A. Statutory Background and Fundamental Case Law in Europe and the U.S.

I. Introduction

As outlined in chapter II above, the tertiary structure is the single most important determinant of a protein's biological function.[159] Research related to drug design that is conducted on grounds of the tertiary folding type has a more reliable basis than studies that solely involve the knowledge of primary structures. The goal of this chapter is to provide an overview of the legal terrain faced by those seeking to patent protein 3-D structure related claims. The requirements of the patentability of proteomic claims depend on statutory background on the one hand and existing case law related to chemical, biotechnology and software inventions on the other. Thus, as a first step, the applicable law will be presented regarding the patentable subject matter, industrial application/utility, specification/written description, enablement and novelty and/or inventive step.

Next, the major case law will be examined. Cases related to biotechnological material will be used to exemplify how patent law systems have coped with the new genomic technologies. Since proteins are considered chemical compounds, the legal treatment of molecular structures will also be reviewed. One particular focus will be the patenting of primary structure-related protein inventions, where problems have mainly occurred regarding the novelty and inventive step requirement. Patent examiners have resolved these issues by applying certain principles, which will be developed in detail below. Such a comprehensive description will form the basis of subsequent chapters, which discuss the applicability of traditional patent law standards to 3-D, or proteomic, structures.

II. Applicable law in the U.S. and Europe

In order to be granted a patent in compliance with American patent law, at least the following criteria must be met: subject matter eligibility and utility (35 U.S.C. § 101), written description (35 U.S.C. § 112 1), enablement (35 U.S.C. § 112 1), clarity (35 U.S.C. § 112 2) novelty, no loss of rights (35 U.S.C. § 102), and non-obviousness (35 U.S.C. § 103). European patents are granted for any invention that is susceptible to industrial application, is new and involves an inventive step (Art. 52 I EPC). According to the practice of the EPO, an invention as understood in patent

159 See at Chapter 1 B II 2.

law is a "practical teaching, which requires the claimed subject-matter or activity to have a technical character, and which is capable of being realized and repeatable and provides a solution to a problem based on technical consideration."[160]

1. Patentable Subject Matter

a) U.S.

The fundamental principle of U.S. patent law is that one may patent that which is new. According to § 101, a patentable subject matter is determined as "any useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof".[161] As for the patenting of genes or proteins in the human organism, the intuitively appealing objection is that they themselves are not new. The human genome and the encoded proteins have existed in humans apart from any inventive effort of anyone who might seek to patent them.[162] The reasoning in *Funk Brothers Seed Co. v. Kalo Inoculant Co.* in 1948 was based on this argument.[163] The Supreme Court found the patent claims that were directed to a mixed culture of different strains of bacteria invalid and argued that patents cannot be issued for the discovery of a phenomenon of nature

> "The qualities of these bacteria, like the heat of the sun, electricity, or the qualities of metals, are part of the storehouse of knowledge of all men. They are manifestations of law of nature, free to all men and reversed exclusively to none."[164]

In light of a broad reading of *Funk Brothers*, DNA sequences and human proteins could not be considered as patentable subject matters. Although the *Funk Brother* decision never has been officially overruled, subsequent patent law does not deny the patentability of all inventions consisting of naturally occurring products or laws of nature. In the 1980 decision of *Diamond v. Chakrabarty*[165], the Supreme Court again touched the question of patentability of biotechnological inventions. The patent claim referred to living microorganisms into which the inventor had introduced multiple naturally occurring plasmids. These rings of bacterial DNA encompassed genetic information that resulted in the organism's ability to break down multiple components of crude oil. The USPTO found the plasmids not to be "products of nature", since bacteria containing the introduced plasmids did not occur in nature. Nevertheless, it rejected the claims on the ground that living organisms as such

