procedures and allow for better determination of the target patient population.

e) Derivatives

The research around docetaxel did not diminish the efforts in basic research to find new innovative drugs. Attempts to improve various aspects (for example the anti-tumoural activity) of docetaxel resulted in nine patent families dealing with novel derivatives of taxoids.[54] This research work successfully led to the marketing of Jevtana (cabazitaxel), approved in the U.S. in June 2010. Cabazitaxel was first disclosed in the patent WO 96/30335 (oral formulation WO 00/41482). Despite attempts to switch to the new therapy, docetaxel is still part of the widely used first line therapy. Cabazitaxel currently finds more use in retreatment of patients previously treated with a docetaxel-containing regime.[55] For some types of cancer there is currently no data (no studies done) at hand which proves an added benefit of cabazitaxel over docetaxel, while for others it has been demonstrated that the life time is significantly improved for cases of refractory cancer.[56]

3. Use of Procedural Provisions: Supplementary Protection Certificates (SPCs)/Patent Term Extension

In Europe, Supplementary Protection Certificates can be requested from the national patent offices under Regulation (EC) 496/2009

54 WO 92/09589, WO 93/23389, WO 94/08984, WO 94/11547, WO 94/20484, WO 95/01969, WO 95/11247, WO 96/03395 and WO 97/23473.

55 Institute for Quality and Efficiency in Health Care, IQWiG Reports – Commission No. A11-24 Cabazitaxel – Benefit assessment according to § 35a Social Code Book V, (Jan. 12, 2012), found at https://www.iqwig.de/download/A11-24_Extract_Cabazitaxel_Benefit_assessment_35a_Social_Code_Book_V.pdf, (last visited Sept. 11, 2012).

56 *Id*.

which codifies Council Regulation (EEC) 1768/92.[57] The SPC had been introduced for the purpose of allowing originator pharmaceutical companies to benefit of a maximum market exclusivity of 15 years from marketing authorisation, whereby the certificate may have duration up to 5 years.[58] Both Regulations foresaw transitional periods.[59, 60]

The keystone of the patent protection for docetaxel in Europe is EP 0253738 which has been filed in July 1987. Said patent was to expire after a patent term of 20 years in July 2007. Market approval for docetaxel in Europe was obtained only in November 1995,[61] after more than eight years of research to determine safety and efficacy of the drug in various clinical trials, which were necessary to fulfil the regulatory obligations. To facilitate the recovery of the high cost of R&D the originator company could avail itself of the application for an SPC. Further protection of docetaxel until November 2010 was obtained in 9 EU Member States, while in Switzerland the extension was granted until December 2011.[62] The rights conferred by the SPC did however

57 Regulation (EC) 469/2009, 2009 O.J. (L 152) 1 supersedes Council Regulation (EEC) 1768/92, 1992, O.J. (L 182) 1.

58 SPCs must be requested within 6 months after a valid authorization to place a medicinal product on the market has been granted in accordance with the Directive 2001/83/EC, see Council Regulation (EEC) 469/2009, Articles 7(1) and 3(b), 2009 O.J. (L 152) 1, 2-3.

59 Council Regulation (EEC) 1768/92, Article 19, 1992, O.J. (L152) 1, 6: it was stipulated that for products which had received marketing authorisation after 01 January 1985 the 6 month period would start from the date the Regulation entered into force. Initially, only 4 exceptions were foreseen: for Belgium and Italy, the first marketing authorisation might have been received as early as 01 January 1982; for Denmark and Germany, not earlier than 01 January 1988. Exceptions were later also applied for three countries of the European Economic Area established in 1994 which at that point in time were not members of the European Union: Austria, Finland and Norway. The former two countries have since then joined the European Union (1. January 1995), the latter has remained a European Free Trade Association (EFTA)-state within the European Economic Area. For Austria, the 1982 limit data is relevant, for Norway and Finland 1988 is the limit date.

60 For provisions regarding transitional periods relating to the enlargement of the community see Regulation (EC) 469/2009, Article 20, 2009 O.J. (L 152).

61 *Supra* note 32.

