priority date knew that – and why – antibodies, resulting from a particular species (here: mouse), were not only not amenable to *in vivo* use, but also that he would have known that monoclonal antibodies may be produced by replacing regions of the murine antibody by human sequences in order to make them suitable for an *in vivo* use. However, the Court concluded:

[In such situation] the person skilled in the art would have expected that the patent, had it contemplated extending the protection also to those [i.e. mixed murine/humanized] antibodies, would contain hints in this direction. Given that no such hints exist, the person skilled in the art could expect that the scope of protection would only comprise monoclonal antibodies which only contain sequences of one (single) species.

In its recent decision *Occlusion Device*³³, the German Federal Supreme Court considered a patent protecting a collapsible medical device. According to the patent, clamps were adapted to clamp strands at opposing ends of the device. However, the attacked device was not clamped. Rather, the strands were folded over, a socket was slid over the ends and the ends of the strands were welded. Welding of the strands was disclosed in the description, but not recited in the claims. The Court held that the attacked device did not infringe: If the patent disclosed various technical solutions (clamping, welding) to obtain a specific technical result, but only one of them (clamping) found its way into the claims, the claims covered only one of them, namely clamping. The Court reasoned that it was the Applicant’s decision to claim one out of a number of disclosed technical solutions, and this needed to be taken into account, with the result that technical solutions that were only disclosed in the description, but not claimed, were not covered under the doctrine of equivalents.

It is almost impossible to reconcile these two decisions: In *Murine Monoclonal Antibody*, the doctrine of equivalents was excluded because the variant (humanized antibody) was not disclosed, whereas in *Occlusion Device* it was excluded because the variant was disclosed, but not explicitly claimed.

³³ German Federal Supreme Court, GRUR 2011, 701, ICC 2011, 851 – *Occlusion Device*.

In its *Diglycide Compounds* decision³⁴, the Federal Supreme Court dealt with the situation that the attacked embodiment contained a feature that was mentioned neither in the claims nor in the specification. The court held that in such a situation, one needed to analyze whether the effects of this feature are more similar to the feature in the claim than the alternative features that are disclosed in the specification. In the latter case, the doctrine of equivalents would be excluded.

What remains undecided by the German Federal Supreme Court is how to evaluate equivalence in the event that the description fails to mention any alternative means to the means of the claims at all. In a very recent decision³⁵ the Court of Appeals Düsseldorf had to deal with such a case. In the end, it denied infringement under the doctrine of equivalents because the alternative means of the attacked embodiment was regarded to contradict the patent's core teaching. Moreover, the Court took into account that the Patentee had limited the claim particularly to a specific feature in prior opposition proceedings in the EPO.

In the Netherlands, there is no statutory basis for the concept of infringement under the doctrine of equivalents. However, in the event that one (or more) feature(s) of the patent claim is (are) not literally fulfilled in the attacked embodiment, the Dutch courts will establish whether (or not) use of the claim has been made (by equivalent measures). Dutch courts apply the so-called “function-way-result test”, meaning equivalent measures are measures which perform essentially the same function, in essentially the same way to lead to essentially the same result. It seems that the Dutch Supreme Court has never made a clear distinction between literal infringement and infringement by equivalence. However, in its decision *Dreizler v. Remeha*³⁶ the Dutch Supreme Court did not object to the “function-way-result test” applied by the Court of Appeals.

In *Yamanouchi v. Biogen*³⁷ the District Court in The Hague considered whether this test is appropriate when the patent protects a chemical compound. It held that in such cases, instead of applying the “function-way-result test”, a court may apply the so-called “insubstantial differences test”.

France also applies the doctrine of equivalents. One of the most recent reported cases is *Technogenia v. Ateliers Joseph Mary et al*³⁸. In this case, the Court of Appeals Paris addressed the deviation from the limits of the patented medical range for various attacked devices. The patent required an organic binder to be present in the range of 0.5–1.5 wt%. One attacked variant, however, contained 1.74 wt% organic binder and was held to infringe. Interestingly, the Court did not refer to

³⁴ German Federal Supreme Court, GRUR 2012, 45 – *Diglycide Compounds*.

³⁵ Court of Appeals Düsseldorf, decision of September 13, 2013, docket no. I-2 U 23/13, BeckRS 2013, 18740.

³⁶ Dutch Supreme Court, decision of January 13, 1995, BIE 1995, p. 63.

³⁷ District Court of The Hague, decision of October 28, 1998, docket no. 98/0398.

³⁸ Paris Court of Appeal (Cour d' Appel), decision of January 10, 2007, docket no. 04/696, IIC 2010, 844.

the doctrine of equivalents. Another attacked variant contained between 2.0 wt% and 2.5 wt% of organic binder. This was held to infringe under the doctrine of equivalents.

The Court stressed that the low proportion of organic binder had the effect of avoiding a blowing phenomena of the welding components and that, therefore,

the difference in the proportion of binder in the coating, as long as the proportion remains low, does not have an impact on the function (ensuring the cohesion of the coating) or on the result sought³⁹.

Despite the rather large deviation in the amount of organic binder, the Court held that the attacked variant fulfilled the same function (no blowing of the welding components) to achieve a similar result (easy and good welding quality) in the same manner as the patent, which justified assuming infringement under the doctrine of equivalents. Interestingly and as opposed to, for example, the German, UK and Dutch courts, the French courts do not seem to apply the view of the person skilled in the art.

In the same decision, the court needed to determine the scope of protection of another feature of the patent, i.e. a coating containing between 0.2 and 1% glycerin. One of the attacked products contained only 0.1%. The suit was dismissed. The Court of Appeals Paris held that the variant supposedly did not benefit from the effect of added plasticizers in the given range, which was to afford flexibility and homogeneity to the patented rod.

In the UK, the most comprehensive decision in the area of equivalence is the House of Lords' ruling in *Kirin-Amgen*⁴⁰. The patent related to the production of the protein erythropoietin ("EPO") by recombinant DNA technology. EPO is a protein stimulating the production of red blood cells. It is useful in the treatment of anaemia. It has attracted attention for being used in doping.

The approach followed by the House of Lords is somewhat different from other infringement courts in the EU. The House of Lords established that claims should be given a "purposive construction". In *Kirin-Amgen*, Lord Hoffman stated that "purposive construction" is the one binding principle in determining the scope of protection:

[T]here is only one compulsory question, namely that set by Article 69 [EPC] and its Protocol: What would a person skilled in the art have understood the Patentee to have used the language of the claim to mean? Everything else [...] is only guidance to a judge trying to answer that question⁴¹.

It is probably fair to conclude that "*Kirin-Amgen*" implied a two-step approach in determining patent scope. The first step is the "conventional (literal) meaning":

³⁹ *id.*, page 848.

⁴⁰ In following the House of Lords decision *Kirin-Amgen v. Hoechst Marion Roussel*, [2004] UKHL 46.

⁴¹ *id.*, para. 69.

So, to make any sense of the terms “primary, literal or acontextual meaning” in the Protocol questions, it must be taken to mean a construction which assumes that the author used words strictly in accordance with their conventional meanings⁴².

The Court emphasized that patent claims need to be construed on the basis of the same general principles as any other declaration in a document or contract, considering in particular the author’s intended meaning. In patent law, the purpose of a patent specification was to describe and delineate the invention for the person skilled in the art. The Patentee was responsible for the words since he could freely choose them – and only exceptionally could a patent be understood to have used words in an unconventional sense or as including unessential elements.

The second step would be “purposive construction”, described by Lord Hoffman in *Kirin-Amgen* as follows⁴³:

“Purposive construction” does not mean that one is extending or going beyond the definition of the technical matter for which the Patentee seeks protection in the claims. The question is always what the person skilled in the art would have understood the Patentee to be using the language of the claim to mean. And for this purpose, the language he has chosen is usually of critical importance.

In *Kirin-Amgen*, the patent taught the isolation of the EPO gene from a human source and its introduction into a suitable host cell, which then expressed the exogenous EPO gene, thereby producing EPO. The Defendants used a different method, called “gene activation”. Instead of introducing an (exogenous) EPO gene into a host cell, the existing EPO gene in the human cell was activated. This caused the human cell to express the endogenous EPO gene. When the Plaintiff’s patent application was filed, this “gene activation” technique was still unknown. The question was whether claims 19 and 26 (both product-by-process claims) were infringed. Lord Hoffman concluded that this was not the case, because

[t]he man skilled in the art would not have understood the claim as sufficiently general to include gene activation. He would have understood it to be limited to the expression of an exogenous DNA sequence which coded for EPO⁴⁴.

Whether it is called “doctrine of equivalents” or “purposive construction”, the result is similar. Both prevent an alleged Infringer from avoiding infringement by making only minor and/or insubstantial changes. The difficulty in practice really is to predict the outcome of a case based on infringement under the doctrine of equivalents or by applying a purposive claim construction. All of these cases are, by definition, borderline, and there are often as many good arguments to find for infringement as to find against it.

⁴² id., para. 64.

⁴³ id., para. 34.

⁴⁴ id., para. 80.

E.II.3. Specific Claim Categories

E.II.3.a. Product Claims/Compound Claims

The scope of protection for new chemical compounds of known structure seems to be relatively straightforward in Europe. The EPO held in its decision **G 2/88 (Friction reducing additive/MOBIL OIL CORPORATION III)**⁴⁵:

An initial question to be considered in such a case is the protection which is conferred by a claim to a physical entity such as a compound, per se. It is generally accepted as a principle underlying the EPC that a patent which claims a physical entity per se, confers absolute protection upon such physical entity; that is, wherever it exists and whatever its context (and therefore for all uses of such physical entity, whether known or unknown).

German courts follow the viewpoint that the scope of protection for chemical compounds is absolute. In the landmark case “*Imidazoline*”⁴⁶ the German Federal Supreme Court held that protection for compounds produced by chemical means is not linked to a specific utility:

The scope of the subject matter of a chemical product invention, as outlined above, results in an unrestricted exclusive right of a patent owner with respect to the commercial use of the chemical products covered by the invention. The patent owner may enjoin any commercial use of the chemical products according to the invention whether or not such use may have been anticipated by him. Even if another discovers a non-obvious, and, therefore, inventive use for the chemical product covered by the invention, he cannot commercially exploit the same without the prior consent of the Patentee. Thus, product protection is in principle absolute.

It should be noted that the absolute protection is limited in the area of human gene sequences to the use/purpose as disclosed in the patent and stated in the claims (cf. *infra* at E.II.5.e.).

Situations may arise where only traces (residues) of a protected compound can be found in a product. There have been some reported cases in both the Netherlands and Germany where courts denied patent protection where only small amounts of a patented compound can actually be detected in the attacked product, resulting in an argument that the compound does not possess the relevant technical effect specified in the patent. A Dutch court held in *Handley Page vs. KLM*⁴⁷ that it was not sufficient to hold for infringement for the sole reason that the allegedly infringing product contains a product that is identical to the patented product. Even if this were the case, i.e. all elements of the claimed invention are present in the allegedly infringing product, the attacked product still needed to function in conformity with the teaching of the patent for infringement to be acknowledged.

⁴⁵ Decision of December 11, 1989, OJ EPO 1990, 93.

⁴⁶ German Federal Supreme Court, decision of March 14, 1972, IIC 1972, 386 – *Imidazoline*.

⁴⁷ BIE 1942, para. 118, p. 147.

A similar ruling was handed down by the German District Court Düsseldorf in its *Grasherbizid* decision⁴⁸:

The scope of protection of a product patent on an intermediate product does not extend to an end product, if it has been chemically transformed into a new substance, whose physical characteristics and technical applicability differ from that of the intermediate product. The use of such an end-product does not constitute an act of infringement even if the end-product contains a residue of the incomplete detransformed intermediate product, which however has no function for the end-product.

However, it should be noted that even though such a *de minimis* exception is discussed, it has not been adopted by higher courts and, therefore, is far from constituting established law in Germany.

E.II.3.b. Composition claims

Compositions are usually not as accurately defined as chemical compounds. Ranges are often used in the claim to describe proportions of various components or the concentration of selected components. If this is the case, the question is if and to what extent an allegedly infringing composition with components in different ranges nevertheless falls within the scope of the patent. A good example is the landmark *Custodiol II* decision of the German Federal Supreme Court⁴⁹. The patent was directed to a solution with 11 additives specified in the claim. The respective contents of these additives were specified by mmol/l, each with additional tolerances resulting in an upper and lower limit for each additive. The patent provided, *inter alia*, for 10 ± 2 mmol/l of magnesium chloride and 16 ± 11 mmol/l histidine hydrochloride. The attacked embodiment only used 4 mmol/l magnesium chloride and replaced the histidine hydrochloride by another additive. The *Custodiol II* decision is one of the landmark cases regarding equivalence in Germany and has been discussed *supra*, E.II.2. The Court held⁵⁰:

An interpretation that a value must be complied with exactly will above all correspond to the interpretation of the person skilled in the art following the realization that this is a “critical” value. Accordingly, the way in which a specific figure or dimension in the patent claim is to be understood is a question of the interpretation by the person skilled in the art in the individual case, which is a matter to be determined by the trial judge.

In the case at hand, the attacked embodiment was held not to infringe:

In the light of the circumstances explained above in closer detail, and the present large discrepancy that can no longer be related to the quantity of magnesium chloride contained in the patent claim, the contested embodiment can no longer be included within the extent of protection of the patent at issue⁵¹.

⁴⁸ District Court Düsseldorf, GRUR 1987, 898 – *Grasherbizid*.

⁴⁹ German Federal Supreme Court, March 12, 2002, docket no. X ZR 73/01; IIC 2003, 197 – *Custodiol II*, cf. ³⁰.

⁵⁰ *id.*, p. 200.

⁵¹ *id.*, p. 203.

E.II.3.c. Product-by-Process Claims

In the life sciences, product-by-process claims are more frequent than in other technical areas. Product-by-process claims are directed to a product, which is (either in total or at least in part) defined by its production process. Oftentimes, a product-by-process claim makes reference to a process which is protected separately. Rather often, the question is whether the process as defined in the claim actually limits the scope of protection of such a claim, i.e. whether a Defendant that makes use of a different method, but obtains the same product, infringes. This is far from clear, and the approaches of different EU-courts vary significantly.

In Germany, it seems widely acknowledged that a rather broad wording such as “*product x obtainable by process y*” suggests that the specific product may (but need not) be obtained by making use of the recited process. In such a case, it cannot matter for patentability whether the process is new and inventive, given that the specifically disclosed process is only one way to obtain the product. Rather, the product as such must be new and inventive. When using the term “*obtainable*”, this is entirely clear in the wording. Consequently, when turning to infringement, it should not matter whether process y is actually used, or whether the Defendant performs some other process leading to the same product.

However, one also finds claims that seem rather limited in that they recite wording such as “*product x obtained by process y*”, i.e. they disclose and put under protection a product that is described to be the result of one (single) specific process. The question in such cases is whether the use of such wording actually limits the claims. In Germany, the case law relating to this question has shifted over time. In the *Trioxan* decision⁵² of the German Federal Supreme Court, the wording “*obtained by*” and “*obtainable by*” were regarded as clearly different. According to this view, an Applicant reciting “*obtained by*”, “*unmistakably*” shows that he seeks protection only for products obtained by the process described in the claim. However, in 1993, in *Tetraploide Kamille*⁵³, the German Federal Supreme Court, in revocation proceedings, indicated a shift in this position, since it regarded the phrases “*obtained by*” and “*obtainable by*” to be absolutely equal. More specifically, the Court believed the wording “*obtained by*” does not limit the scope of protection to products that result from the recited process.

However, it is not entirely clear whether German infringement courts will necessarily follow this approach. In its 1996 decision *Oberflächenaktives Material*⁵⁴, the District Court Düsseldorf held that the definition of the process indirectly circumscribes the patented product. According to this Court:

⁵² German Federal Supreme Court, BGH GRUR 1972, 80 ff. – *Trioxan*.

⁵³ German Federal Supreme Court, BGH GRUR 1993, 651, 655 – *Tetraploide Kamille*.

⁵⁴ District Court Düsseldorf, decision of August 6, 1996, docket no. 4 O 265/95, BeckRS 2010, 24439 – *Oberflächenaktives Material*.

[it] is to be determined by interpretation of the claim and the description for each individual case, to what extent the disclosed manufacturing process results in physical or chemical features of the protected product which need to be present to hold that a product obtained by a different manufacturing process infringes.“

In its more recent decision “*Aufzeichnungsträger*”⁵⁵, the German Federal Supreme Court took a very similar approach. It held that one would need to interpret the patent with respect to what features of the resulting product were coined by the referenced process:

[I]t is to be determined by construction of the claim, whether and to what extent the referenced process results in features of the product⁵⁶.

In contrast to Germany, UK courts seem to interpret product-by-process claims rather narrowly in the aftermath of the decision “*Kirin-Amgen*”⁵⁷ mentioned above. Claim 26 in *Kirin-Amgen* was directed to

a polypeptide product of the expression in a eucaryotic host cell of a DNA sequence according to any of claims 1, 2, 3, 5, 6 and 7

and the referenced claims 1–7 described the process.

The House of Lords held that the patent only affords protection against products that have been obtained by the referenced process. In essence, the decision stresses the importance of the process and is certainly narrower than the scope of protection granted by German courts for a product-by-process claim.

E.II.3.d. (Second Medical) Use Claims/“Off label” Use

A compound can be linked not only to a specific manufacturing process, but also to a specific purpose for use. Such claims are referred to as “purpose-limited claims” or “use claims”. There exist a variety of reasons as to why an Applicant might choose such claims. Often, the compound as such is not new – what is new, however, is the specific purpose/function. The question is whether the purpose/function contained in the claim limits the scope of protection, i.e. whether the same compound which is or may be used for another purpose/function still infringes.

In Germany, the leading case in this regard is *Antivirussmittel*⁵⁸. The patent claimed an antiviral compound containing 1-aminodamantane or 1-aminoadamantane hydrochloride. Some years after the filing date, it was discovered that the claimed compounds may also be used to treat Parkinson’s disease, and the Defendant marketed a drug containing 1-aminoadamantanesulfate for use against Parkinson’s disease. The German Federal Supreme Court dismissed the

⁵⁵ German Federal Supreme Court, BGH GRUR 2005, 749 – *Aufzeichnungsträger*.

⁵⁶ id., p. 750/751.

⁵⁷ In following the House of Lords decision *Kirin-Amgen v. Hoechst Marion Roussel*, [2004] UKHL 46.

⁵⁸ German Federal Supreme Court, decision of June 16, 1987, docket no. X ZR 51/86; GRUR 1987, 794 – *Antivirussmittel*.

suit, because it saw the functional claim type in question as limited by the function stated in the claim:

„Functional claims“ contain a final element, namely realization of a particular purpose. This is an essential element of the protected invention, which is only realized by carrying into effect the inherent purpose. If this purpose is neither pursued nor fully achieved, but a purpose different from the one identified in the claim is achieved, a use of the patent needs to be ruled out.

The Court held that the specific goal of the patented invention needs to be realized to a “practically considerable degree”. In the case at hand, the court held that a drug designed to be used against Parkinson’s disease is not designed to be used against a virus disease. Even if some of the patients suffering from Parkinson’s may also coincidentally suffer from a virus disease, this does not mean that the attacked drug infringes:

The fact that the [attacked product] which is for use against Parkinson’s disease is occasionally also used for prevention of virus diseases, cannot be regarded as a realization of the purpose of the patent to prevent virus diseases, to a practically considerable extent.

One may summarize this decision as follows: There is no infringement if the purpose of the patent is neither intended nor fully achieved.

In later decisions, the lower courts have elaborated on this concept. However, case law is very limited indeed. One of the few decisions, which is often cited, is *Ribavirin*⁵⁹ of the District Court Düsseldorf. There, the use claim (in a so-called “Swiss-type format”) read as follows:

The use of ribavirin *in combination* with pegylated interferon alpha for the manufacture of a pharmaceutical composition for treating a patient having chronic hepatitis C infection, characterized in that the composition is for administration for a time period of 40–50 weeks, *and the patent is a naïve patient having a genotype 1 infection* and a viral load of more than 2 million copies per ml serum. (summarized by the author, emphasis added)

The Defendant offered ribavirin capsules and distributed them for use for patients with a chronic hepatitis C infection. The Court rejected the Plaintiff’s infringement claims. Even though the attached package insert provided, *inter alia*:

For the treatment of patients with chronic hepatitis C who have not responded to treatment with alpha-interferon on account of a contra-indication or intolerance. As an accompanying therapy for patients with chronic hepatitis C who are being treated with alpha-interferon.