160 Schulte/Moufang, PatG mit EPÜ, § 1, No. 19.
161 Chisum, Donald/Nard, Craig Allen/Schwartz, Herbert F./Newman, Pauline/Kieff, F. Scott, Principles of Patent Law, New York 2001, Chapter 3.
162 Eisenberg, Rebecca, Patenting the Human Genome, 39 Emory Law Journal 1990, 721, 723.
163 Funk Brothers Seed Co. V. Kalo Inoculat Co., 333 U.S. 127 (1948).
164 Funk Brothers Seed Co. V. Kalo Inoculat Co., 333 U.S. 127, 130.
165 Diamond v. Chakrabarty, 447 U.S. 303 (1980).

would not be patentable subject matter.[166] The Supreme Court concluded that a living, genetically modified organism may be patentable as a new "manufacture" or "composition of matter" under section 101. The Court distinguished *Funk Brothers* on the grounds set forth as follows: while the patent holder in *Funk Brothers* had not modified the function of any of the species of root-nodule bacteria in the mixed-culture inoculant, Chakrabarty had formed "a new bacterium with markedly different characteristics from any found in nature". The discovery thus was "not nature's handiwork, but his own; accordingly it is patentable subject matter …." In order to support this wide range of the categories of patentable subject matter, the Court relied on the language from committee reports accompanying the 1952 Patent Act, to the effect that Congress intended statutory subject matter to "include anything under the sun that is made by man." The question of distinguishing patentable subject matter and products of nature depends on whether the claimed invention is the result of human invention. With regard to human DNA sequences, one might still reason that they should not be patentable as such, although they might be a patentable subject matter in the creation of recombinant material that incorporates human genes. Nevertheless, a substantial amount of case law concludes that newly isolated or purified materials may be patented even though those materials exist in nature in an impure state. As long as the purified material offers some advantages, it is sufficient that a patent applicant has made the sequences available in an isolated or purified form that does not exist in nature.[167] In *Merck & Co. v. Olin Mathieson Chemical Corp.,* a patent was granted on purified vitamin B12 isolated from fermentation materials. The Court upheld the validity of the patent, arguing that the patent product was advantageous to the previously available vitamin B12 from cattle due to its relatively abundant supply, cheap price, freedom from toxic substances, and amenability to control potency and dosage. As a whole, the Courts' reasoning suggested that there should be no bar to patenting a "product of nature" assuming the invention is new, useful, falls within the categories of patentable subject matter under section 101, and complies with all further statutory patent requirements.[168]

In sum, *Diamond v. Chakrabarty* opened the door for the patenting of biological material. It thus can be considered as a decisive step in the rise of the biotechnological industry. Its economic implications have indeed been much further reaching than those of the German *Red Dove* decision, which will be discussed next.[169]

166 Eisenberg, Rebecca, Patenting the Human Genome, Emory Law Journal, 39 Emory Law Journal 1990, 721, 725.

167 Eisenberg, Rebecca, Patenting the Human Genome, 39 Emory Law Journal 1990, 721, 726-727.

168 Merck & Co. V. Olin Mathieson Chemical Corp. 253 F.2d 156 (4th Cir. 1958).

169 Straus, Joseph, Biotechnology and Patents, 54 Chimia 2000, 293, 293.

b) Europe

aa) Patentability of biological material

In Europe, for many decades, inventions involving biological material were not considered patentable on grounds that they were not 'technical' but 'a product of nature'. This approach has been radically changed by the landmark decision of *Red Dove*[170], where the patent application was directed to a method for breeding a dove with red plumage.[171] The German Federal Supreme Court clearly extended the field of technology so as to cover biological phenomena and forces, defining them as

> "… [a] teaching to methodically utilize controllable natural forces to achieve a causal, perceivable result, …, provided that teaching meets the general prerequisites of industrial application, novelty, [etc.]."[172]

The court reasoned that there generally are three possibilities of biological inventions that have been considered patentable in theory and practice:

-If the course of biological events is affected with means other than animate matter;

- if inanimate matter is influenced by biological means and

- if the means as well as the final result lie within the field of biology.