62 EPO registry.

not stop the Israeli generic pharmaceuticals company Teva Pharma to request (*via* its Dutch subsidiary) and obtain market authorization for docetaxel from the French authorities. Presuming an imminent infringement of its rights, Sanofi-Aventis filed a lawsuit against Teva Pharma with the *Tribunal de Grande Instance de Paris*.[63] The court however, following French case law, ruled in favour of the defendant and decided that the request for a market authorization does not constitute an infringement. According to the court a market authorization requested by and granted to the defendant does not automatically allow to assume that a generic product will actually be marketed prior to the expiry of the claimant's rights.[64, 65] Permission for paediatric studies targeting nasopharyngeal carcinoma was granted by the EMA in May 2008.[66] Results of the studies are not yet in the public domain.

A similar patent term extension is available also in the U.S.[67] The basic patent US 4,814,470 was due to expire in July 2007 and the marketing approval of Taxotere was obtained in 1996. Therefore, the requirements of extension of the patent term were met and an extension of 1035 days was granted.[68] A further paediatric exclusivity[69] (6

63 Aventis v. Teva: Tribunal de Grande Instance de Paris, Mar. 17, 2011, http://kluwerpatentblog.com/files/2010/12/2010-08-19_TGI_Paris_Aventis_Teva_translation.pdf (last visited Feb. 9, 2012).

64 Pierre Véron, *Submission of a tender: imminent infringement?,* Wolters Kluwer Patent Blog, (Dec. 8, 2010) http://kluwerpatentblog.com/2010/12/08/submission-of-a-tender-imminent-infringement/ (last visited Feb. 9, 2012).

65 Simon Klopschinski, *Arzneimittelrechtliche Genehmigungsverfahren, staatliche Preisfestsetzung und Kostenerstattung für Arzneimittel im Lichte des Patentschutzes – Rechtsprechungsübersicht Belgien, Deutschland, Frankreich und Österreich*, GRURInt. 993, 1000, (2011).

66 EMA, EMA decision of 16 May 2008 on the application for agreement of a Paediatric Investigation Plan for Docetaxel, Taxotere (EMEA-000029-PIP01-07) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council as amended, found at http://www.ema.europa.eu/docs/en_GB/document_library/PIP_decision/WC500005480.pdf, (last visited Aug. 3, 2012).

67 35 U.S.C. § 156: Extension of patent term.

68 See Image File Wrapper at the Public Patent Application Information Retrieval (PublicPAIR) of the USPTO.

69 21 U.S.C § 355A: Pediatric studies of drugs.

months) for the treatment of solid tumours extended the patent protection of Taxotere to November 2010.[70]

4. Conclusion

In its patent strategy Sanofi-Aventis focused mainly on three innovation tracks: formulations, combinations and process. Use of SPCs was also important to prolong in Europe and in the U.S. the life of the patent application that first disclosed docetaxel.

The patent filing trends for docetaxel (figure 2) show a first increment of filing activity in 1996 after launch followed by a second surge in 2002 and a third one in 2006. However, around 280 entities contributed actually to such filing whose distribution is shown in figure 3.[71] Of particular note is the large number of individual and academic inventors in the case of docetaxel, which is likely due to the particular interest cancer research attracts both in terms of public grants and in terms of public visibility. However, just contributing to total patent numbers, most of these patents appear to be neither a real challenge for the position of the originator, nor are they of particular commercial interest. There seem to be only a few cases, where, in the phase after marketing had started, Aventis secured patents through collaboration with university partners.[72]

As already mentioned, a substantial number of patents (75%) is directed towards the research fields of formulation, combination and process (figure 2). However, only a limited amount of these has been submitted by the originator company. In the formulation track for example, although the number of patent families is very high, only three patent families belong to the originator company after 1996 (launch year). Other two companies, Forest Laboratories (14 patents) and

70 See Zhikong He *supra* note 40.

71 The data forming the basis for the graphic display of the patent filing trends has been kindly provided by the Patent Department of Boehringer Ingelheim GmbH.

72 For example WO 02/070498 has been obtained by collaboration with a group at the State University of New York.