> "Certain practices that do not equal *per se* patent misuse may constitute misuse if a court determines that such practices do not reasonably relate to the subject matter within the scope of the patent claims. If "the practice has the effect of extending the patentee's statutory rights and does so with an anti-competitive effect, ... the finder of fact must decide whether the questioned practice imposes an unreasonable restraint on competition".[717]

For the reasons set forth above, the legal treatment of reach-licensing agreements is yet not clear. Hence, it is advisable to handle such strategy with caution.

## IV. Conclusion

Based on the study of the different approaches provided by the European and the U.S. patent offices, it can be concluded that both offices largely share the same views with respect to the patentability requirements of 3-D protein structures-related claims.[718] Yet, different approaches exist with regard to the patentability of *in-silico* screening methods. The European Patent office accepts the claim, assuming a patentable subject matter due to a further technical effect of the computerized invention. The USPTO, by contrast, rejects the claim, concluding there is obviousness due to the understanding that the algorithm is considered as non-functional descriptive material.

The study shows that an inventor seeking patent protection for 3-D protein structures should obey the following guidelines.[719] Generally, a patent applicant should provide accurate and precise information regarding the 3-D structural coordinates. Furthermore, a precise description of how the structural analysis was carried out should be provided in the patent specification. Isolated and determined 3-D protein structures establish novelty, if the inventor proves that the tertiary structure coordinates are a more unambiguous parameter than the amino acid sequence already disclosed in the prior art.

The further rule that novelty can be derived from physical morphology applies principles developed in the field of chemical inventions. The possibility of creating novelty through the principles of selection inventions are also in line with classical chemical patent principles. The question of dependency from the patent covering the whole protein is another key factor and will be discussed below.

717 Bayer v. Housey, 169 F.Supp.2d 328, 331 (District Court of Deleware 2001).

718 European Patent Office, Japan Patent Office, United States Patent and Trademark Office, Trilateral Project WM4, Comparative Studies in New Technologies (Biotechnology, Business Methods, etc.), Report on Comparative Study on Protein 3-Dimensional (3-D) Structure Related Claims, Vienna 2002, 32; also Vinarov, Sara D., Patent protection for structural genomics-related inventions, Journal of structural and functional genomics 2003, 191, 206.

719 Vinarov, Sara D., Patent protection for structural genomics-related inventions, Journal of structural and functional genomics 2003, 191, 207, who emphasizes that understanding how patent offices will analyze structural genomics-based inventions is crucial for formulating strategies in patent prosecution and litigation.

As for proteomics claims in the field of bioinformatics, principles from both computer-implemented inventions and inventions involving biological material should apply. Therefore, the author suggests that a further technical effect, as well as the acknowledgement of functional descriptive material, may be derived from the biological function the protein performs *in-vivo*.

As for compounds screened by *in-silico* methods, the strategy to draft reach-through claims should be handled with caution. With strict conditions set out for the written description/sufficient disclosure requirement and enablement factor, it may be advisable to use other approaches such as milestone payments or reach-through licensing methods. As long as the claim defines the identified compound by size and shape, it is not considered a reach-through claim. In order to meet the patentability requirements of written description/sufficient disclosure and enablement, it is advisable for applicants to disclose theoretical information about the size and shape of binding sites within the computerized method and in responding compounds. Inventors, however, must take into account that such claims involve a high risk that they will be rendered invalid. Even if only one prior art ligand has the shape and size demonstrated by the claim and would therefore respond to the *in-silico* protein, the claim lacks novelty. With many molecules being reported in prior art, but not all of them defined by size and shape, the concrete risk of a destruction of novelty is difficult to assess.[720]