The patent application at issue belonged to the third category of possibilities in which a biological result is obtained either solely by or primarily as the result of biological means. Thus, patentability would in principal be possible. Nevertheless, it was necessary that the method of breeding be recurrent. Lacking such requirement, a patent could not be granted. Although a patent was not granted for the claim at issue, the decision clearly approved the patentability of biological inventions as eligible subject matters. [173]

With the goal of providing high and harmonized standards of protection for biotechnology comparable to those in the U.S. and Japan, the European Commission adopted the Directive on the Legal protection of Biotechnology Inventions (98/44/EC) ('the Directive') in 1998.[174] The Directive, which became effective on

170 BGH, 1 IIC 136 (1970) - Red Dove (Rote Taube); see also Herrlinger, Karolina A., Die Patentierung von Krankheitsgenen: dargestellt am Beispiel der Patentierung der Brustkrebsgene BRCA 1 und BRCA 2, München 2005, 115.

171 Straus, Joseph, Biotechnology and Patents, 54 Chimia 2000, 293, 293; the "Red Dove case" also is the starting point for the modern jurisdiction on the patentablility of biological inventions in Germany, Straus, Joseph, Patenting Human Genes in Europe - Past Developments and Prospects for the Future, 26 IIC 920, 920 (1995); Benkart/Melullis, EPÜ, Art. 53, No. 44.

172 BGH 1 IIC 136, 137 (1970) - Red Dove (Rote Taube); see also Busse/Keukenschrijver, PatG, § 1, No. 24.

173 BGH 1 IIC, 137ff (1970) - Red Dove (Rote Taube).

174 Benkard/Schäfers, PatG, § 34 No. 37e; Jaenichen, Hans-Rainer/Mcdonell, Leslie A./Haley, James F., Jr., From Clones to Claims, Cologne, Berlin, Bonn, Munich 2002, 2; Straus, Joseph, Biotechnology and Patents, 54 Chimia 2000, 293, 295.

July 6, 1998, strikes a balance between the commercial needs of scientists and industry and the ethical concerns of some of the public that strongly opposed the idea of patenting living material.[175] The contracting states of the EU were supposed to put the Directive into practice within two years of the date of publication by changing the national practice and law where necessary. Irrespectively, the process of implementation in each of the member states took much longer than expected. After three years, only four member states, United Kingdom, Finland, Denmark and Ireland, had actually put the rule into practice. The European Court of Justice rejected an action of annulment against the Directive that was filed by the Netherlands and supported by Italy and Norway.[176] In 2004, Germany was convicted by the European Court of Justice for having failed to implement the Directive into national law. Consequently, the German legislature reacted and implemented the Directive in February 2005 by amending the German Patent Act.[177]

With the EPO not being linked to the European Union, the Directive does not have any direct influence on the EPC.[178] However, in order to harmonize the EPO's practice with the EU Directive, the Implementing Regulations to the EPC were amended by a decision of the Administrative Council of the European Patent Organization on June 16, 1999. For this amendment, the EPO introduced several new rules. On December 13, 2007, a revised version of these rules entered into force.[179] To incorporate the Directive into the EPC, the EPO introduced Rule 26 (former 23b) (General and definitions), Rule 27 (former 23c) (Patentable biotechnological inven-

175 As for the concerns of the different groups of interest in Germany, see particularly 'Entwurf eines Gesetzes zur Umsetzung der Richtlinie über den rechtlichen Schutz biotechnologischer Erfindungen', Bundestagsdrucksache 14/5642 (November 23, 2001), 1-24 (reasons and statements provided by the German Federal Council and the German Federal Government; see also Straus, Joseph, Biotechnology and Patents, 54 Chimia 2000, 293, 295.