Citing the aforementioned *Antivirumittel* decision, the Court held that the package insert only related to and described the use of ribavirin in monotherapy for treatment of hepatitis C as one potential use. As far as use of ribavirin in combination with another product was described, use would be within the limit of what had already been known in the prior art. The Court continued by emphasizing that

⁵⁹ District Court Düsseldorf, GRUR-RR 2004, 193 – *Ribavirin*.

any reference to the claimed specific use to treat a specific group of patients as is claimed under claim 1 [is lacking]. An instruction target-oriented to actually fulfilling the specific use of ribavirin according to claim 1 of the patent, does not exist.

It is important to note that according to Plaintiff's allegation, this particular group of patients was already contained in the larger group of "non-responders". However, the Court nevertheless held that one could not derive from the package insert Defendant's intention to actually treat this particular sub-group of patients. Even though it could not be ruled out that the attacked ribavirin capsules would actually be used to treat the specific group of patients mentioned in the patent, this was not decisive for the issue of infringement. Rather, citing the aforementioned *Antiviriumsmittel* decision, the District Court Düsseldorf concluded that no "purposeful use" was achieved. The Court very much emphasized the package insert:

The Plaintiff cannot successfully argue that the patented use is imposed [on the buyers] or that [they] will objectively use the attacked product accordingly. ... Even though it cannot be ruled out that patients will be treated with the attacked product which belong to the subgroup of patients defined in the patent, this is not decisive for patent infringement. [...] What lacks [to establish infringement] is [treatment of the defined subgroup of patients in a combination therapy] in a *considerable range and goal-oriented use*. (emphasis added)

In order not to extend the scope of protection too far, German courts require that any document providing evidence that the product shall be used according to the teaching of the patent be clearly tied to the product. Therefore, rather general advertisements informing potential customers as to potential uses of a particular compound, without reference and without being (physically) attached to or enclosed with a particular product, do not infringe a functional claim⁶⁰.

In the area of generics, one should be aware of Art. 3 para. 3)b of EU Regulation (EU) 726/2004: The general rule is that the summary of product characteristics of the generic must be consistent with the original product. This will also include the intended use (indications, dosage). However, the generic company may rely on the "carve-out" provision of Art. 11 EU Directive 2004/27, providing, in relevant part:

For authorisations under Article 10, those parts of the summary of product characteristics of the reference medicinal product referring to indications or dosage forms which were still covered by patent law at the time when a generic medicine was marketed need not be included.

Consequently, the manufacturer of a generic may refrain from actually including the purpose of the pharmaceutical for the patented (second medical) use in the product information leaflet. The question is whether or not the sole fact that the patented (second medical) use is not mentioned actually suffices to escape liability for patent infringement. *Prima facie*, one may tend to agree. How-

⁶⁰ Court of Appeals Düsseldorf, decision of January 31, 2013, docket no. I-2 U 54/11, BeckRS 2013, 11782 – *Cistus*.

ever, in many cases either the prescribing doctor or the pharmacist knows of the suitability of the compound contained in the generic for the patented (second medical) use, with the effect that, at least to some extent, it may and actually will be prescribed and sold for the patented purpose irrespective of whether a carve-out has been used. One speaks of so-called “off label” or “cross label” use, i.e. a use by the patient that is not recommended in the labelling of the generic.

There are no reported cases on “off label use” by German courts so far.

However, there is a 2010 *Ribavirin* decision of the (Dutch) Hague District Court⁶¹ (*Schering v. Teva*). As regards the claims, please refer to the German *Ribavirin* decision (*supra*). The Defendant in this case explicitly “carved-out” Plaintiff’s patented indication (combination therapy for a particular subgroup). The Dutch court denied infringement since the Defendant had

excluded the specific patient category (naïve and having genotype 1 infection) claimed by [Plaintiff]. That is sufficient to fall outside the protective scope of the patent. In other words: [Defendant] does not have a market authorization to manufacture generic ribavirin for the specific indication claimed in the patent.

However, the Dutch court makes reference to the actual market situation by mentioning:

This [non-infringement] could be different in the hypothetical situation – which is not the case here – that it had been proven that because of the clinical research mentioned in [the pharmacodynamic chapter of the SmPC] and the conclusions from that research, Teva’s generic ribavirin – induced to it or not – would nevertheless also be prescribed for naïve patients having a genotype 1 infection.

E.II.3.e. Companion Diagnostic Claims

Companion diagnostic claims have been discussed *supra* (C.I.2.d.). They may be characterized by, e.g., the following claim structure:

Compound X for use in treating patients with disease Z that have been tested positively for marker Y.

When it comes to infringement, things are rather complicated indeed, given that there are usually three potential infringers, none of which fulfils all features of the claim: First, the pharmaceutical company that actually manufactures the compound (in the above example: “Compound X”). Second, a diagnostic laboratory that determines whether the patients have tested positive for marker Y. Third, the doctors who prescribe the compound X for the patients testing positive. So far, it would seem that such claims have not been tried in European courts. Most likely, they should be treated similarly to use claims.

In practice, it should be possible to enforce a claim reading

Compound X for use in the treatment of disease Y wherein the patient has the genetic marker Z

⁶¹ Decision of November 10, 2010, [http://www.ie-forum.nl/backoffice/uploads/file/IE-Forum/IEForum%20Uitspraken/Octrooirecht/10-437%20Schering_Teva%20cs%20_ribavirine%20+%20interferon%20alpha_%20def%20versie%20\(2\).](http://www.ie-forum.nl/backoffice/uploads/file/IE-Forum/IEForum%20Uitspraken/Octrooirecht/10-437%20Schering_Teva%20cs%20_ribavirine%20+%20interferon%20alpha_%20def%20versie%20(2).)

against a pharmaceutical company if it identifies the group of patients in the package insert. In that case, it may be liable for infringement. In contrast, in the event the claim identifies – as is currently preferred by the EPO – process steps, e.g.

Compound X for use in the treatment of disease Y wherein the patient is tested for genetic marker Z comprising the steps ...

it is unlikely that any package insert mentions these steps, making it difficult to enforce such a claim against the pharmaceutical company.

E.II.3.f. Screening Processes and Reach-Through Claims

Highly debated in practice is the scope of protection of patents for screening processes. Most of these claims are directed to identifying/isolating a substance of interest (such as a protein).

The term “reach through claims” relates to claims that attempt to extend the scope of protection, e.g. of a screening process patent, to the compounds as such identified by the screening process.

“Direct” reach-through claims may have the following wording:

Use of a compound that has been identified in a process according to claim x, to manufacture a pharmaceutical that is suitable to be used in treating disease y,

or more specifically:

Use of a receptor agonist identified by the method of claim ...

Moreover, there exist claims which are not clearly formulated as reach-through claims. One may call them “tarnished” reach through claims. However, they are alleged by the Patentee to extend (“reach through”) to identified products, such as the following:

A method of determining whether a substance is an inhibitor or activator of a protein whose presence in a cell evokes a responsive change in a phenotypic characteristic other than the level of said protein in said cell per se,

which comprises:

- (a) providing a first cell which overproduces said protein and exhibits said phenotypic response to the protein;
- (b) providing a second cell which produces the protein at a lower level than the first cell, or does not produce the protein at all, and which exhibits said phenotypic response to the protein to a lesser degree or not at all;
- (c) incubating the first and second cell with the substance; and
- (d) comparing the phenotypic response of the first cell to the substance with the phenotypic response of the second cell to the substance.

Even though this claim is, *prima facie*, limited to a process that seeks to detect the characteristics (inhibitor or activator) of a particular product, such claims have been used by Patentees to seek protection against pharmaceuticals that have been developed by making use of the patented screening process.

As regards the “direct” reach-through claims, it will often be questionable whether they are actually valid. However, they have been granted by the EPO,

although the EPO is becoming more restrictive in allowing such claims. Often times, they may not be clearly identifiable as reach-through claims.

As regards the “tarnished” reach-through claims, one must perform a careful analysis. In a first step, one must ascertain whether the identified substance may be understood to be directly obtained by a process according to Article 64 (2) EPC. In most cases, this is probably not the case, since the underlying screening process is directed to identifying a substance, but is not directed to manufacturing it. The identified product will thus not normally qualify as a product “directly obtained” by the patented process.

However, borderline cases may exist in which the patent is not limited to mere screening, but also arguably leads to manufacturing of substances. In such cases, things may be different if the resulting substance is also contained in the attacked product (oftentimes a pharmaceutical).

A good example is the rather recent *Ranibizumab* decision⁶² of the District Court Düsseldorf. The Court was called to decide on infringement relating to a method comprising phage display technology. An appeal was filed, but later withdrawn. Reportedly, there was parallel litigation in the UK, France, China and the Netherlands. Relevant claim 1 reads as follows:

A method for producing a molecule with binding specificity for a particular target, which method comprises:

(feature 1.1.)

producing a population of filamentous bacteriophage particles displaying at their surface a population of binding molecules having a range of binding properties, wherein the binding molecules comprise antibody antigen-binding domains for complementary specific binding pair members, wherein the binding molecules are displayed at the surface of the filamentous bacteriophage particles by fusion with a gene III protein of the filamentous bacteriophage particles, and wherein each filamentous bacteriophage particle contains nucleic acid encoding the binding molecule expressed from the nucleic acid and displayed by the particle at its surface;

(feature 1.2.)

selecting for a filamentous bacteriophage particle displaying a binding molecule with a desired binding property by contacting the population of filamentous bacteriophage particles with a particular target so that individual binding molecules displayed on filamentous bacteriophage particles with the desired binding property bind to said target;

(feature 1.3.)

separating bound filamentous bacteriophage particles from the target;

(feature 1.4.)

recovering separated filamentous bacteriophage particles displaying a binding molecule with the desired binding property;

(feature 1.5.)

isolating nucleic acid encoding the binding molecule from separated filamentous bacteriophage particles;

⁶² District Court Düsseldorf, docket no. 4a 143/10, decision of November 10, 2011, BeckRS 2012, 20233 – *Ranibizumab*.

(feature 1.6.)

inserting nucleic acid encoding the binding molecule, or a fragment or derivative thereof with binding specificity for the target, in a recombinant system; and

(feature 1.7.)

producing in the recombinant system separate from filamentous bacteriophage particles a molecule with binding specificity for the target, wherein the molecule is said binding molecule or a fragment or derivative thereof with binding specificity for the target.

The patent was found to be infringed by import and sale of a direct product of the process (ranibizumab). One of the Defendant's main defences was that Plaintiff's claim was a reach-through claim, and that the Plaintiff sought to extend the scope of protection to commercially interesting products even though the invention allegedly failed to make a substantial contribution to the resulting product. Rather, phage display was a screening method and therefore a pure research tool that allowed one to select binding molecules, but did not result in their preparation.

The Court found for infringement, because it regarded the claim to constitute a manufacturing process:

Based on these considerations, the protected method constitutes a manufacturing process and not only a working process. Even though "screening methods" [by some] are regarded to constitute working processes [...] the requirements [to qualify the claim as a working process] do not apply. Even though according to features 1.1. and 1.2. a screening ("phage display") takes place, [...] claim 1 is not limited to mere screening. Rather, subsequently an isolation of the nucleic acid (according to features 1.3. to 1.5.) takes place and binding molecules or fragments or derivatives thereof with binding specificity for the target are generated. The result is a process that serves for producing a binding molecule which is specific for certain targets. Therefore, the process is not limited to exert an impact on an object without altering it, but rather leads to a product.

The Court regarded the Defendant's attacked product, which comprised the active component ranibizumab, as resulting directly from performing the protected process.

As opposed to the German courts, the UK High Court⁶³, in a parallel case, held that ranibizumab was not produced by a process falling under this claim (and also found the claim to be invalid). However, the Court indicated that

if ranibizumab was produced by a process falling within [...] claim 1 [...], it would be a product obtained directly by means of that process. On that hypothesis, Novartis would have infringed those claims.

In effect, this means that the UK court, in line with the German court, interpreted the claim to cover products obtained directly by the claimed process, even though the claim was directed (among other things) to a screening technique.

Given that some uncertainty as regards the exact scope of protection of "screening patents" cannot be ruled out, it seems advisable in practice to add

⁶³ Decision of July 5, 2011, HC09 C04770 [2011] EWHC 1669 (Pat).

claims with steps that result in the production of the final (commercial) product. This certainly helps to maximize protection.

E.II.3.g. SPCs

According to Art. 4 and 5 of Regulation (EC) No. 469/2009 (in the following: “SPC-Regulation”, see Annex 7) an SPC affords extended patent lifetime. The SPC-Regulation is directly applicable in the member states of the EU.

However, Art. 4 (subject matter of protection) and Art. 5 (effects of the certificate) are not entirely clear in cases where the SPC was granted for a product consisting of an active ingredient A, whereas the alleged infringer used a combination product containing not only A, but also other separate ingredients (B, C etc.). This matter has now been resolved by the CJEU in *Novartis AG v. Actavis UK Ltd*⁶⁴.

Both the UK and the German courts had referred, in essence, identical questions to the CJEU⁶⁵:

Are Articles 4 and 5 of Regulation (EC) No. 469/2009 to be interpreted as meaning that the protection conferred by a supplementary protection certificate, which has been granted for a single active ingredient (in this case: valsartan), extends to a form which contains a combination of active ingredients featuring that single active ingredient (in this case: valsartan+hydrochlorothiazide)?

This was answered in the positive by the CJEU in the *Actavis*-holding of February 9, 2012 (case C-574/11)⁶⁶ as follows:

Articles 4 and 5 of Regulation (EC) No 469/2009 of the European Parliament and of the Council of 6 May 2009 concerning the supplementary protection certificate for medicinal products must be interpreted as meaning that, where a ‘product’ consisting of an active ingredient was protected by a basic patent and the Holder of that patent was able to rely on the protection conferred by that patent for that ‘product’ in order to oppose the marketing of a medicinal product containing that active ingredient in combination with one or more other active ingredients, a supplementary protection certificate granted for that ‘product’ enables its Holder, after the basic patent has expired, to oppose the marketing by a third party of a medicinal product containing that product for a use of the ‘product’, as a medicinal product, which was authorised before that certificate expired.

The holding is somewhat difficult to read. Basically, the Court says that the Owner of an SPC for, say, an antigen A, may enforce that SPC against a product comprising antigen A in combination with other antigens or other active ingredients.

Further details regarding the scope of SPCs may be found in section C.II.1.

⁶⁴ Order of February 9, 2012, Case C-442/11, BeckRS 2012, 80847.

⁶⁵ cf. District Court Düsseldorf, decision of November 8, 2011, docket no. 4b O 66/11, LSK 2012,100260.

⁶⁶ BeckRS 2012, 80847.

E.II.3.h. Plant Variety Rights

On a European level, plant varieties are governed by Regulation (EC) 2100/94⁶⁷ (Plant Variety Right Regulation, see Annex 8 (CPVR)). It should be noted that plants may also be protected under the national laws of the EU member states.

Once granted, the plant variety is protected according to Article 13 *et seq.* of the CPVR.

The scope of protection is determined by the grant decision, i.e. the infringement court is bound by the decision that a specific combination of features of the plant shall be protected. However, in view of the fact that a certain variability is intrinsic to plants, courts acknowledge that the scope of protection shall be extended to cover, to some limited extent, “variations that are to be expected”. This resembles the doctrine of equivalents in patent cases. German courts use the term “tolerance range”⁶⁸. To define the tolerance range, the court determines the features of the plant variety that are listed in the grant decision as they appear when cultivated under the current climatic and other conditions (i.e. in reality). The German Federal Supreme Court acknowledged that the trial judge is generally free to decide how he wants to determine whether a plant variety right is infringed⁶⁹. Courts in Düsseldorf apply the Guidelines of the German *Bundessortenamt* (= Federal Office for Plant Varieties) on Examination on Distinctiveness, Uniformity and Stability to determine whether the attacked plant actually infringes the plant variety right⁷⁰. In contrast to the Düsseldorf courts, the (German) Court of Appeals Karlsruhe⁷¹ determined in a 2004 decision the scope of protection by a botanical comparison of the respective features.

The courts examine feature by feature whether differences exist. This requires that both the protected plant variety and the attacked material are cultivated at the same place and during the same growing season, and are then compared (“comparing cultivation”).

Two different kinds of infringing acts may occur:

First, according to Art. 13 para. 2 CPVR, “variety constituents” or “harvested material of the protected variety” require authorization of the Holder of the variety right as regards:

⁶⁷ Regulation (EC) 2100/94 of July 27, 1994 on Community Plant Variety Rights.

⁶⁸ German Federal Supreme Court, decision of April 23, 2009, docket no. Xa ZR 14/07, BeckRS 2009, 13342; Court of Appeals Düsseldorf, decision of December 21, 2006, docket no. I-2 U 94/05, BeckRS 2007, 02436 – *Lemon Symphony*.

⁶⁹ German Federal Supreme Court, decision of February 14, 2006, docket no. X ZR 94/04, GRUR-RR 2006, 575 – *Melanie*.

⁷⁰ However, the Court of Appeals Düsseldorf held in a decision of April 26, 2007 (docket no. I-2 U 87/01, BeckRS 2007, 18589) that the infringement court is not bound by the amount of plants to be cultivated according to these Guidelines.

⁷¹ Court of Appeals Karlsruhe, decision of May 26, 2004, docket no. 6 U 216/03, GRUR-RR 2004, 283 – *Botanischer Vergleich*.

- a) production or reproduction (multiplication);
- b) conditioning for the purpose of propagation;
- c) offering for sale;
- d) selling or other marketing;
- e) exporting from the community;
- f) importing to the community;
- g) stocking for any of the purposes mentioned in a) to f).

With respect to “harvested material”, protection is only afforded in the event that (1) it was obtained through the unauthorized use of variety constituents, and (2) the Holder of the right did not have sufficient opportunity to exercise his right in relation to said variety constituents (cf. Art. 13 para. 2 CPVR). This limitation prevents the Holder of the right suing based on material harvested from plants that originate from authorized “variety constituents”.

Second, Art. 18 para. 3 CPVR, enjoins use of designations for a botanical species that might be confused with designations of a registered plant variety right.

E.II.4. Effects of the Patent – Overview

According to Art. 64 (1) EPC, any published European patent shall have the same right as a national patent of the designated states. Leaving minor differences between the member states aside, the following acts constitute a use of the invention:

- with respect to a product: to manufacture, offer, market, import/export or use or possess it;
- with respect to a process: to either perform the process, or offer the process to third parties.

According to Art. 64 (2) EPC, protection also extends to the products that directly result from a protected process. Art. 5^{quarter} Paris Convention affords the Patentee protection against importation of such products that are imported and distributed domestically even if the patented process is performed abroad (including in countries where no patent protection exists).

Moreover, contributory (indirect) use of the patent is a well known concept in Europe. The basic concept of contributory (indirect) use extends the scope of protection of a patent to include an offering or delivery of means (products) that put the recipient in a position to make use of the invention.

E.II.5. Issues particular to the life sciences

E.II.5.a. Bolar Provision

In the area of drugs, the research exemption is of particular importance. It is also known as the Bolar Provision or Roche–Bolar–Provision, named after the case *Roche Products v. Bolar Pharmaceutical*⁷². According to this exemption, performing research and tests as part of obtaining approval does not constitute infringement for a limited term before the end of the patent term. It essentially allows generic drug manufacturers to perform certain acts that would otherwise be regarded as an infringement. In Europe, the exemptions are laid down in a number of Directives⁷³ that have been converted into the national laws of the member states of the EU. According to decision **T 223/11 (Ibandronic acid/HOFFMANN – LA ROCHE)**,

the principle behind the Bolar exemption is that generic companies should be in a position to take the necessary preparatory measures in order to be able to enter the market without delay once patent protection expires⁷⁴.

According to Art. 10(6) Directive 2004/27/EC

conducting the necessary studies and trials with a view to the application of paragraphs 1, 2, 3 and 4 [that relate to authorization of generics and biosimilars in the EU] and the consequential practical requirements shall not be regarded as contrary to patent rights or to supplementary protection certificates for medicinal products.

The activities thus exempted are not necessarily covered by (the usual) experimental use exemptions because the exempted studies and trials have a clear commercial motivation, i.e. are not of a purely scientific nature, and may not necessarily lead to more knowledge about the patented drug.