Finally, it must again be emphasized that the patentability of 3-D protein structure is a key factor in the treatment of a number of frequently occurring neurodegenerative disorders. With the increased aging of society, Alzheimer's, one of the diseases based on amyloid brain plaques, is increasingly reported worldwide. Prion-based diseases, such as BSE or CJD, accompany industrial developments such as intensive mass animal farming.[721] In view of these diseases, there clearly is a need for cost-effective drugs related to the treatment of prion diseases. Because the tertiary folding stage of the infectious proteins is the major cause of this diseases, effective treatment must be based on knowledge of their 3-D structure. Research must specifically emphasize the visualization of the structural transition from the normal, cellular prion, Prp C to the diseased form, Prp Sc. As yet, the understanding of the structural biology of the pathogenic conversion, however, remains incomplete in many

720 Eisenberg, Rebecca S., Reaching through the Genome, In: Perspectives on Properties of the Human Genome Project; Kieff, F. Scott, ed. Amsterdam 2003; 209, 225.

721 A major risk for the development of CJD is the treatment with growth hormones. Two doctors in France were charged with involuntary manslaughter of a child who had been treated with growth hormones derived from corpses. The child contracted Creutzfeldt-Jakob Disease. According to French studies, there have been 24 reported cases of CJD in children who had been subject of growth hormone treatments between 1983 and mid-1985. Fifteen of these persons have died. It now appears possible that hundreds of children in France have been treated with growth hormone derived from dead bodies at the risk of contracting CID; see U.S. Patent 6916419 "Device for Removal of Prions from Blood, Plasma and other Liquids" by Prusiner, Stanley B./Safar, Jiri G., Oakland, CA 2005.

ways.[722] There exist a large number of patents related to prions.[723]Inventions range from methods related to the modification[724] and detection[725] of prions or models of prion diseases[726], to methods related to antibodies[727] or devices for removal of prions from blood, plasma and other liquids.[728] Only recently, have scientists developed an artificial protein that can trigger a neurological disorder similar to BSE. They produced a normal prion protein fragment in bacteria and folded it into larger, abnormally shaped structures. These structures were then injected into the brains of mice. The animals began to show symptoms similar to those occurring in BSE.[729] Hence, the field of prion research plays a crucial role in the proteomic era and it can be expected that a plurality of patent applications will be filed in the near future. In view of the importance of these technologies, the patent law systems must provide adequate protection. Since the tertiary stage is the crucial element, this protection is only achieved if the 3-D structure is sufficient to create novelty, irrespective of whether the primary sequence of the protein is already included in the prior art.

722 For example, it is unknown exactly which structural regions of PrP C bear the crucial properties for the conformational change to occur. It is also not disclosed which regions of PrP Sc bear the infectious properties; see U.S. Patent 6916419, "Device for Removal of Prions from Blood, Plasma and other Liquids" by Prusiner, Stanley B./Safar, Jiri G., Oakland, CA 2005.

723 The Nobel laureate Stanley B. Prusiner has been involved in the development of at least 40 patents granted in between 1996 and 2005, available at http://patft.uspto.gov/, last checked on January 21, 2008.

724 International Patent Application WO/2002/049460 "Method for modifying the protein structure of prions PrP in a targeted manner" by Kortschak, Fritz, Berlin 2003.

725 U.S. Patent 7208281 „Ligands used for detecting prions" by Kiesewetter, Holger/Salamar, Abdulgabar, Berlin 2003.

726 U.S. Patent 6767712 "Models of prion disease" by Prusiner, Stanley B./Carsten, Korth, Oakland, CA 2004.

727 U.S. Patent 6858397, PrusinerAntibodies specific for native PrPsc by Stanley B/Williamson, R. Anthony/Burton, Dennis R., Oakland; La Jolla 2005.

728 U.S. Patent 6916419 "Device for Removal of Prions from Blood, Plasma and other Liquids" by Prusiner, Stanley B./Safar, Jiri G Oakland, CA 2005.

729 See BBC News from July 30, 2004, available at: http://news.bbc.co.uk/go/pr/fr/-/1/hi/health/3936519.stm, last checked on August 1, 2005.