176 EuGH C-377/98 in: GRUR Int 01, 1043 = BIPMZ 01, 357 Biotechnology Directive; see also Schulte/Moufang, PatG mit EPÜ, § 1 No. 79. According to the French view, the patenting of human genes is violating human dignity. Consequently, France rejected the implemenation of the rule into its national law and asked the Commission to reconsider the Directive. In a statement that strongly supported this policy, the French National Committee on Ethics in the Life and Health Sciences summarized the underlying considerations. For example, it stated: "L'exigence qui porte à exclure cette connaissance du gène de la brevetabilité rejoint deux autres préoccupations éthiques le souci de maintenir le corps humain, ses éléments et ses produits hors des circuits marchands, l'apparition d'une aspiration au partage des bienfaits attendus de la connaissance du genome," Comité Consultatif National d'Ethique pour les sciences de la vie et de la santé, "Avis sur l'avant-projet de loi portant transposition, dans le code de la propriété intellectuelle de la directive 98/44/CE du Parlement européen et du Conseil, en date du 6 juillet 1998, relative à la protection juridique des inventions biotechnologiques," 8 Juin 2000, para 6), available at http://www.ccne-ethique.fr/francais/start.htm, last checked on December 10, 2006.

177 The details of the European Court of Justice's verdict and of the German Patent Act amendment will be discussed in Chapter IV D below.

178 Benkard/Melullis, EPÜ, Art. 53, No. 39; Straus, Joseph, Biotechnology and Patents, 54 Chimia 2000, 293, 295.

179 Decision of the Administrative Council, Act revising the European Patent Convention of 29 November 2000.

tions), Rule 28 (former 23d) (Exceptions to patentability) and Rule 29 (former 23e) (The human body and its elements).[180] Rule 26(1), second sentence (former 23 b (1)) establishes the general principle that the Directive "shall be used as a supplementary means of interpretation" of the EPC.[181] The basic principles of the Directive are listed in Recitals 35-46. These include the exclusion from patentability for processes for treatment of the human or animal body by surgery or therapy and diagnostic methods (Recital 35) and the guarantee of *ordre public* or morality (Recitals 37 and 39). The Directive also contains a commitment to the special importance of the "ethical clause", where it is indicated that all ethical aspects of biotechnology must be interpreted in light of the specified principles of patent law and specifically evaluated by the Commission's European Group on Ethics in Science and new Technologies (Recital 44).[182] With regard to biological material, the Directive confirms the practices that were approved in the German *Red Dove* decision by introducing the patentability of biological material or processes.[183] The principle applies also to biological material, provided it is isolated from the natural environment or produced by means of a technical process (Art. 2(1)(a)(Rule 23b (3) EPC; Art. 3(1) (2); Rule 27(a) EPC (former Rule 23c (a)).[184]

bb) Exclusions from patentability

The approach to what constitutes patentable subject matter can be considered a major difference between the European and the U.S. patent law system. As illustrated in *Diamond v. Chakrabarty*, the U.S. Patent Act does not contain any specific exclusions or exceptions from patentability.[185] Rather, the courts are responsible for setting the limits inherent in the principles of the patent system. In contrast, European patent law is characterized by several of such exclusions and exceptions and many are specifically directed to the field of biotechnology.[186]

Section 52 EPC excludes certain matters from patentability. Items on this list include, in particular, discoveries, scientific theories, mathematical methods, aesthetic

180 Jaenichen, Hans-Rainer/Mcdonell, Leslie A./Haley, James F., Jr., From Clones to Claims, Cologne, Berlin, Bonn, Munich 2002, 3.

181 Schulte/Moufang, PatG mit EPÜ, § 1, No. 6, citing Rule 23b(1) Second Sentence; see also Straus, Joseph, Biotechnology and Patents, 54 Chimia 2000, 293, 295.

182 For the "ethical dimension of the patent law system" as expressed in Art. 53(a) EPC see Moufang, Rainer, Patentierung menschlicher Gene, Zellen, und Körperteile? - Zur ethischen Dimension des Patentrechts, GRUR 1993, 439, 442. Despite Art. 53(a) EPC the European Patent Office issued large numbers of gene patents without raising any ethical issues; Straus, Joseph, Patenting Human Genes in Europe - Past Developments and Prospects for the Future, 26 IIC 920, 926 (1995).