Art. 10(6) Directive 2004/27/EC has been implemented very differently by each member state.

In Germany, the Bolar exemption relates to

studies and trials and the respective practical requirements, that are necessary for obtaining drug authorization for the bringing into commerce in the European Union or for obtaining drug authorization in the EU Member States or in third countries.

The German provision is widely regarded (1) not to distinguish between marketing authorization for generic and innovative drugs and (2) to apply irrespective of whether these authorizations are obtained in Europe or elsewhere.

Other European member states, such as the Netherlands and Belgium are reported to have taken a narrower approach to the Bolar exemption.

⁷² *Roche Products v. Bolar Pharmaceutical*, 733 F 2d 858 (Fed. Cir. 1984), a US case related to the manufacturing of generic pharmaceuticals.

⁷³ EC Directive 2001/82/EC (as amended by Directive 2004/28/EC) and Directive 2001/83/EC (as amended by Directive 2002/98/EC, 2003/63/EC, 2004/24/EC and 2004/27/EC).

⁷⁴ *id.*, point 2, 5th para.

The respective national Bolar exemptions have rather far-reaching economic implications. So far, the Bolar exemptions are clearly not applied equally in all EU countries. It is therefore necessary to obtain specific guidance before entering a particular EU market.

In a still pending case, the Düsseldorf courts (first and second instance) were called to decide whether the Bolar or experimental use exemption only applies to the person actually conducting experiments or research, or whether they also cover a third party selling and/or offering the patented substances to the generic company that wants to obtain drug approval. The District Court Düsseldorf⁷⁵ elaborated in great detail on the Bolar and experimental use exemptions in German Patent Law and noted that deliveries of patented products or substances do not automatically fall under these exemptions. However, it construed the exemptions narrowly: Preparatory actions such as delivery of patented products or substances were not covered by the exemption. As far as other persons – such as a seller of these patented products/substances – were concerned, they would only benefit from the exemptions if they could be seen as co-organizers of the experiments/trials, e.g. if they had their own interest in the pursued approval or authorization or in the results of the studies and trials. However, if the seller pursued an economic profit from the transaction, and the studies/trials that were performed by the buyer were merely desirable or advantageous to him, there was no sufficient reason to exempt such actions from constituting an infringement.

On appeal, the Court of Appeals Düsseldorf⁷⁶ decided to stay the proceedings and refer the following questions to the CJEU:

1. Must Art. 10 para. 6 of Directive 2001/83/EC be interpreted as meaning that those acts of delivery are also excluded from patent protection by which a third party offers or delivers a patented active substance to a manufacturer of generic products for purely commercial reasons, which the manufacturer of generics intends to use for studies or trials in order to obtain a marketing authorisation or approval within the meaning of Art. 10 para. 6 of Directive 2001/83/EC?
2. If this first question is to be answered in the affirmative:
 - a) Does the privileged status of the third party depend on whether the manufacturer of generics supplied indeed uses the provided active substance in privileged studies or trials within the meaning of Art. 10 para. 6 of Directive 2001/83/EC? In such a case, does the exclusion from patent protection also apply if the third party is unaware of its customer's intended privileged use and has not ascertained whether this is the case? Or does the privileged status of the third party merely depend on whether, at the time of the act of delivery, the third party can rightly assume that, judging all of the circumstances (i.e. profile of the supplied company, small amount of the provided active substance, imminent expiration of the patent protection of the relevant active substance, experience gained concerning the customer's reliability), the supplied manufacturer of generics will use the provided active substance for privileged trials and studies in the context of a marketing approval only?

⁷⁵ District Court Düsseldorf, decision of July 26, 2012, docket no. 4a O 282/10, IIC 2013, 361 – *Solifenacin*.

⁷⁶ Court of Appeals Düsseldorf, decision of December 5, 2013, docket no. I-2 U 68/12, BeckRS 2013, 21605.

- b) In the context of its act of delivery, is the third party obliged to take separate precautions to ensure that its customer will indeed use the active substance for privileged trials and studies only or do the precautionary measures of the third party differ, depending on whether the patented active substance is merely offered or actually delivered?

The Court of Appeals summarized its view as follows:

(3) Opinion of the referring court [i.e. Court of Appeals Düsseldorf]

The referring court supports the following approach: Commercial third party acts of delivery are principally also subject to the marketing authorisation privilege pursuant to Sec. 11 No. 2b PatG, Art. 10 Para. 6 of Directive 2001/83/EC. However, when the third party commits the act of delivery, it must be able to assume, given the circumstances, that the delivered active substance will indeed exclusively be used for privileged trials and studies for approval. In this context, the profile of the supplied company, the small amount of the delivered active substance, the imminent expiration of patent protection for the active substance in question and the already acquired experience concerning the reliability of the customer can be relevant. In addition, the third party itself has to take precautionary measures in order to avoid non-privileged use of the delivered active substance wherein the measures to be taken differ, depending on whether the third party merely offers or supplies the patented active substance. In case of offering it suffices to clearly indicate that only small quantities of the product will be delivered and those merely for the purpose of marketing authorisation studies. In case of delivery, the third party and the customer will regularly have to enter into an agreement of use that is subject to an adequate contractual penalty. In individual cases with particular circumstances other measures might be required.

It remains to be seen how the CJEU will decide on this matter. The question at issue in this referral is definitely of importance for the generic industry in Europe, because many generic drug companies rely on deliveries of (patented) compositions from third parties.

In Ireland, the exemption (entered into Irish law in 2006) was interpreted narrowly and only exempted acts carried out by a generic company with a view to obtaining regulatory approval for generic pharmaceutical products. In July 2013, the Irish Government (after an extensive review) approved proposals to amend the National Patent Act in order to expand the reach of the Bolar provisions. It will be expanded to include

all studies, tests, experiments, clinical and field trials and the consequential practical requirements which are necessary for the purpose of obtaining market authorization for new and generic products. In addition, a revised, expanded research exemption will cover acts done in this country relating to the acquisition of a marketing authorization in a Non-EU-country.

A corresponding bill is expected to be implemented in 2015.

In the UK, the initial legislative approach (in 2005) was to adopt only the minimum required by EU legislation. The UK exemption covered only those trials carried out to obtain EU marketing authorizations for generic medicinal products.

The new legislation⁷⁷ was approved by the UK Government on July 14, 2014, and came into effect on October 1, 2014. The legislative change follows

⁷⁷ The Legislative Reform (Patents) Order 2014.

consultations by the UK IP Office (IPO) with pharmaceutical industry stakeholders in 2011 and 2012. The responses to the consultation were in favor of extending the exemption to innovative drugs and bring the UK in line with other EU countries with a more liberal approach to clinical trials. Most notably, the new legislation widens the scope of the UK exemption in the following ways:

- The territorial reach is extended – it now covers acts carried out to provide data to regulatory bodies both within and outside the EU;
- The exemption applies to tests relating to any type of medicinal product – it is no longer limited to generics, but also relates to all new drugs and new combination products;
- It also covers post-authorization testing and health technology assessments.

France exempts from infringement:

Studies and trials needed to obtain a marketing authorization for a medicinal product in any Member State of the European Community or any Member State of the European Economic Area, as well as any acts needed to perform them.

The French version is regarded to cover generic and innovator products. However, it is limited in that it only extends to authorizations for the EU or European Economic Area.

E.II.5.b. Experimental Use

Even before the implementation of Bolar Provisions in Europe, some EU member states provided for experimental use exemptions, for example UK and Germany. These provisions are still in place⁷⁸ and (for instance in Germany, Sec. 11(2) (a) German Patent Act) tie the exemption to

[...] activities performed for experimental purposes relating to the subject matter of the invention [...]

In Germany, the *Clinical Trials I* decision⁷⁹ of the Federal Supreme Court held that tests that implement the invention only as a “means” to conduct studies relating to subject matter different from that of the invention do not benefit from the experimental use exemptions:

[T]he subject matter of the invention must be the object of the test activity for the purpose of gaining knowledge.

Basically, this means that in order to be exempted, experiments must be directed to gaining knowledge *about*, not *with* the invention. In particular, this also has the consequence that patented research tools tend not to be exempted, be-

⁷⁸ E.g., UK: Patents Act of 1977, Sec. 60(5)(b) and Germany: Sec. 11(2)(a) German Patent Act.

⁷⁹ IIC 1997, 103.

cause in using a patented research tool, one takes advantage of the invention to gain information about something else outside of the invention.

However, it is regarded to be permitted (i.e. exempted) if commercial goals are also followed.

Only the compound or process on which the experiments are conducted can benefit from the exemption. The difficulty is to clearly distinguish in cases of biotechnological research which substance is the subject of the research and which substance only serves as a tool.

E.II.5.c. Research Tools

The term “research tools” encompasses products and processes that are used to conduct further research. This includes the whole range of “classical” auxiliary means for scientists such as reagents, test kits, but now also extends to biological research tools such as monoclonal antibodies, enzymes, drug targets, PCR, etc., e.g. means that may help to identify/provide an active agent for a pharmaceutical. The question is, then, whether their use may be exempted under either the Bolar or the experimental use provisions of the EU member states.

It is acknowledged that such research tools are patentable in Europe. If the patent claim protects a research tool as such, the matter is relatively clear-cut: Any research tool that makes use of this claim infringes. In contrast, experiments relating to the patented research tool itself may be exempted, but such cases are probably rare.

However, if the patent protects an object other than the research tool itself, it is debatable whether use of the patent by means of a research tool may be exempted.

There does not seem to be any EU case law on this issue so far. In order for an experimental use to be exempted, Germany requires that it is tied to “the subject matter of the invention”. Therefore, it should be clear that any use of (patented) research tools that is directed towards obtaining scientific findings on objects *other* than the research tool itself, shall not fall under the experimental use exemption, simply because such use is not directed towards obtaining information pertaining to the invention itself. Things may be different, though, when research tools are being used in the context of obtaining drug authorizations. In such cases, the Bolar Provision may apply. However, it would probably overstretch the scope of activities that are exempted under the Bolar Provision if the purpose of obtaining a drug market authorization justified *any* use of patented research tools in the context of obtaining drug approval. In Germany, the scope of exempted activities is limited to those that are “necessary” for obtaining drug authorization but this does not mean that any tool that is used for obtaining the drug for which approval is desired is also exempted from patent infringement.

E.II.5.d. EU Biotech Directive

When dealing with biotechnological material in gene sequences, certain particular provisions come into play: Directive 98/44/EC⁸⁰ (EU Biotech Directive) contains particular articles relating to the scope of protection in Articles 8 *et seq.*

The EU Biotech Directive was adopted by the European Parliament in 1998 after more than 10 years of discussion and needed to be transposed into the national laws of the EU member states by July 30, 2000. Germany, however, implemented this Directive as late as 2005. By now, all EU member states have enacted respective provisions in their national laws.

Art. 8 governs the protection of “biological material”, which is defined by Art. 2(1)(a) to mean “any material containing genetic information and capable of reproducing itself or being reproduced in a biological system”.

The Holder of a patent to such biological material shall be entitled to prohibit the use of patented self-reproducing material as long as the reproduced material is in an identical or divergent form and possesses the same characteristics as the patented biological material (cf. Art. 8(1) EU Biotech Directive).

Art. 8(2) EU Biotech Directive extends the protection of a patent to a process that enables biological material to such reproduced biological material that is derived from the biological material which is directly obtained from the patented process (again, as long as this reproduced material is present in an identical or divergent form and possesses the same characteristics).

With respect to genetic information (e.g. DNA sequences), Art. 9 EU Biotech Directive provides that the protection extends to all material in which the product is incorporated and in which the genetic information is contained and performs its function.

Art. 10 EU Biotech Directive provides for exhaustion of patent protection concerning biological material obtained by propagation. Even though exhaustion provisions had been common in national patent laws of the EU member states even before the Directive was adopted, a particular provision for biological material was necessary because of the material’s ability to reproduce. If biological material is marketed for the purpose of being propagated, the Patentee may not enjoin the distribution of the propagated material within the EU once he (or a third person with his consent) has marketed the biological material in an EU member state. However, material obtained by second-generation propagation is not covered by Art. 10.

Art. 11 establishes the so-called “farmer’s privilege”.

⁸⁰ Directive 98/44/EC of the European Parliament and of the Council of July 6, 1998 on the legal protection of biotechnological inventions (OJ 1998 L 213, p. 13).

E.II.5.e. Limitations of patent protection available to gene sequences – the Monsanto decision

Art. 9 of the aforementioned EU Biotech Directive provides:

The protection conferred by a patent on a product containing or consisting of genetic information shall extend to all material [...] in which the product is incorporated and in which the genetic information is contained and performs its function.

In *Monsanto*⁸¹, the Court was called on to explore the limits of protection in the following scenario: Monsanto held a European patent relating to a DNA sequence which, once introduced into the DNA of a soybean plant, renders it resistant to the herbicide glyphosate. Glyphosate is commonly used in agriculture for killing non-resistant weed. The benefit of the patent is that soybean plants that contain the protected DNA sequence become resistant to the herbicide, allowing selective killing of weeds while the desired soybean plants remain unharmed. Cultivated soybean plants that were genetically modified according to its patent were called “Round up ready (RR) soybean plant”. The Defendant companies imported soy meal from Argentina, where no patent protection for Monsanto existed, into the Netherlands. This soy meal showed traces of the DNA in “RR soybean plants”, indicating that the imported soy meal had been produced using that type of soybean plant.

The fundamental question in this case was how to construe the requirement of Art. 9 of the EU Biotech Directive, providing that the product falling under the scope of protection not only contains the genetic information, but also *performs its function*. The Court held that the genetic information contained in the imported soy meal did not perform its function in the meal. The Court noted that the function of Monsanto’s invention was performed when the protected enzymes were active, i.e. when the genetic information contained in that material provided resistance against the effect of the glyphosate herbicide. However, such resistance was no longer conferred to the soy meal by the DNA sequences contained in this meal not exhibiting any herbicide resistance. Soy meal was the product of several treatment processes and was a dead material. Consequently, it was held that the genetic information contained in such soy meal had ceased to perform the function it performed before, when the soy bean plant was alive.

Monsanto argued that the genetic information contained in the soy meal could eventually and possibly, under proper conditions, perform its function again. However, the Court considered this indecisive, because such “revival” of the functioning of the DNA sequence would actually require it being introduced into another plant.

The Court also stated that adopting the EU Biotech Directive prevented an EU member state from granting absolute protection to a patented DNA sequence as such, i.e. regardless of whether it performs its function in the material

⁸¹ *Monsanto Technology LLC v. Cefetra et al.*, C-428/08, judgment of the court (Grand Chamber) of July 6, 2010.

containing it. This means that the Court regards the EU Biotech Directive as constituting an exhaustive harmonization of the matter in the European Union, and that, consequently, the member states may not implement legislation that extends protection beyond what is provided for in Art. 9 of the EU Biotech Directive.

E.III. Enforcement options

E.III.1. Introduction

A Patentee has various options for enforcing its rights in EU countries. Again, laws of the EU member states vary significantly, even though some EU Regulations and EU Directives have afforded a certain degree of harmonization.

E.III.2. Cease and Desist Letter

Oftentimes, a Patentee may try to resolve a potential patent dispute out of court by sending a cease and desist letter to the suspected Infringer. In such a letter, the Patentee briefly explains the patent and sets out the reasons why it is infringed. The Patentee usually demands that the suspected Infringer

- undertakes to cease ongoing infringement and desist from future infringement;
- renders information about the distribution chain and turnover and profit made with the infringing product;
- recalls the infringing products from the channels of trade;
- destroys any remaining infringing products it has in its possession; and
- compensates it for damages suffered.

The downside of such a cease and desist letter is that it puts the suspected Infringer on notice, i.e. alerts it that it may be sued. This may trigger its decision to initiate a “torpedo action” (cf. chapter E.I.2.c.). However, in Germany, cease and desist requests are still widely used.

E.III.3. Criminal Proceedings

The EU member states differ with respect to whether a patent infringement constitutes a criminal offense. In Germany, for example, infringing a patent intentionally is a criminal offense and is punished either by imposing a fine on the Infringer or even imprisonment of up to 5 years. However, despite the theoretical availability of criminal proceedings in Germany, they are clearly the exception rather than the rule. In the UK, no criminal liability is tied to infringement of patent rights.

E.III.4. Border Seizure

European Regulation EU/608/2013 provides for border seizure by customs. The owner of an IP right may apply for seizure of goods that are imported from or exported to countries that are not member states of the EU or the EEA. Customs may actually seize goods that are (only) suspected of infringing an IP right (among them patents, SPCs for both medical products and plant protection products, plant variety rights (both EU and national)). Seized goods may be destroyed under customs control if both the IP Owner and the Declarant (or Holder) of the goods agree to the destruction. In case the Declarant (or Holder) of the seized goods disagrees, the Patentee shall initiate legal action for patent infringement against him within a period of 10 days, which may be extended by an additional 10 day period. The IP Owner needs to inform customs of the initiation of proceedings, otherwise, the goods are released. Even in the event proceedings have been initiated, the Declarant (or Holder) of the goods may request customs to re-release them if he provides a guarantee that protects the interests of the Patentee, all custom formalities have been completed and no precautionary measures (e.g. a preliminary injunction) have been ordered by a court.

Regulation EU/608/2013 provides for a specific and rapid procedure for the destruction of goods in small consignments. However, this is not applicable for technical intellectual property rights (patents, in particular).

In general, EU custom seizure often turns out to be a fairly efficient means to prevent infringing goods from coming into the EU. Things may be somewhat more complicated in the event the patent is difficult to read and understand or when the imported product must be analysed before it is suspected of infringement. In practice, whether or not border seizure promises to be an effective tool in protecting against patent infringement needs to be decided on a case-by-case basis.

For pharmaceuticals, the 2012 statistics of the customs authorities in Germany reveal that they account for

- 0.84% (equalling € 1.12 m) of the overall value of seized goods
- 1.04% (equalling 272) of the number of overall seizures.

For the EU, the number of seizures of counterfeit pharmaceuticals in recent years is reported to be as follows:

Year	Number of seizures
2005	148
2006	497
2007	2.043
2008	3.207

Year	Number of seizures
2009	3.374
2010	1.812
2011	2.494
2012	2.530
2013	1.175

The retail volume of counterfeit pharmaceuticals was € 27.6 m in 2011, € 8.2 m in 2012 and € 12.0 m in 2013.

It is important to know that some countries have additional – domestic – border measures that may apply in addition to EU laws. National counsel needs to be consulted in any event.

Finally, it is important to note that the EU has to a large extent done away with internal border control measures (Schengen Convention), meaning that once a product has entered the EU, it can cross internal EU borders without being checked by customs. This requires a Patentee to ascertain beforehand at which EU port suspected infringing products are likely to enter the EU, and to instruct local customs accordingly.

E.III.5. Decision on the merits

Most patent litigation is decided by a “full trial” leading to a decision on the merits rendered by the competent civil court. As outlined above (cf. chapter E.I.1.), a Plaintiff which considers taking action against a suspected Infringer should consider carefully where to sue. Length of the trial, potential outcome, expertise of the courts and costs are all factors that a Plaintiff will take into account. Current space constraints preclude even an attempt to describe the different formats of proceedings in the various EU member states. However, we would like to at least highlight which aspects seem of most practical interest for clients.

E.III.5.a. Bifurcation

Some courts in the EU deal with infringement and validity together (such as the UK, France, the Netherlands) while others (most notably Germany) do not. One may certainly take the position that the scope of protection of a patent, given that it plays a role both for infringement and validity, should be determined by one – rather than two – courts, and favor that both are tried before the same court. However, one may also stress that more competent authorities (staffed with technical experts like the EPO or the patent courts of a EU member state) than infringement courts may exist to hear validity issues, and that one

may, in most cases, assume that a granted patent is *prima facie* valid. These considerations tend to favor a decision on infringement and validity by different authorities.

Irrespective of the “better” outcome of a trial (whatever that is), strategic considerations also enter into play when deciding whether a Plaintiff should enforce his patent in a bifurcated system such as Germany or in a non-bifurcated system such as the UK. In a bifurcated system, the civil court may only stay the infringement proceedings until the outcome of the validity proceedings, and in practice will do so only if severe doubts exist that the patent will actually be upheld. As opposed to this, no such delay is to be expected by, say, UK courts, which decide on both infringement and validity; this certainly makes sense to some extent, most notably because the scope of protection is defined by one single court, and differing opinions of different courts on this highly relevant issue are avoided. However, it also means that validity is determined by a judge which is not a technical expert, which may be seen as a disadvantage.

E.III.5.b. Discovery

What also plays a role and is different throughout the EU is the availability and handling of (pre-trial) discovery.

In Germany, for example, one of the fundamental principles is that the Plaintiff bears the sole responsibility of obtaining evidence that establishes infringement. Hence, pre-trial discovery in the meaning commonly used is not permitted under German law. However, some changes were brought about by the Enforcement Directive (Directive 2004/48/EC). Following this, German courts allow for submission of documents or inspection of an object (on particular premises) or even a process (performed on a suspected Infringer's property), always provided that there is an adequate probability that the patent is infringed. This means that, in any event, a Patentee needs to substantiate the claims brought forward and cannot just request inspection of goods and processes without detailed explanation of why infringement is likely to occur. Practice shows that in Germany such requests for inspection, which are granted by way of preliminary injunctions, are not filed frequently. Of the requests made, however, the grant rate is reported to be high.

In contrast, UK courts have known a search and seizure order (formerly known as Anton Piller order) even before the Enforcement Directive came into effect. Such order requires the Defendant to allow Plaintiff's counsel (together with an independent supervisor) to enter Defendant's premises and to allow a search for infringing items and other material (in particular infringing products). To obtain such an order, a Plaintiff needs to provide a very strong *prima facie* case and also needs to establish that the damage resulting from suspected patent infringement may turn out to be very significant. Moreover, the Plaintiff must furnish evidence to the extent that the items and other material to be inspected may be destroyed before any application *inter partes* can be made.

In France, the *saisie-contrefaçon* is ordered to establish proof of infringement. The *saisie-contrefaçon* allows the Patentee to call upon a bailiff to record an infringement. This proceeding is almost always used to establish proof of infringement. It is ordered in *ex parte* proceedings essentially based on a valid title only and can be obtained by the Patentee within a day. The bailiff provides a written description (a report) on what he found and/or may even seize the items in question depending on the terms of the order. Unless the alleged Infringer raises confidentiality issues, the report and/or seized items are handed over to the Patentee to be able to make up his mind concerning infringement. The *saisie-contrefaçon* is reported to be remarkably effective and therefore widely used in patent infringement litigation, as the seizure report and/or seized items provide the court with facts beyond what the parties present. Seizure only remains valid in case court proceedings are initiated within 20 working days or 31 calendar days, whatever comes later.

On request, the bailiff may be accompanied by the Patentee's patent attorney to obtain assistance in technical issues. The bailiff may also request to be accompanied by photographers, technicians or the police.

Both the Anton Piller order and the *saisie-contrefaçon* were known prior to the Enforcement Directive (2004/48/EC). Other countries (such as Italy, Belgium and Spain) had employed measures with a similar effect. Throughout Europe, "measures for preserving evidence" are now provided by the member states due to enactment of the Enforcement Directive.

E.III.5.c. Preliminary Relief/Preliminary Injunctions

Often, a Patentee is interested in resolving the patent dispute quickly. This is true, in particular, for pharma companies in their effort to enforce their patents against generic companies.

There exist important differences as regards availability of preliminary measures. One should, however, take the following into account:

In the Netherlands, *ex parte* injunctions are only available in exceptional cases, for example they may be issued against a distributor when infringement against the manufacturer has already been decided. More frequent in the Netherlands are the so-called "kort geding"-proceedings, which are judgments rendered within a period of about 2–4 months. A Dutch "kort geding" is often deemed very efficient because the Dutch courts accept urgency easily and a trial date is obtained within weeks upon filing the motion by the Plaintiff.

Also, Dutch law allows for accelerated proceedings on the merits with a judgment rendered within 10–11 months.

In the UK, preliminary injunctions in patent matters are available as well. In its recent case *BASF v. Sipcam (UK) Limited* an injunction was granted by the UK High Court⁸² even though the judge left the issue of infringement unde-

⁸² Decision of September 12, 2013, [2013] EWHC 2863 (Pat).

cided. What the judge found conclusive was the conduct of the Defendant, *inter alia* that it had not allowed inspection of its commercial processes and had violated undertakings not to sell its attacked product prior to a certain date.

In *Novartis AG v. Hospira UK Limited*⁸³, the UK Court of Appeal held that a preliminary injunction is not barred even if, in first instance, the patent in suit has been revoked. Two Novartis patents had been invalidated by the High Court. Novartis had appealed this decision and brought infringement proceedings and applied for a preliminary injunction against Defendant Hospira. Initially, the preliminary injunction request was dismissed by the High Court. Despite the fact that the invalidity decision was still on appeal, the Court of Appeal reversed the decision of the High Court and granted the preliminary injunction. The Court of Appeal reasoned that there existed an unquantifiable risk of damage to Novartis (primarily the price erosion to be expected) which outweighed the potential damage to Hospira. The Court of Appeal sided with the Plaintiff in that it regarded the generic manufacturers to have the duty to clear the way before launching new products:

The way to market for a generic manufacturer is not clear until all arguable objections from the Patentee have been eliminated. If the generic manufacturer allows the trial of the action at first instance to coincide with the intended launch date he runs the risk that a successful appeal could get in the way, even if judgment at first instance is given in his favour.

In *Merck and Bristol-Myers Squibb v. Teva et al.*⁸⁴, the UK High Court issued a preliminary injunction against generic manufacturer Teva. The Court found various issues in favor of Patentees. Defendants had been granted a marketing authorization a rather long period of time (22 months) in advance of Patentee's SPC expiry. Despite respective requests of Plaintiffs, Defendants had failed to state their intentions as regards a potential market entry. And, finally, the Court took into account that in another case (unrelated to this litigation), Defendant Teva had launched a generic version of a blockbuster despite previously having provided the Plaintiff/Patentee with an assurance to wait with market entry until expiration of the patent.

In Germany, a preliminary injunction is granted only in urgent matters when the infringement is apparent and the patent is clearly valid. It may be granted within few days upon filing. The threshold requirement is that one does not seriously expect that the preliminary injunction turns out to be unjustified *ex post*. Validity, in particular, is an issue after the landmark *Harnkatheterset*⁸⁵ decision of the Court of Appeals Düsseldorf. It requires, in general, that preliminary injunctions are only available for a patent if it has survived opposition or nullity actions. It is only in exceptional circumstances (such as the fact that renowned companies have taken licenses) that a court may deviate from this rule.

⁸³ Decision of May 22, 2013, [2013] EWCA Civ 583.

⁸⁴ Decision of November 7, 2013, [2013] EWHC 1958 (Pat).

⁸⁵ Court of Appeals Düsseldorf, BeckRS 2010, 15862 – *Harnkatheterset*.

In the area of entry of generics into the market, however, German courts seem to be less hesitant to grant preliminary injunctions than in other areas. According to the *Flupirtin-Maleat* decision of the Court of Appeals Düsseldorf⁸⁶, a preliminary injunction may also be granted if the validity of the patent remains somewhat unclear:

[Exceptional circumstances] are present in case of an infringement by a generic company. While the damage will be enormous in case the patent is upheld and such damage will not be recoverable (in view of the decline of sales prices by determination of fixed prices), a preliminary injunction that turns out to be unjustified in view of a subsequent nullification of the patent-in-suit will only have the effect that the generic company will be kept away from the market without justification, which may be compensated by damage claims against the Patentee. If one takes also into account that the generic company, in general, has not taken any economic risks for being present on the market (because the pharmaceutical has been tested and established on the market by the Patentee), a preliminary injunction needs to be granted, even if no absolute certainty about the validity of the patent may be obtained by the infringement court, but if according to his assessment there are more arguments in favour of validity than against it.

In France, preliminary injunctions may be granted based on Art. L.615–3 of the French Intellectual Property Code, which serves as a basis to grant provisional measures in the event an infringing act has already been committed or is about to be committed. This provision also allows for rendering of *ex parte* decisions. However, French courts are reported to be rather reluctant to render preliminary injunctions. The statutory provision requires the Applicant (Patentee) to establish that it is “likely” that his patent is infringed (or about to be infringed). Reportedly, in the past there have been noticeable differences among the French courts as to whether or not an in-depth examination of validity must be made when determining whether an infringement is “likely”. In its recent *Novartis v. Mylan and Qualimed* decision⁸⁷, the Paris Court of Appeal considered it to be sufficient that, *prima facie*, the patent seems to be valid. Moreover, the court held in this case that the respondents should have challenged the validity of Novartis’ patent sufficiently in advance for obtaining a judgment on validity before launching their product.

In France, a requirement to obtain a preliminary injunction is, in any event, that an action on the merits has been lodged. It takes the courts between 2–4 months to render a decision.

In particular in the area of generics coming on the market, one is well advised to scrutinize differences between the courts, which may be crucial for winning a case.

In most European jurisdictions, applying for or obtaining a market authorization for a generic is not an act of infringement⁸⁸. In its recent *Virostatikum*

⁸⁶ Court of Appeals Düsseldorf, GRUR-RR 2013, 236 – *Flupirtin-Maleat*.

⁸⁷ Court of Appeal of Paris, Decision of March 21, 2012, docket no. 11/12942 (unpublished).

⁸⁸ German Federal Supreme Court, GRUR 1990, 997 – *Ethofumesat*.

decision, the Court of Appeals Düsseldorf⁸⁹ clarified that the mere granting of a market authorization was not enough to establish imminent infringement, even if the generic company did not respond to a warning letter. Moreover, the Court rejected the Applicant's argument that threatened entry into the UK market would constitute an imminent danger of an entry into the German market.

As opposed to this, it was held by the German Federal Supreme Court in *Simvastatin*⁹⁰ that entry of a generic in a pharmaceutical database ("Lauer-Taxe") for distribution constitutes an offering for sale and thus an infringing act in Germany.

Likewise, in the same decision the Court held that even an advertisement published *before* expiration of the patent as regards distribution of a patented product only *after* expiration of the patent would nevertheless constitute infringement. The German court apparently differs on this issue from the UK Patent Court⁹¹.

In its *Desogestrel* decision⁹², the District Court Düsseldorf granted a preliminary injunction taking into account, *inter alia*, that the Respondent (a generic company) had not filed a nullity action, even though there had been opportunity to do so when applying for market authorization many months before coming on the market. The Court acknowledged that in many cases a preliminary injunction is the only means for an Applicant to effectively challenge a generic.

E.IV. Antitrust

E.IV.1. Introduction

Antitrust considerations become even more important in the area of life sciences. On the EU level, the central provisions are Art. 101 and 102 of the Treaty on the Functioning of the European Union ("TFEU"). Violations of these provisions may be fined by the EU Commission. Moreover, if an agreement violates Article 101 TFEU, it may be deemed void. This is particularly important in the area of license agreements.

Highly relevant are also the so-called Block Exemption Regulations of the EU. In the life sciences, the most important of these is Regulation (EC) 772/2004 ("Technology Transfer Regulation"), replaced as per May 1, 2014 by Reg-

⁸⁹ Court of Appeals Düsseldorf, GRUR-RR 2013, 241 – *Virostatikum*.

⁹⁰ German Federal Supreme Court, GRUR 2007, 221 – *Simvastatin*.

⁹¹ Decision of July 20, 1995, Gerber Garment Technology Inc. v. Lectra Systems Ltd., RPC 1995, 383 [412].

⁹² District Court Düsseldorf, BeckRS 2013, 02395 – *Desogestrel*.

ulation (EU) 316/2014⁹³. To provide guidance for practitioners, official Guidelines that elaborate in detail on antitrust issues in technology transfer agreements have been published⁹⁴.

The Technology Transfer Regulation provides for exemption of certain potentially anti-competitive clauses in technology transfer agreements, most notably license agreements. A prerequisite is that the parties to the agreement together have less than 20% (if they are competing undertakings) or less than 30% (if they are not) of the market share. Agreements concluded between parties that exceed these values need to be assessed on a case-by-case basis. In its Art. 4, the Technology Transfer Regulation defines a set of hardcore restrictions that are anti-competitive, making the whole agreement invalid. In Art. 5, certain restrictions are defined that do not benefit from the exemption, but do not make the agreement as such void.

It should be emphasized that restrictions imposed on the Licensee as regards attacks on validity are seen more critically under the new Regulation: No-challenge clauses continue to reap no benefit from the exemption. The right of a Licensors to terminate the license in the event a Licensee undertakes to invalidate the licensed patent is however only automatically exempted in the context of exclusive licenses under the new Regulation.

Chapter 4 of the Guidelines⁹⁵ contains an interesting summary of the Commission's view on patent pools.

E.IV.2. Sector Inquiry (Pharmaceuticals)

In the area of pharmaceuticals, the EU conducted a "sector inquiry" in 2008. Notably, it looked at delays in the market entry of generics. The results of the enquiry have been published by the European Commission in the "Final Report Concluding the Pharmaceutical Sector Inquiry" dated July 8, 2009⁹⁶.

Of particular importance are settlement agreements (i.e. agreements to settle patent-related disputes concerning infringement/validity), because they are suspected of raising antitrust concerns. In this respect, the Commission defines settlements by type, namely

- Type "A": Characteristics: No limitation of generic entry
- Type "B.I.": Characteristics: Limitation of generic entry, but no value transfer from the originator to the generic
- Type "B.II.": Characteristics: Limitation of generic entry and value transfer from the originator to the generic

⁹³ Commission Regulation (EU) No. 316/2014, OJ 2014 L 93, p. 17.

⁹⁴ cf. Guidelines of the Commission, 2004/C 101/02

⁹⁵ Cf. ⁹³.

⁹⁶ Available under http://ec.europa.eu/competition/sectors/pharmaceuticals/inquiry/communication_en.pdf.

On December 9, 2013, DG COMP⁹⁷ published its 4th report on the monitoring in Europe of patent settlements. It perpetuates the distinction between the aforementioned three categories of settlements (A., B.I. and B.II.) depending on whether they contain (1) a limitation on the generic's ability to enter the market with its own product, and (2) a value transfer from the originator to the generic. Agreements containing both are classified as B.II.-Type settlements and regarded as "likely to attract the highest degree of antitrust scrutiny." In contrast, A-Type settlements and B.I.-Type settlements are regarded as rather uncritical because in essence, either the generic company or the originator gives up ("surrenders").

The term "value transfer" is broadly defined and includes all sorts of concessions made by the originator to the generic such as money payments or a grant of license. If the generic's freedom is restricted and the originator makes some concession to reach a compromise, the agreement will be categorized as B.II.-Type. Probably as a consequence of this very strict application of antitrust rules to settlement agreements, B.II.-Type settlements have now practically disappeared.

In practice, one certainly has to act cautiously when settling pharma litigation, and should take into account the Commission's view as expressed in its reports.

E.IV.3. "Pay-for-delay"/ Lundbeck decision

On June 19, 2013, the Commission fined parties of a "pay-for-delay" agreement in the *Lundbeck*-decision⁹⁸. The fines imposed amounted to EUR 145 m. Lundbeck was the originator of Citalopram. Generic competitors were close to entering the market with generic versions of Citalopram. Instead of enforcing its patents against the generic companies, Lundbeck entered into agreements with them to the extent that it paid the generic companies to not compete. The Commission regarded this to be anti-competitive. It stressed that such clauses would go to the detriment of patients, who would be deprived of access to cheaper medicine, and also pointed out that the public health system was harmed because it had to bear the costs of an artificially expensive medicine for a long period of time. Such "pay-for-delay" deals were regarded to constitute a severe infringement of EU Competition Law (Art. 101 TFEU).

⁹⁷ Abbreviation for Directorate-General for Competition, which is responsible for establishing a coherent competition policy for the EU.

⁹⁸ EC Commission, decision of June 19, 2013, COMP/AT.39226 – *Lundbeck*, reasoning unpublished.

E.V. Unitary Patent and Unified Patent Court

E.V.1. Introduction

A few years ago, the European Commission and the European Parliament passed legislation providing an European Patent with unitary effect, commonly referred to as “Unitary Patent”, as well as a Unified Patent Court (UPC). All that is required for the Unitary Patent and the UPC to come into effect is that a sufficient number of EU member states ratify – this is widely expected for 2016.

This will change the European litigation landscape significantly. As was explained in Section E.I., litigation in the EU is currently still fragmented and – leaving cross border injunctions aside – requires a Patentee to enforce its patent in each EPO country separately. This will change with the introduction of the Unitary Patent and the UPC.

Regulation (EU) 1257/2012 is the fundamental legal instrument that establishes the Unitary Patent. It is valid for and grants protection in the territories of all participating EU member states⁹⁹. It will be granted by the EPO upon request by the Applicant. The unitary effect of the European Patent will also be registered at the EPO.

The fees for obtaining a Unitary Patent are still to be determined. It is to be expected that the amount of fees due for the Unitary Patent will influence its acceptance in the industry.

E.V.2. Language

Regulation (EU) 1260/2012 addresses applicable translation arrangements. The general rule is that no further translations are needed when the Unitary Patent is published¹⁰⁰. However, there is a transitional period of up to 12 years during which translations must be furnished, according to the following rules:

- if the language of proceedings in the EPO is French or German, an English translation must be provided;
- if the language of proceedings in the EPO is English, a translation into any other official language of the EU must be provided.

Exceptions will apply in the event of an alleged infringement. According to Art. 4 of Regulation (EU) 1260/2012, the Patentee shall provide, under certain conditions, at its own costs and upon the request of either the alleged Infringer or the court, a full translation of the Unitary Patent. Practitioners should pay attention to Art. 4(4) of Regulation (EU) 1260/2012: In the event the Defendant

⁹⁹ Currently, only Spain and Italy have not acceded.

¹⁰⁰ Cf. Article 3 Regulation (EU) 1260/2012.

is held to infringe a patent written in a foreign language, damage claims may be reduced or excluded until the Plaintiff has provided a translation. This may notably be the case if the Defendant is an NPO, university, small or medium sized entity or an individual.

E.V.3. Unified Patent Court (UPC)

E.V.3.a. Introduction

The UPC is governed by an agreement (UPC Agreement). There will exist a common court for all signatories to the UPC Agreement¹⁰¹. It should be emphasized that it does not have jurisdiction in respect of designations of the European Patent for any other, non-signatory state.

The UPC will have exclusive competence with respect to litigation relating to (classical) European Patents, Unitary Patents and supplementary protection certificates. In particular, this encompasses actions for actual or threatened infringement (and related defences), actions for declaration of non-infringement, actions for provisional and protective measures and injunctions, revocation actions and counterclaims for revocation (cf. Art. 32 UPC Agreement).

National courts will remain competent to hear actions which do not come within the exclusive competence of the UPC. In essence, national courts will continue to hear patent disputes regarding national patents, classical European Patents for which an “opt out” has been notified (cf. below) and, if available, national utility models.

E.V.3.b. Structure

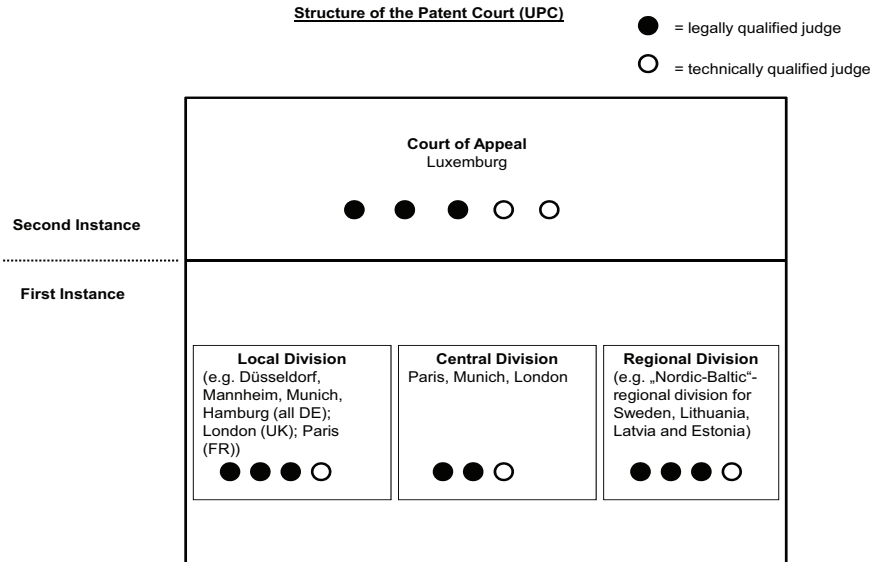
UPCs of first instance will be distributed throughout the EU. There will be a central division located in Paris, with branch offices in London (for chemical/pharmaceutical patents) and Munich (for mechanical engineering patents). The backbone of the UPC, however, is the body of local and regional divisions. In Germany, there will be four local divisions (Munich, Mannheim, Düsseldorf, Hamburg), in the UK and France there will be one each. Other countries will also host a local division. Countries with a limited amount of patent litigation may establish (joint) regional divisions¹⁰². The court of appeals will be located in Luxembourg. In selected cases, the CJEU will hear cases.

The following schematic depicts the structural relationships described above:

¹⁰¹ These are all EU member states except Spain, Poland and Croatia.

¹⁰² Example: Sweden, Finland, Lithuania, Latvia and Estonia announced to create a (joint) regional division. Denmark has announced that it wishes to join this Nordic-Baltic regional division.

Structure of the Patent Court (UPC)



E.V.3.c. Jurisdiction

As a general rule, the central division will be competent to hear (only) stand-alone nullity and non-infringement actions, whereas all other cases are to be brought before the local/regional division.

The general rule is that actions shall be brought before the local/regional division where the infringement has occurred or where the Defendant has its residence or place of business (Art. 33(1) UPC Agreement). If, however, the Defendant has no residence or place of business within one of the contracting member states, the action shall be brought either before the local/regional division where the infringement has occurred or before the central division. If no local/regional division in the contracting member states which would have jurisdiction has been established, the case is heard by the central division.

As noted above, actions for revocation and non-infringement shall be brought before the central division. However, if an infringement action between the same parties and referring to the same patent has been brought before a local/regional division, these actions may only be brought before the local/regional division where the infringement matter is pending.

If, in the course of an infringement action, a counterclaim for revocation is launched (and this will almost always be the case), the local/regional division may (cf. Art. 33(3) UPC-Agreement)

- proceed with both (infringement and revocation) actions;
- refer the counterclaim for revocation to the central division; or

- should the parties agree, refer the whole case (infringement and revocation) to the central division.

Parties may also agree to bring actions before the division of their choice, including the central division.

E.V.3.d. Transitional Period and “opt out”

Exceptions apply during the transitional period, which will last for either 7 or 14 years. During the transitional period, infringement or revocation actions with regard to classical European Patents may still be brought before national courts (Art. 83(1) UPC Agreement). Moreover, the Patentee/Applicant of a classical European Patent may “opt out” from the UPC, unless an action has already been brought before it (Art. 83(3) UPC Agreement). To do so, the Patentee/Applicant must notify the EPO Registry. Such notification to “opt out” may be withdrawn later, subject to certain conditions (sometimes referred to as “opt in”, for further details cf. Art. 83(4) UPC Agreement). One should remember that an “opt out” may be declared only for (classical) European Patents, meaning that it is not available for Unitary Patents.

The “opt out” provision (Art. 83 UPC Agreement) is rather extensively discussed among practitioners. The reason is that the decision as to whether or not to opt out is influenced by the patent strategy under the EPC. Basically, if a Patentee wants to benefit from the EU-wide enforcement option (“one stop shop” for the EU), it will not opt out, i.e. do nothing. In consequence, it risks invalidation of its classical European Patent by the UPC; it puts all its proverbial eggs in one basket. In contrast, if the Patentee of a classical European Patent opts out, the risk is minimized because the UPC is no longer competent to invalidate it throughout Europe; at the same time, an opted out classical European Patent must be enforced as is currently the case, i.e. on a country-by-country basis.

Unfortunately, the wording of Art. 83 UPC Agreement is somewhat unclear and has led to the view that the consequence of opting out is that while the UPC is no longer competent for a specific case in question, the UPC Agreement as such remains applicable. The opposite view is that in the event of an opt out, the UPC Agreement no longer applies, with the effect that the courts must apply their national laws. It remains to be seen how this controversy as regards interpretation of the effect of an opt out on the applicable law will be decided in the end. It would seem that if an opt out is declared, the UPC Agreement as a whole no longer applies, leading to an application of national laws by the national courts. This is also the opinion expressed by the Preparatory Committee in its interpretative note dated January 29, 2014¹⁰³.

¹⁰³ Cf. <http://www.unified-patent-court.org/> NEWS.

E.V.3.e. Panels

The panels of the UPC shall be multinational, i.e. composed of judges with different nationalities.

Moreover, the panels will comprise legally and technically qualified judges. In the local/regional divisions, the panel will comprise three legally qualified judges and additionally one technically qualified judge upon the parties' request or upon the panel's initiative. In the central division, there shall be two legally qualified judges and one technically qualified judge. The appeal panel shall comprise three legally qualified judges and two technically qualified judges¹⁰⁴.

E.V.4. Sources of Law

The UPC will base its decisions on the laws of the European Union, the UPC Agreement, the EPC, certain international agreements and national laws, cf. Art. 24 UPC Agreement.

One should emphasize that the UPC Agreement contains material patent law provisions regarding

- direct infringement (Art. 25),
- contributory infringement (Art. 26), and
- certain exemptions (Art. 27), most notably relating to
 - experimental use (Art. 27 lit. b),
 - the “use of biological material for the purpose of breeding or discovering and developing other plant varieties” (Art. 27 lit. c),
 - a Bolar provision in Art. 27 lit. d), allowing acts according to Art. 13(6) of Directive 2001/82/EC or Art. 10(6) of Directive 2001/83/EC “in respect of any patent covering the product within the meaning of either of those Directives”,
 - a farmer's privilege (Art. 27 lit. i),
 - and also actions exempted under Art. 10 Biotech Directive 98/44/EC (Art. 27 lit. l).

It remains to be seen how the courts will apply the material provisions of the UPC Agreement. So far, there was only EU-wide harmonization as regards interpretation of the EU Directives and Regulations that needed to be transposed into the national laws of the member states. Only a few cases made their way up to the CJEU, namely when a national court identified the need for guidance on an aspect of EU laws. This will change, given that all divisions of the UPC will apply the same laws. Therefore, it is probably fair to expect the development of a new body of case law in the upcoming years. For the most part, it will be for

¹⁰⁴ A training center for the UPC opened in Budapest in March, 2014 – the center will function as a coordinating office for the training of judges and candidate judges of the UPC system.

the UPC of Appeals in Luxembourg to provide guidance. But one should take into account that the CJEU may also decide on selected legal issues.

E.V.5. Provisional Measures

The UPC Agreement empowers the UPC to

- order a party to produce evidence (Art. 59);
- order provisional measures to preserve evidence and the inspection of premises (Art. 60);
- enjoin a party from removing, from the UPC's jurisdiction, any kind of assets (Art. 61);
- order preliminary injunctions and render certain protective measures (Art. 62).

Of particular importance will be preliminary injunctions. According to Art. 62(2) UPC Agreement, the UPC, when considering whether to grant an injunction, shall weigh up the interests of the parties, and shall take into account, in particular, the potential harm for either of the parties resulting from the granting or the refusal of the injunction. According to Rule 209 of the Draft Rules of Procedure of the UPC¹⁰⁵

- the outcome of any opposition proceeding before the EPO (or any other revocation action before a national court);
- the urgency of the case;
- whether the Defendant has been heard; and
- whether any protective letter has been filed

shall be taken into account.

Preliminary injunctions may be granted *ex parte* (i.e. without the Respondent being heard before the UPC issues a preliminary injunction), if this turns out to be necessary. This shall be the case, in particular, if otherwise a delay occurred which caused irreparable harm for the Patentee, or when there is a demonstrable risk of evidence being destroyed (cf. Art. 60(5) UPC Agreement).

E.V.6. Parties and their Representation before the UPC

Apart from the Patentee, the Holder of an exclusive license is entitled to bring actions before the UPC (Art. 47(2) UPC Agreement). The Holder of a non-exclusive license is not entitled to bring actions before the UPC, unless the Patentee has given prior notice and the license agreement permits bringing such

¹⁰⁵ Please note that the Rules of Procedure of the UPC are still under review and have not been enacted; the current version No. 16 can be found under <http://www.unified-patent-court.org/consultations>.

action (Art. 47(3) UPC Agreement). If an action is brought by a licensee, the Patentee shall be entitled to join the action (Art. 47(4) UPC Agreement).

Professional representation before the UPC will be mandatory. A party shall be represented by either a lawyer (which is authorized to practice before a court of a contracting member state) or a European patent attorney who has acquired additional appropriate qualifications¹⁰⁶.

E.V.7. Procedural Issues

Most of the procedural issues will be determined by the Rules of Procedure, which are still under review. The statements made herein are based on the 17th draft dated October 31, 2014. The draft has been published by the Preparatory Committee. The current version has been prepared in response to a wide consultation with practitioners and industry on the previous draft. The current (17th) draft is to be reviewed further. We deliberately refrain from going into detail, simply because by the time this book is published, a new draft will probably be in place. However, we would like to mention the following:

The Rules of Procedure contain detailed provisions (rules) on crucial procedural aspects of patent litigation. One should bear in mind that these rules govern all patent litigation before the UPC, i.e. patent litigation in as many as 25 different member states. However, all of these member states have established their own (national) procedural laws and certain “dos and don’ts” in (patent) litigation over the past years. Therefore, it is indispensable that detailed provisions are enacted that govern the rules to be taken into account by any party making an appearance before the (new) UPC. Nonetheless, it remains to be seen how the attorneys and judges from the various member states actually practice the rules.

Part 1 of the Rules of Procedure deals with the procedures before the court of first instance. It is divided into several chapters:

- Chapter 1 deals with written procedures in the various types of action available:
 - infringement actions (Sec. 1)
 - revocation actions (Sec. 2)
 - action for declaration of non-infringement (Sec. 3)
 - actions within Articles 33(5) (i.e. counterclaim for revocation) and 33(6) UPC-Agreement (i.e. stay of non-infringement action in case of a follow-up infringement action) (Sec. 4)
 - actions for compensation for licenses (Sec. 5)
 - actions against decisions of the EPO (Sec. 6)

¹⁰⁶ Cf. Article 48 UPC Agreement, mentioning, as an example, an European Patent Litigation Certificate; however details are still uncertain.

- The next step in the proceedings shall be “interim procedures”, regulated in Chapter 2.
- Next comes the oral procedure (hearing) regulated in Chapter 3.
- Chapter 4 regulates specific procedures for the determination of damages and compensation.
- Chapter 5 regulates the procedure for the cost decision and Chapter 6 for the security for costs.

Part 2 deals with evidence, i.e.

- witnesses and experts of the parties (Chapter 1)
- court experts (Chapter 2)
- orders to produce evidence and to communicate information (Chapter 3)
- orders to preserve evidence (*saisie*) and order for inspection (Chapter 4)

Part 3 contains rules for provisional measures.

Part 4 covers the procedures before the court of appeal.

Part 5 contains general provisions on important procedural issue such as

- service (Chapter 2)
- rights and obligations of representatives (Chapter 3)
- stay of proceedings (Chapter 4)
- (calculation of) time periods (Chapter 5)
- parties to proceedings (Chapter 6)
- miscellaneous provisions on languages (Chapter 7)
- case management (Chapter 8)
- rules relating to the organisation of the court (Chapter 9)
- decisions and orders (Chapter 10)
- decisions by default (Chapter 11)
- actions bound to fail or manifestly inadmissible (Chapter 12)
- settlements (Chapter 13)

Finally, Part 6 contains rules on fees and legal aid.

ANNEX 1

Relevant Provisions of the EPC: Articles

Article 2

European patent

- (1) Patents granted under this Convention shall be called European patents.
- (2) The European patent shall, in each of the Contracting States for which it is granted, have the effect of and be subject to the same conditions as a national patent granted by that State, unless this Convention provides otherwise.

Article 52

Patentable inventions

- (1) European patents shall be granted for any inventions, in all fields of technology, provided that they are new, involve an inventive step and are susceptible of industrial application.
- (2) The following in particular shall not be regarded as inventions within the meaning of paragraph 1:
 - (a) discoveries, scientific theories and mathematical methods;
 - (b) aesthetic creations;
 - (c) schemes, rules and methods for performing mental acts, playing games or doing business, and programs for computers;
 - (d) presentations of information.
- (3) Paragraph 2 shall exclude the patentability of the subject-matter or activities referred to therein only to the extent to which a European patent application or European patent relates to such subject-matter or activities as such.

See decisions of the Enlarged Board of Appeal G 1/98, G 1/03, G 2/03

Article 53

Exceptions to patentability

- European patents shall not be granted in respect of:
- (a) inventions the commercial exploitation of which would be contrary to “ordre public” or morality; such exploitation shall not be deemed to be so contrary merely because it is prohibited by law or regulation in some or all of the Contracting States;
 - (b) plant or animal varieties or essentially biological processes for the production of plants or animals; this provision shall not apply to microbiological processes or the products thereof;
 - (c) methods for treatment of the human or animal body by surgery or therapy and diagnostic methods practised on the human or animal body; this provision

shall not apply to products, in particular substances or compositions, for use in any of these methods.

See decisions of the Enlarged Board of Appeal G 3/95, G 1/98, G 1/03, G 2/03, G 1/04, G 2/06, G 01/07, G 2/08

Article 54

Novelty

(1) An invention shall be considered to be new if it does not form part of the state of the art.

(2) The state of the art shall be held to comprise everything made available to the public by means of a written or oral description, by use, or in any other way, before the date of filing of the European patent application.

(3) Additionally, the content of European patent applications as filed, the dates of filing of which are prior to the date referred to in paragraph 2 and which were published on or after that date, shall be considered as comprised in the state of the art.

(4) Paragraphs 2 and 3 shall not exclude the patentability of any substance or composition, comprised in the state of the art, for use in a method referred to in Article 53(c), provided that its use for any such method is not comprised in the state of the art.

(5) Paragraphs 2 and 3 shall also not exclude the patentability of any substance or composition referred to in paragraph 4 for any specific use in a method referred to in Article 53(c), provided that such use is not comprised in the state of the art.

See decisions/opinions of the Enlarged Board of Appeal G 2/88, G 6/88, G 1/92, G 3/93, G 1/98, G 2/98, G 3/98, G 2/99, G 1/03, G 2/03, G 2/08

Article 55

Non-prejudicial disclosures

(1) For the application of Article 54, a disclosure of the invention shall not be taken into consideration if it occurred no earlier than six months preceding the filing of the European patent application and if it was due to, or in consequence of:

(a) an evident abuse in relation to the applicant or his legal predecessor, or

(b) the fact that the applicant or his legal predecessor has displayed the invention at an official, or officially recognised, international exhibition falling within the terms of the Convention on international exhibitions signed at Paris on 22 November 1928 and last revised on 30 November 1972.

(2) In the case of paragraph 1(b), paragraph 1 shall apply only if the applicant states, when filing the European patent application, that the invention has been so displayed and files a supporting certificate within the time limit and under the conditions laid down in the Implementing Regulations.

See decisions of the Enlarged Board of Appeal G 3/98, G 2/99

Article 56**Inventive step**

An invention shall be considered as involving an inventive step if, having regard to the state of the art, it is not obvious to a person skilled in the art. If the state of the art also includes documents within the meaning of Article 54, paragraph 3, these documents shall not be considered in deciding whether there has been an inventive step.

See decisions/opinions of the Enlarged Board of Appeal G 2/98, G 3/98, G 2/99, G 1/03, G 2/03

Article 57**Industrial application**

An invention shall be considered as susceptible of industrial application if it can be made or used in any kind of industry, including agriculture.

See decisions of the Enlarged Board of Appeal G 1/03, G 2/03, G 1/04

Article 63**Term of the European patent**

(1) The term of the European patent shall be 20 years from the date of filing of the application.

(2) Nothing in the preceding paragraph shall limit the right of a Contracting State to extend the term of a European patent, or to grant corresponding protection which follows immediately on expiry of the term of the patent, under the same conditions as those applying to national patents:

(a) in order to take account of a state of war or similar emergency conditions affecting that State;

(b) if the subject-matter of the European patent is a product or a process for manufacturing a product or a use of a product which has to undergo an administrative authorisation procedure required by law before it can be put on the market in that State.

(3) Paragraph 2 shall apply *mutatis mutandis* to European patents granted jointly for a group of Contracting States in accordance with Article 142.

(4) A Contracting State which makes provision for extension of the term or corresponding protection under paragraph 2(b) may, in accordance with an agreement concluded with the Organisation, entrust to the European Patent Office tasks associated with implementation of the relevant provisions.

Article 64**Rights conferred by a European patent**

(1) A European patent shall, subject to the provisions of paragraph 2, confer on its proprietor from the date on which the mention of its grant is published in the European Patent Bulletin, in each Contracting State in respect of which it is granted, the same rights as would be conferred by a national patent granted in that State.

(2) If the subject-matter of the European patent is a process, the protection conferred by the patent shall extend to the products directly obtained by such process.

(3) Any infringement of a European patent shall be dealt with by national law.

See decisions of the Enlarged Board of Appeal G 2/88, G 1/98

Article 69

Extent of protection

(1) The extent of the protection conferred by a European patent or a European patent application shall be determined by the claims. Nevertheless, the description and drawings shall be used to interpret the claims.

(2) For the period up to grant of the European patent, the extent of the protection conferred by the European patent application shall be determined by the claims contained in the application as published. However, the European patent as granted or as amended in opposition, limitation or revocation proceedings shall determine retroactively the protection conferred by the application, in so far as such protection is not thereby extended.

The Protocol on the Interpretation of Article 69 EPC is an integral part of the Convention pursuant to Article 164, paragraph 1).

See decisions of the Enlarged Board of Appeal G 2/88, G 6/88

Protocol on the Interpretation of Article 69 EPC of 5 October 1973 as revised by the Act revising the EPC of 29 November 2000

Article 1

General principles

Article 69 should not be interpreted as meaning that the extent of the protection conferred by a European patent is to be understood as that defined by the strict, literal meaning of the wording used in the claims, the description and drawings being employed only for the purpose of resolving an ambiguity found in the claims. Nor should it be taken to mean that the claims serve only as a guideline and that the actual protection conferred may extend to what, from a consideration of the description and drawings by a person skilled in the art, the patent proprietor has contemplated. On the contrary, it is to be interpreted as defining a position between these extremes which combines a fair protection for the patent proprietor with a reasonable degree of legal certainty for third parties.

Article 2

Equivalents

For the purpose of determining the extent of protection conferred by a European patent, due account shall be taken of any element which is equivalent to an element specified in the claims.

Article 82**Unity of invention**

The European patent application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept.

See decision/opinion of the Enlarged Board of Appeal G 1/91, G 2/92

Article 83**Disclosure of the invention**

The European patent application shall disclose the invention in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art.

See decision/opinion of the Enlarged Board of Appeal G 2/93, G 2/98

Article 84**Claims**

The claims shall define the matter for which protection is sought. They shall be clear and concise and be supported by the description.

See decisions/opinions of the Enlarged Board of Appeal G 2/98, G 1/03, G 2/03, G 1/04

Article 87**Priority right**

(1) Any person who has duly filed, in or for

(a) any State party to the Paris Convention for the Protection of Industrial Property or

(b) any Member of the World Trade Organization,

an application for a patent, a utility model or a utility certificate, or his successor in title, shall enjoy, for the purpose of filing a European patent application in respect of the same invention, a right of priority during a period of twelve months from the date of filing of the first application.

(2) Every filing that is equivalent to a regular national filing under the national law of the State where it was made or under bilateral or multilateral agreements, including this Convention, shall be recognised as giving rise to a right of priority.

(3) A regular national filing shall mean any filing that is sufficient to establish the date on which the application was filed, whatever the outcome of the application may be.

(4) A subsequent application in respect of the same subject-matter as a previous first application and filed in or for the same State shall be considered as the first application for the purposes of determining priority, provided that, at the date of filing the subsequent application, the previous application has been withdrawn, abandoned or refused, without being open to public inspection and without leaving any rights outstanding, and has not served as a basis for claiming a right of priority. The previous application may not thereafter serve as a basis for claiming a right of priority.

(5) If the first filing has been made with an industrial property authority which is not subject to the Paris Convention for the Protection of Industrial Property or the Agreement Establishing the World Trade Organization, paragraphs 1 to 4 shall apply if that authority, according to a communication issued by the President of the European Patent Office, recognises that a first filing made with the European Patent Office gives rise to a right of priority under conditions and with effects equivalent to those laid down in the Paris Convention.

See decisions/opinions of the Enlarged Board of Appeal G 3/93, G 2/95, G 2/98, G 1/03, G 2/03

Article 88

Claiming priority

(1) An applicant desiring to take advantage of the priority of a previous application shall file a declaration of priority and any other document required, in accordance with the Implementing Regulations.

(2) Multiple priorities may be claimed in respect of a European patent application, notwithstanding the fact that they originated in different countries. Where appropriate, multiple priorities may be claimed for any one claim. Where multiple priorities are claimed, time limits which run from the date of priority shall run from the earliest date of priority.

(3) If one or more priorities are claimed in respect of a European patent application, the right of priority shall cover only those elements of the European patent application which are included in the application or applications whose priority is claimed.

(4) If certain elements of the invention for which priority is claimed do not appear among the claims formulated in the previous application, priority may nonetheless be granted, provided that the documents of the previous application as a whole specifically disclose such elements.

See decision/opinion of the Enlarged Board of Appeal G 3/93, G 2/98

See decision of the President of the EPO dated 17.03.2009, OJ EPO 2009, 236

Article 89

Effect of priority right

The right of priority shall have the effect that the date of priority shall count as the date of filing of the European patent application for the purposes of Article 54, paragraphs 2 and 3, and Article 60, paragraph 2.

See decisions/opinions of the Enlarged Board of Appeal G 3/93, G 2/98, G 3/98, G 2/99

Article 153

The European Patent Office as designated Office or elected Office

(1) The European Patent Office shall be

(a) a designated Office for any State party to this Convention in respect of which the PCT is in force, which is designated in the international application and for which the applicant wishes to obtain a European patent, and

(b) an elected Office, if the applicant has elected a State designated pursuant to letter (a).

(2) An international application for which the European Patent Office is a designated or elected Office, and which has been accorded an international date of filing, shall be equivalent to a regular European application (Euro-PCT application).

(3) The international publication of a Euro-PCT application in an official language of the European Patent Office shall take the place of the publication of the European patent application and shall be mentioned in the European Patent Bulletin.

(4) If the Euro-PCT application is published in another language, a translation into one of the official languages shall be filed with the European Patent Office, which shall publish it. Subject to Article 67, paragraph 3, the provisional protection under Article 67, paragraphs 1 and 2, shall be effective from the date of that publication.

(5) The Euro-PCT application shall be treated as a European patent application and shall be considered as comprised in the state of the art under Article 54, paragraph 3, if the conditions laid down in paragraph 3 or 4 and in the Implementing Regulations are fulfilled.

(6) The international search report drawn up in respect of a Euro-PCT application or the declaration replacing it, and their international publication, shall take the place of the European search report and the mention of its publication in the European Patent Bulletin.

(7) A supplementary European search report shall be drawn up in respect of any Euro-PCT application under paragraph 5. The Administrative Council may decide that the supplementary search report is to be dispensed with or that the search fee is to be reduced.

See decision of the Enlarged Board of Appeal G 4/08.

Article 164

Implementing Regulations and Protocols

(1) The Implementing Regulations, the Protocol on Recognition, the Protocol on Privileges and Immunities, the Protocol on Centralisation, the Protocol on the Interpretation of Article 69 and the Protocol on Staff Complement shall be integral parts of this Convention.

(2) In case of conflict between the provisions of this Convention and those of the Implementing Regulations, the provisions of this Convention shall prevail.

See decisions/opinions of the Enlarged Board of Appeal G 2/95, G 6/95, G 1/02

ANNEX 2

Relevant Provisions of the EPC: Rules relating to Biotechnological Inventions – Patentability

Rule 26

General and definitions

(1) For European patent applications and patents concerning biotechnological inventions, the relevant provisions of the Convention shall be applied and interpreted in accordance with the provisions of this Chapter. Directive 98/44/EC of 6 July 1998* on the legal protection of biotechnological inventions shall be used as a supplementary means of interpretation.

(2) “Biotechnological inventions” are inventions which concern a product consisting of or containing biological material or a process by means of which biological material is produced, processed or used.

(3) “Biological material” means any material containing genetic information and capable of reproducing itself or being reproduced in a biological system.

(4) “Plant variety” means any plant grouping within a single botanical taxon of the lowest known rank, which grouping, irrespective of whether the conditions for the grant of a plant variety right are fully met, can be:

(a) defined by the expression of the characteristics that results from a given genotype or combination of genotypes,

(b) distinguished from any other plant grouping by the expression of at least one of the said characteristics, and

(c) considered as a unit with regard to its suitability for being propagated unchanged.

(5) A process for the production of plants or animals is essentially biological if it consists entirely of natural phenomena such as crossing or selection.

(6) “Microbiological process” means any process involving or performed upon or resulting in microbiological material.

*: see ANNEX 6, EU Regulations

See decisions of the Enlarged Board of Appeal G 1/98, G 2/06

Rule 27

Patentable biotechnological inventions

Biotechnological inventions shall also be patentable if they concern:

(a) biological material which is isolated from its natural environment or produced by means of a technical process even if it previously occurred in nature;

(b) plants or animals if the technical feasibility of the invention is not confined to a particular plant or animal variety;

(c) a microbiological or other technical process, or a product obtained by means of such a process other than a plant or animal variety.

Rule 28

Exceptions to patentability

Under Article 53(a), European patents shall not be granted in respect of biotechnological inventions which, in particular, concern the following:

- (a) processes for cloning human beings;
- (b) processes for modifying the germ line genetic identity of human beings;
- (c) uses of human embryos for industrial or commercial purposes;
- (d) processes for modifying the genetic identity of animals which are likely to cause them suffering without any substantial medical benefit to man or animal, and also animals resulting from such processes.

See decision of the Enlarged Board of Appeal G 2/06

Rule 29

The human body and its elements

(1) The human body, at the various stages of its formation and development, and the simple discovery of one of its elements, including the sequence or partial sequence of a gene, cannot constitute patentable inventions.

(2) An element isolated from the human body or otherwise produced by means of a technical process, including the sequence or partial sequence of a gene, may constitute a patentable invention, even if the structure of that element is identical to that of a natural element.

(3) The industrial application of a sequence or a partial sequence of a gene must be disclosed in the patent application.

ANNEX 3

Relevant Provisions of the EPC: Rules relating to Biotechnological Inventions – Biological Sequences

Rule 30

Requirements of European patent applications relating to nucleotide and amino acid sequences

(1) If nucleotide or amino acid sequences are disclosed in the European patent application, the description shall contain a sequence listing conforming to the rules laid down by the President of the European Patent Office for the standardised representation of nucleotide and amino acid sequences.

(2) A sequence listing filed after the date of filing shall not form part of the description.

(3) Where the applicant has not filed a sequence listing complying with the requirements under paragraph 1 at the date of filing, the European Patent Office shall invite the applicant to furnish such a sequence listing and pay the late furnishing fee. If the applicant does not furnish the required sequence listing and pay the required late furnishing fee within a period of two months after such an invitation, the application shall be refused.

See decision of the President of the EPO, OJ EPO 2011, 372, and the notice from the EPO, OJ EPO 2011, 376

OJ EPO 2011, 372 – Decision of the President of the European Patent Office dated 28 April 2011 on the filing of sequence listings

The President of the European Patent Office (EPO), having regard to Article 10(2) EPC, Rules 2, 30(1), 68(2), 73(2) and 163(3) EPC and Rule 13ter PCT, has decided as follows:

Article 1 Filing of sequence listings in respect of European patent applications

(1) If nucleotide or amino acid sequences are disclosed in a European patent application, the description must contain a sequence listing in electronic form complying with WIPO Standard ST.25⁸.

(2) The sequence listing under (1) is to be filed on an admissible electronic data carrier¹. If the sequence listing is also filed on paper, the applicant shall submit a statement that the sequence listings in electronic form and on paper are identical.

Article 2 Subsequent filing of sequence listings

(1) Where the applicant has not filed a Standard-compliant sequence listing in electronic form at the date of filing the European patent application, the EPO shall invite the applicant under Rule 30(3) EPC to file such a sequence listing and to pay the late furnishing fee within a non-extendable period of two months from the invitation.

(2) Sequence listings filed after the date of filing of the European patent application must be accompanied by a statement that the sequence listing does not include matter which goes beyond the content of the application as filed.

Article 3 Unreadable, incomplete or infected files

(1) If a file containing a sequence listing is unreadable or incomplete, the unreadable or incomplete part shall be deemed not to have been filed.

(2) If a file containing a sequence listing is infected with a computer virus or if it contains other harmful software, the file shall be deemed to be unreadable. The EPO shall not be obliged to open or process it.

(3) If a file containing a sequence listing is defective within the meaning of (1) or (2) at the time of filing, the applicant shall be informed forthwith. Article 2 of the present decision shall apply *mutatis mutandis*.

Article 4 Furnishing of sequence listings to the EPO acting as international authority under the PCT

Where a sequence listing in electronic form and compliant with WIPO Standard ST.25 is not available to the EPO as International Searching Authority, Supplementary International Searching Authority or International Preliminary Examining Authority, the applicant shall be invited to furnish such a sequence listing under Rule 13ter.1(a) PCT and to pay the late furnishing fee under Rule 13ter.1(c) PCT within a non-extendable period of one month from the date of the invitation.

Article 5 Filing sequence listings with the EPO as designated or elected Office

On invitation to file a Standard-compliant sequence listing under Rule 163(3) EPC, Articles 1, 2 and 3 of the present decision shall apply *mutatis mutandis*.

Article 6 Publication and conversion of sequence listings by the EPO

(1) A sequence listing filed at the date of filing of the European patent application shall be published with the application documents (Rule 68(1) EPC) and the patent specification (Rule 73 EPC) as part of the description.

(2) Sequence listings filed in electronic form shall be converted *ex officio* for the purpose of publication and file inspection. A copy of the original file submitted by the applicant shall be made available on request.

Article 7 Previous decisions superseded

With the entry into force of this decision, the decision of the President of the EPO dated 12 July 2007 concerning the filing of sequence listings (Special edi-

tion No. 3, OJ EPO 2007, C.1.) in the version amended by the decision of the President of the EPO dated 26 March 2010 concerning the furnishing of sequence listings to the EPO acting as international authority under the Patent Cooperation Treaty (PCT) (OJ EPO 2010, 328) shall cease to have effect.

Article 8 Entry into force

This decision shall enter into force on 1 June 2011 and apply to all European patent applications and international patent applications filed in accordance with the PCT on or after that date or pending on that date.

Done at Munich, 28 April 2011

Benot BATTISTELLI President

¹ See Article 2 of the decision of the President of the EPO dated 12 July 2007 concerning the electronic signatures, data carriers and software to be used for the electronic filing of patent applications and other documents, Special edition No. 3, OJ EPO 2007, A.5.

& available from WIPO: http://www.wipo.int/standards/en/part_03_standards.html

Notice from the European Patent Office dated 18 October 2013 concerning the filing of sequence listings

This notice complements the decision of the President on the filing of sequence listings¹ (hereinafter referred to as the “decision of the President”) and describes the procedure under the EPC and PCT for the filing of sequence listings. It has been updated in order to take into account recent changes in said procedure triggered, inter alia, by decisions of the EPO’s boards of appeal.

I. European patent grant procedure

1. Filing of sequence listings

1.1 If nucleotide or amino acid sequences are disclosed in a European patent application, the description must contain a sequence listing complying with WIPO Standard ST.25 (Standard for the Presentation of Nucleotide and Amino Acid Sequence Listings in Patent Applications – hereinafter referred to as the “Standard”) (Rule 30(1) EPC in conjunction with Article 1 of the decision of the President).

1.2 You can consult and download the current version of the Standard on the WIPO website under “Patents” – “WIPO Standards”. The Standard describes in detail both the formal requirements for the filing of Standard-compliant sequence listings and how the sequences contained therein are to be presented.

1.3 The EPO recommends the use of BiSSAP software, which can be downloaded free of charge from the EPO website, to generate Standard-compliant se-

quence listings. Using the latest version of this software enables applicants to meet the formal requirements of the Standard. Applicants are still free to use other software such as PatentIn.

1.4 Under Article 1(1) of the decision of the President, sequence listings must be submitted in electronic form, i.e. in text format (TXT). Further information about the document format is set out in the Standard. The sequence listing should no longer be filed on paper or, in the case of electronic filing of the application, in PDF format (see Article 1(1) and (2) of the decision of the President). If the applicant also files the sequence listing of his own accord on paper or in PDF format, he must submit a statement that the sequence listings in electronic form and on paper or in PDF format are identical. In this case, the paper or PDF form will be disregarded in the further procedure.

1.5 A Standard-compliant sequence listing in TXT format must be filed for all sequence information that conforms to the length thresholds defined in the Standard (see No. 2(ii)), irrespective of whether this sequence information is claimed or not. As an exception, sequences which belong to the prior art and can be found in publicly accessible sequence databases do not need to be included in the sequence listing if they have been identified by their database accession number and either the version number or the database release number in the application as originally filed. This applies even if reference is made to these sequences in one or more claims or if the sequences are essential features of the invention or necessary for the prior-art search (see J 8/11 of 30 January 2013). If the European patent application discloses nucleotide or amino acid sequences that are fragments or variants of a prior-art sequence, a sequence listing complying with WIPO Standard ST.25 has to be filed for these sequence fragments or variants.

1.6 A sequence listing filed together with the application documents is part of the description. In calculating the additional fee under Rule 38(2) EPC and Article 2, 1a RFees, the pages of the sequence listing are disregarded as long as the listing complies with the Standard and is filed as a separate part of the description. If the sequence information in the sequence listing is reproduced in the description or in other parts of the application, contrary to the recommendation in the Standard, the pages concerned will be taken into account in the calculation of the additional fee (see the notice from the EPO dated 26 January 2009 concerning the 2009 fee structure, OJ EPO 2009, 118, point 3.2; see also the Guidelines for Examination in the EPO (“Guidelines”), A-III, 13.2).

1.7 The above relates equally to European divisional applications. As an independent European patent application, a divisional application must also satisfy the requirements of Rule 30 EPC in conjunction with the decision of the President (see G 1/05, OJ EPO 2008, 271, point 3.1 of the Reasons). Without prejudice to the requirements of Article 76(1), second sentence, EPC, if a sequence listing is to form part of the description of the divisional application, it must be submitted together with the other documents making up the divisional application, unless reference is made to a previously filed application contain-

ing a sequence listing as part of the application (Rule 40(1)(c) EPC). However, an applicant who has filed a Standard-compliant sequence listing in TXT format under Rule 30 EPC with regard to the earlier application (parent application) is exempted from having to submit said sequence listing for search purposes only (i.e. not as part of the description) in respect of the divisional application. The Office will add a copy of the Standard-compliant sequence listing in TXT format filed in conjunction with the earlier application for search purposes only (i.e. not as part of the application) to the dossier on the divisional application.

2. Subsequently filed sequence listings/correction of errors – late furnishing fee – loss of rights

2.1 Where the applicant has not filed a Standard-compliant sequence listing in TXT format at the date of filing the European patent application, the Receiving Section will inform the applicant of the deficiencies in question and invite him to file a Standard-compliant sequence listing in TXT format and pay the late furnishing fee within a non-extendable period of two months (Rule 30(1) and (3) EPC in conjunction with Article 2(1) of the decision of the President).

2.2 Where the applicant fails to file a Standard-compliant sequence listing in TXT format and pay the late furnishing fee in due time, the application will be refused under Rule 30(3) EPC. This also applies if a sequence listing is subsequently filed in TXT format but still contains deficiencies with respect to the Standard. Such deficiencies will not prompt the EPO to issue another invitation under Rule 30(3) EPC, triggering a new period of two months, unless the previous invitation did not draw the applicant's attention to such remaining deficiencies (see J 7/11 of 24 January 2012, point 10 of the Reasons).

2.3 If the application is refused under Rule 30(3) EPC, the applicant can request further processing under Article 121 and Rule 135 EPC. A further processing fee is payable for each omitted act.

2.4 A subsequently filed sequence listing may contain only the sequence information – in standardised form – contained in the original application documents. It may contain neither more nor fewer sequences than the number of sequences disclosed in the original description, and the numbering of the sequences must remain unchanged. The applicant must ensure that this is the case and submit a statement to that effect under Article 2(2) of the decision of the President. It is recommended that the statement is worded as set out in the footnote².

2.5 A sequence listing filed after the date of filing is not part of the description and therefore cannot be used to determine the originally disclosed content of the application (Rule 30(2) EPC). It can only be used for the purposes of the search, and is not published with the application documents or patent specification.

2.6 Without prejudice to Rule 30 EPC, a sequence listing forming part of the description may be corrected or amended in accordance with Rule 139 and/or Article 123(2) EPC. In this case a complete new sequence listing in TXT format containing the corrections or amendments is to be filed.

II. Procedure before the EPO as international authority under the PCT

1. If the international application discloses one or more nucleotide and/or amino acid sequences and if a Standard-compliant sequence listing in TXT format is not available to the EPO as International Searching Authority (ISA), Authority specified for supplementary search (SISA) or International Preliminary Examining Authority (IPEA), the EPO will invite the applicant to furnish to it such a sequence listing under Rule 13ter.1(a) PCT within a non-extendable period of one month from the date of the invitation (Article 4 of the decision of the President).

2. The furnishing of a sequence listing in response to an invitation by the EPO as ISA, SISA or IPEA under Rule 13ter.1(a) PCT is subject to the payment of the late furnishing fee fixed by the President (see Rule 13ter.1(c) PCT and Article 4 of the decision of the President). The late furnishing fee may be refunded only where the amount was paid by mistake, without cause, or in excess of the amount due (Agreement between the EPO and the IB of WIPO, Annex C, Part II, paragraph (1)³).

3. Any Standard-compliant sequence listing in TXT format furnished by the applicant under Rule 13ter PCT for the purposes of the search only must be accompanied by a statement to the effect that the sequence listing does not include matter which goes beyond the disclosure in the international application as filed and/or that the Standard-compliant sequence listing in TXT format furnished under Rule 13ter PCT is identical to the sequence listing in the international application (Annex C, paragraphs 4(v) and (vi)). Any sequence listing furnished under Rule 13ter PCT is not part of the international application.

4. If the applicant fails to furnish the required Standard-compliant sequence listing in TXT format and pay the late furnishing fee due within the period under Article 4 of the decision of the President, the EPO as ISA will issue no further invitation to furnish the sequence listing, and will search the international application only to the extent that a meaningful search can be carried out without the sequence listing (Rule 13ter.1(d) PCT). In this case, the international search report will either indicate that certain claims were found unsearchable or will be replaced by the declaration under Article 17(2)(a) PCT. However, if the Standard-compliant sequence listing in TXT format is received and the late furnishing fee paid after the applicable period yet before the start of the international search, the Standard-compliant sequence listing will be considered as having been received within that period.

5. A sequence listing in TXT format that contains (minor) deficiencies with respect to the Standard is deemed to comply with this Standard where these deficiencies may be corrected ex officio or under Rule 26 PCT or otherwise rectified under Rule 91.1(b)(ii) to (iv) PCT, as the case may be. In the latter two cases a complete new sequence listing in TXT format containing the corrections or rectifications is to be filed.

6. If, contrary to the statement referred to in paragraph 3 above, the EPO as ISA finds that the sequence listing in TXT format furnished under Rule 13ter PCT is not identical to the sequence listing in the international application under Rule 5.2(a) PCT, it will indicate that finding in the international search report and either proceed with the international search if the (minor) deficiency can be corrected or rectified under paragraph 5 above, or otherwise proceed under paragraph 4 above, as if the sequence listing in TXT format had not been furnished under Rule 13ter PCT.

7. If a sequence listing in TXT format is found to be deficient within the meaning of Article 3(1) or (2) of the decision of the President, the applicant will be invited to submit a replacement listing within the period under Article 4 of the decision of the President or, if such an invitation has already been issued, within the time remaining in the period stipulated in the invitation (see paragraph 4 above).

8. If the international search report has not been drawn up in full or in part (see paragraph 4 above), the EPO as IPEA will perform an international preliminary examination only to the extent that a meaningful examination can be carried out (Rule 66.1(e) PCT). The applicant is informed accordingly and an entry is made in the international preliminary examination report (Rules 66.2(a)(vii) and 70.12(iv) PCT). In such case, no invitation to furnish a sequence listing is issued.

9. If, after receipt of the documents specified in Rule 45bis.4(e)(i) to (iv) PCT, the EPO as SISA finds that a Standard-compliant sequence listing in TXT format is not available to it, it will proceed as above, in particular as under paragraph 1. The EPO as SISA will start the supplementary international search in accordance with Rule 45bis.5(a) PCT only if a Standard-compliant sequence listing in TXT format is available to it, i.e. if it is furnished to the IB of WIPO under Rule 45bis.1(c)(ii) PCT and thereafter transmitted to the EPO under Rule 45bis.4(e)(iii) (Agreement between the EPO and the IB of WIPO, Annex E, paragraph (4))⁴.

III. Procedure before the EPO as designated or elected Office (regional phase)

1. If a Standard-compliant sequence listing in TXT format is contained in the international application under Rule 5.2 PCT, furnished to the EPO under Rule 13ter.1(a) PCT or made accessible to the EPO by other means, the applicant does not have to submit the Standard-compliant sequence listing again in

TXT format on entry into the regional phase before the EPO as designated or elected Office.

2. Where, however, a Standard-compliant sequence listing in TXT format is not available to the EPO on the expiry of the period under Rule 159(1) EPC, the applicant will be invited to file a Standard-compliant sequence listing in TXT format within two months from the invitation and to pay the late furnishing fee. Rule 30(2) and (3) EPC and Article 1 of the decision of the President are to be applied accordingly (see Rule 163(3) EPC in conjunction with Article 5 of the decision of the President).

3. If any deficiencies are not remedied in due time after such an invitation – this also applies to the payment of the late furnishing fee – the application will be refused (Rule 30(3) EPC). The applicant may request further processing of the application under Article 121 EPC.

IV. Publication of sequence listings

1. A sequence listing filed at the date of filing of the European or international patent application will be published with the application documents (Rule 68(1) EPC; Article 153(4) EPC) and the patent specification (Rule 73 EPC) as part of the description (Article 6 of the decision of the President).

2. A sequence listing filed after the date of filing of the European patent application will not be published with the application documents or the patent specification because it is not part of the description (Rule 30(2) EPC).

3. For the purposes of publication (as far as a Standard-compliant sequence listing present on the date of filing is concerned) and file inspection, the Standard-compliant sequence listing filed by the applicant in TXT format is converted by the EPO. The EPO cannot guarantee that the converted version is without error and reflects exactly the original file. On written request to support@epo.org, the EPO will supply a copy of the original file submitted by the applicant.

V. Entry into force, and superseded previous EPO notices

From the date of its entry into force on 1 January 2014, the present notice supersedes the notice from the European Patent Office dated 28 April 2011 concerning the filing of sequence listings (OJ EPO 2011, 376).

¹ *Decision of the President of the EPO dated 28 April 2011 on the filing of sequence listings, OJ EPO 2011, 372.*

² “I hereby declare that the sequence listing does not go beyond the content of the application as filed.”

³ OJ EPO 2010, 304.

⁴ OJ EPO 2010, 304.

ANNEX 4

Relevant Provisions of the EPC: Rules relating to Biotechnological Inventions – Biological Deposits

Rule 31

Deposit of biological material

(1) If an invention involves the use of or concerns biological material which is not available to the public and which cannot be described in the European patent application in such a manner as to enable the invention to be carried out by a person skilled in the art, the invention shall only be regarded as being disclosed as prescribed in Article 83 if:

(a) a sample of the biological material has been deposited with a recognised depositary institution on the same terms as those laid down in the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure of 28 April 1977 not later than the date of filing of the application;

(b) the application as filed gives such relevant information as is available to the applicant on the characteristics of the biological material;

(c) the depositary institution and the accession number of the deposited biological material are stated in the application, and

(d) where the biological material has been deposited by a person other than the applicant, the name and address of the depositor are stated in the application and a document is submitted to the European Patent Office providing evidence that the depositor has authorised the applicant to refer to the deposited biological material in the application and has given his unreserved and irrevocable consent to the deposited material being made available to the public in accordance with Rule 33.

(2) The information referred to in paragraph 1(c) and (d) may be submitted

(a) within sixteen months after the date of filing of the application or, if priority has been claimed, after the priority date, this period being deemed to have been observed if the information is communicated before completion of the technical preparations for publication of the European patent application;

(b) up to the date of submission of a request under Article 93, paragraph 1(b);

(c) within one month after the European Patent Office has communicated to the applicant that the right to inspect the files under Article 128, paragraph 2, exists.

The ruling period shall be the one which is the first to expire. The communication of this information shall be considered as constituting the unreserved

and irrevocable consent of the applicant to the deposited biological material being made available to the public in accordance with Rule 33.

See decision of the Enlarged Board of Appeal G 2/93

Rule 32

Expert solution

(1) Until completion of the technical preparations for publication of the European patent application, the applicant may inform the European Patent Office that,

(a) until the publication of the mention of the grant of the European patent or, where applicable,

(b) for twenty years from the date of filing, if the application is refused or withdrawn or deemed to be withdrawn, the availability referred to in Rule 33 shall be effected only by the issue of a sample to an expert nominated by the requester.

(2) The following may be nominated as an expert:

(a) any natural person, provided that the requester furnishes evidence, when filing the request, that the nomination has the approval of the applicant;

(b) any natural person recognised as an expert by the President of the European Patent Office.

The nomination shall be accompanied by a declaration from the expert vis-à-vis the applicant in which he enters into the undertaking given under Rule 33 until either the date on which the patent expires in all the designated States or, where the application is refused, withdrawn or deemed to be withdrawn, the date referred to in paragraph 1(b), the requester being regarded as a third party.

See Notice from the European Patent Office dated 07.07.2010 concerning inventions which involve the use of or concern biological material (OJ EPO 2010, 498).

See the general conditions set by the President of the EPO for the recognition of experts in accordance with Rule 28 EPC [1973] (OJ EPO 1981, 359 ff.; 1992, 470).

Rule 33

Availability of biological material

(1) Biological material deposited in accordance with Rule 31 shall be available upon request to any person from the date of publication of the European patent application and to any person having the right to inspect the files under Article 128, paragraph 2, prior to that date. Subject to Rule 32, such availability shall be effected by the issue of a sample of the biological material to the person making the request (hereinafter referred to as “the requester”).

(2) Said issue shall be made only if the requester has undertaken vis-à-vis the applicant for or proprietor of the patent not to make the biological material or any biological material derived therefrom available to any third party and to use that material for experimental purposes only, until such time as the patent application is refused or withdrawn or deemed to be withdrawn, or before the Euro-

pean patent has expired in all the designated States, unless the applicant for or proprietor of the patent expressly waives such an undertaking.

The undertaking to use the biological material for experimental purposes only shall not apply in so far as the requester is using that material under a compulsory licence. The term “compulsory licence” shall be construed as including ex officio licences and the right to use patented inventions in the public interest.

(3) For the purposes of paragraph 2, derived biological material shall mean any material which still exhibits those characteristics of the deposited material which are essential to carrying out the invention. The undertaking under paragraph 2 shall not impede any deposit of derived biological material necessary for the purpose of patent procedure.

(4) The request referred to in paragraph 1 shall be submitted to the European Patent Office on a form recognised by that Office. The European Patent Office shall certify on the form that a European patent application referring to the deposit of the biological material has been filed, and that the requester or the expert nominated by him under Rule 32 is entitled to the issue of a sample of that material. After grant of the European patent, the request shall also be submitted to the European Patent Office.

(5) The European Patent Office shall transmit a copy of the request, with the certification provided for in paragraph 4, to the depositary institution and to the applicant for or the proprietor of the patent.

(6) The European Patent Office shall publish in its Official Journal the list of depositary institutions and experts recognised for the purpose of Rules 31 to 34.

Rule 34

New deposit of biological material

If biological material deposited in accordance with Rule 31 ceases to be available from the recognised depositary institution, an interruption in availability shall be deemed not to have occurred if a new deposit of that material is made with a recognised depositary institution on the same terms as those laid down in the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure of 28 April 1977, and if a copy of the receipt of the new deposit issued by the depositary institution is forwarded to the European Patent Office within four months of the date of the new deposit, stating the number of the European patent application or of the European patent.

ANNEX 5

Relevant Provisions of the EPC: Rule relating to form of claims

Rule 43

Form and content of claims

(1) The claims shall define the matter for which protection is sought in terms of the technical features of the invention. Wherever appropriate, claims shall contain:

(a) a statement indicating the designation of the subject-matter of the invention and those technical features which are necessary for the definition of the claimed subject-matter but which, in combination, form part of the prior art;

(b) a characterising portion, beginning with the expression “characterised in that” or “characterised by” and specifying the technical features for which, in combination with the features stated under sub-paragraph (a), protection is sought.

(2) Without prejudice to Article 82, a European patent application may contain more than one independent claim in the same category (product, process, apparatus or use) only if the subject-matter of the application involves one of the following:

(a) a plurality of interrelated products,

(b) different uses of a product or apparatus,

(c) alternative solutions to a particular problem, where it is inappropriate to cover these alternatives by a single claim.

(3) Any claim stating the essential features of an invention may be followed by one or more claims concerning particular embodiments of that invention.

(4) Any claim which includes all the features of any other claim (dependent claim) shall contain, if possible at the beginning, a reference to the other claim and then state the additional features. A dependent claim directly referring to another dependent claim shall also be admissible. All dependent claims referring back to a single previous claim, and all dependent claims referring back to several previous claims, shall be grouped together to the extent and in the most appropriate way possible.

(5) The number of claims shall be reasonable with regard to the nature of the invention claimed. The claims shall be numbered consecutively in Arabic numerals.

(6) Except where absolutely necessary, claims shall not rely on references to the description or drawings in specifying the technical features of the invention. In particular, they shall not contain such expressions as “as described in part ... of the description”, or “as illustrated in figure ... of the drawings”.

(7) Where the European patent application contains drawings including reference signs, the technical features specified in the claims shall preferably be followed by such reference signs relating to these features, placed in parentheses, if the intelligibility of the claim can thereby be increased. These reference signs shall not be construed as limiting the claim.

See decisions of the Enlarged Board of Appeal G 2/03, G 1/04

ANNEX 6

EU Regulations: Directive 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the legal protection of biotechnological inventions – “Biotech Directive”

DIRECTIVE 98/44/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 6 July 1998 on the legal protection of biotechnological inventions

[...]

CHAPTER I Patentability

[...]

Article 2

1. For the purposes of this Directive,
 - (a) ‘biological material’ means any material containing genetic information and capable of reproducing itself or being reproduced in a biological system;
 - (b) ‘microbiological process’ means any process involving or performed upon or resulting in microbiological material.
2. A process for the production of plants or animals is essentially biological if it consists entirely of natural phenomena such as crossing or selection.
3. The concept of ‘plant variety’ is defined by Article 5 of Regulation (EC) No 2100/94.

Article 3

1. For the purposes of this Directive, inventions which are new, which involve an inventive step and which are susceptible of industrial application shall be patentable even if they concern a product consisting of or containing biological material or a process by means of which biological material is produced, processed or used.
2. Biological material which is isolated from its natural environment or produced by means of a technical process may be the subject of an invention even if it previously occurred in nature.

Article 4

1. The following shall not be patentable:
 - (a) plant and animal varieties;
 - (b) essentially biological processes for the production of plants or animals.

2. Inventions which concern plants or animals shall be patentable if the technical feasibility of the invention is not confined to a particular plant or animal variety.

3. Paragraph 1(b) shall be without prejudice to the patentability of inventions which concern a microbiological or other technical process or a product obtained by means of such a process.

Article 5

1. The human body, at the various stages of its formation and development, and the simple discovery of one of its elements, including the sequence or partial sequence of a gene, cannot constitute patentable inventions.

2. An element isolated from the human body or otherwise produced by means of a technical process, including the sequence or partial sequence of a gene, may constitute a patentable invention, even if the structure of that element is identical to that of a natural element.

3. The industrial application of a sequence or a partial sequence of a gene must be disclosed in the patent application.

Article 6

1. Inventions shall be considered unpatentable where their commercial exploitation would be contrary to ordre public or morality; however, exploitation shall not be deemed to be so contrary merely because it is prohibited by law or regulation.

2. On the basis of paragraph 1, the following, in particular, shall be considered unpatentable:

- (a) processes for cloning human beings;
 - (b) processes for modifying the germ line genetic identity of human beings;
 - (c) uses of human embryos for industrial or commercial purposes;
 - (d) processes for modifying the genetic identity of animals which are likely to cause them suffering without any substantial medical benefit to man or animal, and also animals resulting from such processes.
- [...]

CHAPTER II Scope of protection

Article 8

1. The protection conferred by a patent on a biological material possessing specific characteristics as a result of the invention shall extend to any biological material derived from that biological material through propagation or multiplication in an identical or divergent form and possessing those same characteristics.

2. The protection conferred by a patent on a process that enables a biological material to be produced possessing specific characteristics as a result of the invention shall extend to biological material directly obtained through that process and to any other biological material derived from the directly obtained biological

cal material through propagation or multiplication in an identical or divergent form and possessing those same characteristics.

Article 9

The protection conferred by a patent on a product containing or consisting of genetic information shall extend to all material, save as provided in Article 5(1), in which the product is incorporated and in which the genetic information is contained and performs its function.

Article 10

The protection referred to in Articles 8 and 9 shall not extend to biological material obtained from the propagation or multiplication of biological material placed on the market in the territory of a Member State by the holder of the patent or with his consent, where the multiplication or propagation necessarily results from the application for which the biological material was marketed, provided that the material obtained is not subsequently used for other propagation or multiplication.

Article 11

1. By way of derogation from Articles 8 and 9, the sale or other form of commercialisation of plant propagating material to a farmer by the holder of the patent or with his consent for agricultural use implies authorisation for the farmer to use the product of his harvest for propagation or multiplication by him on his own farm, the extent and conditions of this derogation corresponding to those under Article 14 of Regulation (EC) No 2100/94.

2. By way of derogation from Articles 8 and 9, the sale or any other form of commercialisation of breeding stock or other animal reproductive material to a farmer by the holder of the patent or with his consent implies authorisation for the farmer to use the protected livestock for an agricultural purpose. This includes making the animal or other animal reproductive material available for the purposes of pursuing his agricultural activity but not sale within the framework or for the purpose of a commercial reproduction activity.

3. The extent and the conditions of the derogation provided for in paragraph 2 shall be determined by national laws, regulations and practices.

CHAPTER III Compulsory cross-licensing

[...]

CHAPTER IV Deposit, access and re-deposit of a biological material

Article 13

1. Where an invention involves the use of or concerns biological material which is not available to the public and which cannot be described in a patent

application in such a manner as to enable the invention to be reproduced by a person skilled in the art, the description shall be considered inadequate for the purposes of patent law unless:

(a) the biological material has been deposited no later than the date on which the patent application was filed with a recognised depository institution. At least the international depository authorities which acquired this status by virtue of Article 7 of the Budapest Treaty of 28 April 1977 on the international recognition of the deposit of micro-organisms for the purposes of patent procedure, hereinafter referred to as the 'Budapest Treaty', shall be recognised;

(b) the application as filed contains such relevant information as is available to the applicant on the characteristics of the biological material deposited;

(c) the patent application states the name of the depository institution and the accession number.

2. Access to the deposited biological material shall be provided through the supply of a sample:

(a) up to the first publication of the patent application, only to those persons who are authorised under national patent law;

(b) between the first publication of the application and the granting of the patent, to anyone requesting it or, if the applicant so requests, only to an independent expert;

(c) after the patent has been granted, and notwithstanding revocation or cancellation of the patent, to anyone requesting it.

3. The sample shall be supplied only if the person requesting it undertakes, for the term during which the patent is in force:

(a) not to make it or any material derived from it available to third parties; and

(b) not to use it or any material derived from it except for experimental purposes, unless the applicant for or proprietor of the patent, as applicable, expressly waives such an undertaking.

4. At the applicant's request, where an application is refused or withdrawn, access to the deposited material shall be limited to an independent expert for 20 years from the date on which the patent application was filed. In that case, paragraph 3 shall apply.

5. The applicant's requests referred to in point (b) of paragraph 2 and in paragraph 4 may only be made up to the date on which the technical preparations for publishing the patent application are deemed to have been completed.

Article 14

1. If the biological material deposited in accordance with Article 13 ceases to be available from the recognised depository institution, a new deposit of the material shall be permitted on the same terms as those laid down in the Budapest Treaty.

2. Any new deposit shall be accompanied by a statement signed by the depositor certifying that the newly deposited biological material is the same as that originally deposited.

[...]

ANNEX 7

EU Regulations: Acts relating to Supplementary Protection Certificates

Supplementary protection certificate for medicinal products:

- Regulation (EEC) No 469/2009, OJ L152 of 16.6.2009

Supplementary protection certificate for plant protection products:

- Regulation (EC) No 1610/96, OJ L 198 of 8.8.1996

Medicinal products for paediatric use:

- Regulation (EC) No 1901/2006, OJ L 378 of 27.12.2006,
- *Amended by:* Regulation (EC) No 1902/2006, OJ L 378 of 27.12.2006

On the Community code relating to medicinal products for human use

- Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001, OJ L 311 of 28.11.2001
- *Amended by:* Directive 2004/27/EC of the European Parliament and of the Council of 31 March 2004, OJ L 136 of 30.4.2004

On the Community code relating to veterinary medicinal products

- Directive 2001/82/EC of the European Parliament and of the Council of 6 November 2001, OJ L 311 of 28.11.2001
- *Amended by:* Directive 2004/28/EC of the European Parliament and of the Council of 31 March 2004, OJ L 136 of 30.4.2004

Regulation (EC) No 469/2009 of the European Parliament and of the Council of 6 May 2009 concerning the supplementary protection certificate for medicinal products

[...]

Article 1

Definitions

For the purposes of this Regulation, the following definitions shall apply:

(a) “medicinal product” means any substance or combination of substances presented for treating or preventing disease in human beings or animals and any substance or combination of substances which may be administered to human

beings or animals with a view to making a medical diagnosis or to restoring, correcting or modifying physiological functions in humans or in animals;

(b) “product” means the active ingredient or combination of active ingredients of a medicinal product;

(c) “basic patent” means a patent which protects a product as such, a process to obtain a product or an application of a product, and which is designated by its holder for the purpose of the procedure for grant of a certificate;

(d) “certificate” means the supplementary protection certificate;

(e) “application for an extension of the duration” means an application for an extension of the duration of the certificate pursuant to Article 13(3) of this Regulation and Article 36 of Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use.

[...]

Article 4

Subject matter of protection

Within the limits of the protection conferred by the basic patent, the protection conferred by a certificate shall extend only to the product covered by the authorisation to place the corresponding medicinal product on the market and for any use of the product as a medicinal product that has been authorised before the expiry of the certificate.

[...]

Article 13

Duration of the certificate

1. The certificate shall take effect at the end of the lawful term of the basic patent for a period equal to the period which elapsed between the date on which the application for a basic patent was lodged and the date of the first authorisation to place the product on the market in the Community, reduced by a period of five years.

2. Notwithstanding paragraph 1, the duration of the certificate may not exceed five years from the date on which it takes effect.

3. The periods laid down in paragraphs 1 and 2 shall be extended by six months in the case where Article 36 of Regulation (EC) No 1901/2006 applies. In that case, the duration of the period laid down in paragraph 1 of this Article may be extended only once.

4. Where a certificate is granted for a product protected by a patent which, before 2 January 1993, had its term extended or for which such extension was applied for, under national law, the term of protection to be afforded under this certificate shall be reduced by the number of years by which the term of the patent exceeds 20 years.

[...]

**REGULATION (EC) No 1610/96 OF THE EUROPEAN
PARLIAMENT AND OF THE COUNCIL of 23 July 1996
concerning the creation of a supplementary protection
certificate for plant protection products**

[...]

Article 1
Definitions

For the purposes of this Regulation, the following definitions shall apply:

1. 'plant protection products': active substances and preparations containing one or more active substances, put up in the form in which they are supplied to the user, intended to:

(a) protect plants or plant products against all harmful organisms or prevent the action of such organisms, in so far as such substances or preparations are not otherwise defined below;

(b) influence the life processes of plants, other than as a nutrient (e.g. plant growth regulators);

(c) preserve plant products, in so far as such substances or products are not subject to special Council or Commission provisions on preservatives;

(d) destroy undesirable plants; or

(e) destroy parts of plants, check or prevent undesirable growth of plants;

2. 'substances': chemical elements and their compounds, as they occur naturally or by manufacture, including any impurity inevitably resulting from the manufacturing process;

3. 'active substances': substances or micro-organisms including viruses, having general or specific action:

(a) against harmful organisms; or

(b) on plants, parts of plants or plant products;

4. 'preparations': mixtures or solutions composed of two or more substances, of which at least one is an active substance, intended for use as plant protection products;

5. 'plants': live plants and live parts of plants, including fresh fruit and seeds;

6. 'plant products': products in the unprocessed state or having undergone only simple preparation such as milling, drying or pressing, derived from plants, but excluding plants themselves as defined in point 5;

7. 'harmful organisms': pests of plants or plant products belonging to the animal or plant kingdom, and also viruses, bacteria and mycoplasmas and other pathogens;

8. 'product': the active substance as defined in point 3 or combination of active substances of a plant protection product;

9. 'basic patent': a patent which protects a product as defined in point 8 as such, a preparation as defined in point 4, a process to obtain a product or an ap-

plication of a product, and which is designated by its holder for the purpose of the procedure for grant of a certificate;

10. ‘certificate’: the supplementary protection certificate.

Article 4

Subject-matter of protection

Within the limits of the protection conferred by the basic patent, the protection conferred by a certificate shall extend only to the product covered by the authorizations to place the corresponding plant protection product on the market and for any use of the product as a plant protection product that has been authorized before the expiry of the certificate.

Article 13

Duration of the certificate

1. The certificate shall take effect at the end of the lawful term of the basic patent for a period equal to the period which elapsed between the date on which the application for a basic patent was lodged and the date of the first authorization to place the product on the market in the Community, reduced by a period of five years.

2. Notwithstanding paragraph 1, the duration of the certificate may not exceed five years from the date on which it takes effect.

3. For the purposes of calculating the duration of the certificate, account shall be taken of a provisional first marketing authorization only if it is directly followed by a definitive authorization concerning the same product.

ANNEX 8

EU and international Regulations: Acts relating to Plant Varieties

Council Regulation (EC) No 2100/94 of 27 July 1994 on Community plant variety rights Official Journal L 227, 01.09.1994

Amended by

- Council Regulation (EC) No 2506/95 of 25 October 1995 L 258 3 28.10.1995
- Council Regulation (EC) No 807/2003 of 14 April 2003 L 122 36 16.5.2003
- Council Regulation (EC) No 1650/2003 of 18 June 2003 L 245 28 29.9.2003
- Council Regulation (EC) No 873/2004 of 29 April 2004 L 162 38 30.4.2004
- Council Regulation (EC) No 15/2008 of 20 December 2007 L 8 2 11.1.2008

The citations below are from the consolidated version dated 31.1.2008:

[...]

Article 5

Object of Community plant variety rights

1. Varieties of all botanical genera and species, including, inter alia, hybrids between genera or species, may form the object of Community plant variety rights.

2. For the purpose of this Regulation, ‘variety’ shall be taken to mean a plant grouping within a single botanical taxon of the lowest known rank, which grouping, irrespective of whether the conditions for the grant of a plant variety right are fully met, can be:

- defined by the expression of the characteristics that results from a given genotype or combination of genotypes,
- distinguished from any other plant grouping by the expression of at least one of the said characteristics, and
- considered as a unit with regard to its suitability for being propagated unchanged.

3. A plant grouping consists of entire plants or parts of plants as far as such parts are capable of producing entire plants, both referred to hereinafter as ‘variety constituents’.

4. The expression of the characteristics referred to in paragraph 2, first indent, may be either invariable or variable between variety constituents of the same kind provided that also the level of variation results from the genotype or combination of genotypes.

Article 6**Protectable varieties**

Community plant variety rights shall be granted for varieties that are:

- (a) distinct;
- (b) uniform;
- (c) stable; and
- (d) new.

Moreover, the variety must be designated by a denomination in accordance with the provisions of Article 63.

Article 7**Distinctness**

1. A variety shall be deemed to be distinct if it is clearly distinguishable by reference to the expression of the characteristics that results from a particular genotype or combination of genotypes, from any other variety whose existence is a matter of common knowledge on the date of application determined pursuant to Article 51.

2. The existence of another variety shall in particular be deemed to be a matter of common knowledge if on the date of application determined pursuant to Article 51:

(a) it was the object of a plant variety right or entered in an official register of plant varieties, in the Community or any State, or in any intergovernmental organization with relevant competence;

(b) an application for the granting of a plant variety right in its respect or for its entering in such an official register was filed, provided the application has led to the granting or entering in the meantime.

The implementing rules pursuant to Article 114 may specify further cases as examples which shall be deemed to be a matter of common knowledge.

Article 8**Uniformity**

A variety shall be deemed to be uniform if, subject to the variation that may be expected from the particular features of its propagation, it is sufficiently uniform in the expression of those characteristics which are included in the examination for distinctness, as well as any others used for the variety description.

Article 9**Stability**

A variety shall be deemed to be stable if the expression of the characteristics which are included in the examination for distinctness as well as any others used for the variety description, remain unchanged after repeated propagation or, in the case of a particular cycle of propagation, at the end of each such cycle.

Article 10

Novelty

1. A variety shall be deemed to be new if, at the date of application determined pursuant to Article 51, variety constituents or harvested material of the variety have not been sold or otherwise disposed of to others, by or with the consent of the breeder within the meaning of Article 11, for purposes of exploitation of the variety:

(a) earlier than one year before the abovementioned date, within the territory of the Community;

(b) earlier than four years or, in the case of trees or of vines, earlier than six years before the said date, outside the territory of the Community.

2. The disposal of variety constituents to an official body for statutory purposes, or to others on the basis of a contractual or other legal relationship solely for production, reproduction, multiplication, conditioning or storage, shall not be deemed to be a disposal to others within the meaning of paragraph 1, provided that the breeder preserves the exclusive right of disposal of these and other variety constituents, and no further disposal is made. However, such disposal of variety constituents shall be deemed to be a disposal in terms of paragraph 1 if these constituents are repeatedly used in the production of a hybrid variety and if there is disposal of variety constituents or harvested material of the hybrid variety.

Likewise, the disposal of variety constituents by one company or firm within the meaning of the second paragraph of Article 58 of the Treaty to another of such companies or firms shall not be deemed to be a disposal to others, if one of them belongs entirely to the other or if both belong entirely to a third such company or firm, provided no further disposal is made. This provision shall not apply in respect of cooperative societies.

3. The disposal of variety constituents or harvested material of the variety, which have been produced from plants grown for the purposes specified in Article 15 (b) and (c) and which are not used for further reproduction or multiplication, shall not be deemed to be exploitation of the variety, unless reference is made to the variety for purposes of that disposal.

Likewise, no account shall be taken of any disposal to others, if it either was due to, or in consequence of the fact that breeder had displayed the variety at an official or officially recognized exhibition within the meaning of the Convention on International Exhibitions, or at an exhibition in a Member State which was officially recognized as equivalent by that Member State.

Article 11

Right of Priority

(1) [*The right; its period*] Any breeder who has duly filed an application for the protection of a variety in one of the Contracting Parties (the “first application”) shall, for the purpose of filing an application for the grant of a breeder’s right for the same variety with the authority of any other Contracting Party (the “subse-

quent application”), enjoy a right of priority for a period of 12 months. This period shall be computed from the date of filing of the first application. The day of filing shall not be included in the latter period.

(2) [*Claiming the right*] In order to benefit from the right of priority, the breeder shall, in the subsequent application, claim the priority of the first application. The authority with which the subsequent application has been filed may require the breeder to furnish, within a period of not less than three months from the filing date of the subsequent application, a copy of the documents which constitute the first application, certified to be a true copy by the authority with which that application was filed, and samples or other evidence that the variety which is the subject matter of both applications is the same.

(3) [*Documents and material*] The breeder shall be allowed a period of two years after the expiration of the period of priority or, where the first application is rejected or withdrawn, an appropriate time after such rejection or withdrawal, in which to furnish, to the authority of the Contracting Party with which he has filed the subsequent application, any necessary information, document or material required for the purpose of the examination under Article 12, as required by the laws of that Contracting Party.

(4) [*Events occurring during the period*] Events occurring within the period provided for in paragraph (1), such as the filing of another application or the publication or use of the variety that is the subject of the first application, shall not constitute a ground for rejecting the subsequent application. Such events shall also not give rise to any third-party right.

Article 13

Rights of the holder of a Community plant variety right and prohibited acts

1. A Community plant variety right shall have the effect that the holder or holders of the Community plant variety right, hereinafter referred to as ‘the holder’, shall be entitled to effect the acts set out in paragraph 2.

2. Without prejudice to the provisions of Articles 15 and 16, the following acts in respect of variety constituents, or harvested material of the protected variety, both referred to hereinafter as ‘material’, shall require the authorization of the holder:

- (a) production or reproduction (multiplication);
- (b) conditioning for the purpose of propagation;
- (c) offering for sale;
- (d) selling or other marketing;
- (e) exporting from the Community;
- (f) importing to the Community;
- (g) stocking for any of the purposes mentioned in (a) to (f).

The holder may make his authorization subject to conditions and limitations.

3. The provisions of paragraph 2 shall apply in respect of harvested material only if this was obtained through the unauthorized use of variety constituents of

the protected variety, and unless the holder has had reasonable opportunity to exercise his right in relation to the said variety constituents.

4. In the implementing rules pursuant to Article 114, it may be provided that in specific cases the provisions of paragraph 2 of this Article shall also apply in respect of products obtained directly from material of the protected variety. They may apply only if such products were obtained through the unauthorized use of material of the protected variety, and unless the holder has had reasonable opportunity to exercise his right in relation to the said material. To the extent that the provisions of paragraph 2 apply to products directly obtained, they shall also be considered to be ‘material’.

5. The provisions of paragraphs 1 to 4 shall also apply in relation to:

(a) varieties which are essentially derived from the variety in respect of which the Community plant variety right has been granted, where this variety is not itself an essentially derived variety;

(b) varieties which are not distinct in accordance with the provisions of Article 7 from the protected variety; and

(c) varieties whose production requires the repeated use of the protected variety.

6. For the purposes of paragraph 5 (a), a variety shall be deemed to be essentially derived from another variety, referred to hereinafter as ‘the initial variety’ when:

(a) it is predominantly derived from the initial variety, or from a variety that is itself predominantly derived from the initial variety;

(b) it is distinct in accordance with the provisions of Article 7 from the initial variety; and

(c) except for the differences which result from the act of derivation, it conforms essentially to the initial variety in the expression of the characteristics that results from the genotype or combination of genotypes of the initial variety.

7. The implementing rules pursuant to Article 114 may specify possible acts of derivation which come at least under the provisions of paragraph 6.

8. Without prejudice to Article 14 and 29, the exercise of the rights conferred by Community plant variety rights may not violate any provisions adopted on the grounds of public morality, public policy or public security, the protection of health and life of humans, animals or plants, the protection of the environment, the protection of industrial or commercial property, or the safeguarding of competition, of trade or of agricultural production.

[...]

Article 52

The right of priority

1. The right of priority of an application shall be determined by the date of receipt of the application. Where applications have the same date of application, the priorities thereof shall be determined according to the order in which

they were received, if this can be established. Otherwise they shall have the same priority.

2. If the applicant or his predecessor in title has already applied for a property right for the variety in a Member State or in a Member of the International Union for the Protection of New Varieties of Plants, and the date of application is within 12 months of the filing of the earlier application, the applicant shall enjoy a right of priority for the earlier application as regards the application for the Community plant variety right, provided the earlier application still exists on the date of application.

3. The right of priority shall have the effect that the date on which the earlier application was filed shall count as the date of application for the Community plant variety right for the purposes of Articles 7, 10 and 11.

4. Paragraphs 2 and 3 shall also apply in respect of earlier applications that were filed in another State.

5. Any claim for a right of priority earlier than that provided for in paragraph 2 shall lapse if the applicant does not submit to the Office within three months of the date of application copies of the earlier application that have been certified by the authorities responsible for such application. If the earlier application has not been made in one of the official languages of the European Communities, the Office may require, in addition, a translation of the earlier application in one of these languages.

[...]

Article 63

Variety denomination

1. Where a Community plant variety right is granted, the Office shall approve, for the variety in question, the variety denomination proposed by the applicant pursuant to Article 50 (3), if it considers, on the basis of the examination made pursuant to the second sentence of Article 54 (1), that this denomination is suitable.

2. A variety denomination is suitable, if there is no impediment pursuant to paragraphs 3 or 4 of this Article.

3. There is an impediment for the designation of a variety denomination where:

(a) its use in the territory of the Community is precluded by the prior right of a third party;

(b) it may commonly cause its users difficulties as regards recognition or reproduction;

(c) it is identical or may be confused with a variety denomination under which another variety of the same or of a closely related species is entered in an official register of plant varieties or under which material of another variety has been marketed in a Member State or in a Member of the International Unit for the Protection of New Varieties of Plants, unless the other variety no longer remains in existence and its denomination has acquired no special significance;

(d) it is identical or may be confused with other designations which are commonly used for the marketing of goods or which have to be kept free under other legislation;

(e) it is liable to give offence in one of the Member States or is contrary to public policy;

(f) it is liable to mislead or to cause confusion concerning the characteristics, the value or the identity of the variety, or the identity of the breeder or any other party to proceedings.

4. There is another impediment where, in the case of a variety which has already been entered:

(a) in one of the Member States; or

(b) in a Member of the International Union for the Protection of New Varieties of Plants; or

(c) in another State for which it has been established in a Community act that varieties are evaluated there under rules which are equivalent to those laid down in the Directives on common catalogues;

in an official register of plant varieties or material thereof and has been marketed there for commercial purposes, and the proposed variety denomination differs from that which has been registered or used there, unless the latter one is the object of an impediment pursuant to paragraph 3.

5. The Office shall publish the species which it considers ‘closely related’ within the meaning of paragraph 3 (c).

[...]

INTERNATIONAL CONVENTION FOR THE PROTECTION OF NEW VARIETIES OF PLANTS

of December 2, 1961, as Revised at Geneva on November 10, 1972, on October 23, 1978, and on March 19, 1991

Article 1

Definitions

For the purposes of this Act:

(i) “this Convention” means the present (1991) Act of the International Convention for the Protection of New Varieties of Plants;

(ii) “Act of 1961/1972” means the International Convention for the Protection of New Varieties of Plants of December 2, 1961, as amended by the Additional Act of November 10, 1972;

(iii) “Act of 1978” means the Act of October 23, 1978, of the International Convention for the Protection of New Varieties of Plants;

(iv) “breeder” means

– the person who bred, or discovered and developed, a variety,

- the person who is the employer of the aforementioned person or who has commissioned the latter's work, where the laws of the relevant Contracting Party so provide, or
 - the successor in title of the first or second aforementioned person, as the case may be;
- (v) “breeder's right” means the right of the breeder provided for in this Convention;
- (vi) “variety” means a plant grouping within a single botanical taxon of the lowest known rank, which grouping, irrespective of whether the conditions for the grant of a breeder's right are fully met, can be
- defined by the expression of the characteristics resulting from a given genotype or combination of genotypes,
 - distinguished from any other plant grouping by the expression of at least one of the said characteristics and
 - considered as a unit with regard to its suitability for being propagated unchanged;
- (vii) “Contracting Party” means a State or an intergovernmental organization party to this Convention;
- (viii) “territory,” in relation to a Contracting Party, means, where the Contracting Party is a State, the territory of that State and, where the Contracting Party is an intergovernmental organization, the territory in which the constituting treaty of that intergovernmental organization applies;
- (ix) “authority” means the authority referred to in Article 30(1)(ii);
- (x) “Union” means the Union for the Protection of New Varieties of Plants founded by the Act of 1961 and further mentioned in the Act of 1972, the Act of 1978 and in this Convention;
- (xi) “member of the Union” means a State party to the Act of 1961/1972 or the Act of 1978, or a Contracting Party.

Article 5

Conditions of Protection

(1) [*Criteria to be satisfied*] The breeder's right shall be granted where the variety is

- (i) new,
- (ii) distinct,
- (iii) uniform and
- (iv) stable.

(2) [*Other conditions*] The grant of the breeder's right shall not be subject to any further or different conditions, provided that the variety is designated by a denomination in accordance with the provisions of Article 20, that the applicant complies with the formalities provided for by the law of the Contracting Party with whose authority the application has been filed and that he pays the required fees.

Article 6

Novelty

(1) [*Criteria*] The variety shall be deemed to be new if, at the date of filing of the application for a breeder's right, propagating or harvested material of the variety has not been sold or otherwise disposed of to others, by or with the consent of the breeder, for purposes of exploitation of the variety

- (i) in the territory of the Contracting Party in which the application has been filed earlier than one year before that date and
- (ii) in a territory other than that of the Contracting Party in which the application has been filed earlier than four years or, in the case of trees or of vines, earlier than six years before the said date.

(2) [*Varieties of recent creation*] Where a Contracting Party applies this Convention to a plant genus or species to which it did not previously apply this Convention or an earlier Act, it may consider a variety of recent creation existing at the date of such extension of protection to satisfy the condition of novelty defined in paragraph (1) even where the sale or disposal to others described in that paragraph took place earlier than the time limits defined in that paragraph.

(3) [*"Territory" in certain cases*] For the purposes of paragraph (1), all the Contracting Parties which are member States of one and the same intergovernmental organization may act jointly, where the regulations of that organization so require, to assimilate acts done on the territories of the States members of that organization to acts done on their own territories and, should they do so, shall notify the Secretary-General accordingly.

Article 7

Distinctness

The variety shall be deemed to be distinct if it is clearly distinguishable from any other variety whose existence is a matter of common knowledge at the time of the filing of the application. In particular, the filing of an application for the granting of a breeder's right or for the entering of another variety in an official register of varieties, in any country, shall be deemed to render that other variety a matter of common knowledge from the date of the application, provided that the application leads to the granting of a breeder's right or to the entering of the said other variety in the official register of varieties, as the case may be.

Article 8

Uniformity

The variety shall be deemed to be uniform if, subject to the variation that may be expected from the particular features of its propagation, it is sufficiently uniform in its relevant characteristics.

Article 9

Stability

The variety shall be deemed to be stable if its relevant characteristics remain unchanged after repeated propagation or, in the case of a particular cycle of propagation, at the end of each such cycle.

Article 11

Right of Priority

(1) [*The right; its period*] Any breeder who has duly filed an application for the protection of a variety in one of the Contracting Parties (the “first application”) shall, for the purpose of filing an application for the grant of a breeder’s right for the same variety with the authority of any other Contracting Party (the “subsequent application”), enjoy a right of priority for a period of 12 months. This period shall be computed from the date of filing of the first application. The day of filing shall not be included in the latter period.

(2) [*Claiming the right*] In order to benefit from the right of priority, the breeder shall, in the subsequent application, claim the priority of the first application. The authority with which the subsequent application has been filed may require the breeder to furnish, within a period of not less than three months from the filing date of the subsequent application, a copy of the documents which constitute the first application, certified to be a true copy by the authority with which that application was filed, and samples or other evidence that the variety which is the subject matter of both applications is the same.

(3) [*Documents and material*] The breeder shall be allowed a period of two years after the expiration of the period of priority or, where the first application is rejected or withdrawn, an appropriate time after such rejection or withdrawal, in which to furnish, to the authority of the Contracting Party with which he has filed the subsequent application, any necessary information, document or material required for the purpose of the examination under Article 12, as required by the laws of that Contracting Party.

(4) [*Events occurring during the period*] Events occurring within the period provided for in paragraph (1), such as the filing of another application or the publication or use of the variety that is the subject of the first application, shall not constitute a ground for rejecting the subsequent application. Such events shall also not give rise to any third-party right.

ANNEX 9

Bolar Directives

Art. 13(6) EU Directive 2001/82/EC (as amended by Directive 2004/28/EC) and Art. 10(6) EU Directive 2001/83/EC (as amended by Directive 2002/98/EC, 2003/63/EC, 2004/24/EC and 2004/27/EC).

Conducting the necessary studies and trials with a view to the application of paragraphs 1, 2, 3 and 4 and the consequential practical requirements shall not be regarded as contrary to patent rights or to supplementary protection certificates for medicinal products.

ANNEX 10

Register of cited decisions

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