183 Schulte/Moufang, PatG mit EPÜ, § 1 No. 86.

184 Straus, Joseph, Biotechnology and Patents, 54 Chimia 2000, 293, 295.

185 Diamond v. Chakrabarty, 447 U.S. 303 (1980), see Chapter 3 A II 1 a).

186 Schulte/Moufang, PatG mit EPÜ, § 1 Nos. 86ff, see also Straus, Joseph, Biotechnology and Patents, 54 Chimia 2000, 293, 294.

creations, schemes, rules and methods for performing mental acts, playing games or doing business, programs for computers and presentations of information.[187] Lacking a technical character, a discovery does not provide a practical teaching and is therefore not patentable. [188] This is particularly relevant for inventions involving biotechnological substances. Under the foregoing definition, the revealing of a previously unrecognized substance occurring in nature is a mere discovery. If the patent applicant, however, shows in which way the substance was isolated from its natural environment or how a technical process had produced it, patentability is established. Thus, the mere description of biological material is not sufficient. If a repeated success in isolating a biological substance, like a protein or a gene, is not guaranteed, the invention does not establish a technical teaching and lacks patentability.[189] The disclosed technical teaching, i.e. the isolation of the biological substance, must be repeatable.[190]

The House of Lords' decision in the case of *Asahi Kasei Kogyo's Application* can be considered decisive for determining the threshold for genetic sequences disclosures.[191] Here, the application in suit [the 'Asahi-Application'] disclosed and claimed a physiologically active polypeptide produced by genetic engineering and useful in treating human tumors. The Asahi-Application was rejected by the Patent Office on the grounds that they lacked novelty in view of a co-pending application. The co-pending application was filed after the priority date of the application in suit but claimed priority from an earlier application, which disclosed and claimed the polypeptide but failed to explain how to obtain and how to use the genetic sequences coding for it. The applicant appealed to the English House of Lords asserting that the co-pending application was not an effective anticipation because the only document of earlier priority did not contain an enabling disclosure.[192] The House of Lords concluded that, for anticipation "published information is required to contain an enabling disclosure." An invention is "not made available to the public merely by a published statement of its existence, unless the method of working is so self-evident as to require no explanation."[193] As for the description of the polypeptide,

187 Guidelines for Examination in the EPO, Part C-IV, § 2, available at http://www.epo.org/patents/law/legal-texts/guidelines.html, last checked on January 21, 2008. The list established in Art. 52 EPC is not complete, but is seen to provide a number of examples, see Busse/Keukenschrijver, PatG, § 1, No. 39.

188 Singer/Stauder, EPC, Vol 1, Art. 52, No. 24.

189 Schulte/Moufang, PatG mit EPÜ, § 1 No. 93. A patent applicant establishes patentability for natural substances if he provides "the discovery of a technical application of the discovery." The patent is granted, because the substance was "previously not available." Therefore, the public is not being denied access to something previously accessible; see Singer/Stauder, EPC, Vol 1, Art. 52, No. 25.

190 Schulte/Moufang, PatG mit EPÜ, § 1 No. 98.

191 Asahi Kasei Kogyo's Application, [1991] R.P.C. 485 (House of Lords). See also Cornish, William/Llewelyn, David, Intellectual Property: Patents, Copyright, Trade Marks and Allied Rights, 6th ed., London 2007, 190.

192 Asahi Kasei Kogyo's Application, [19 91], R.P.C. 485, 486.

193 Asahi Kasei Kogyo's Application, [1991], R.P.C. 485, 486.

the court stated "[f]or a chemical product (as what the polypeptide was treated) the invention does not consist in the formula itself, but in a description of a method", because a person skilled in the art will need to know "a method by which it can be produced."[194] In light of these principles, the co-pending application did not destroy the novelty of the Asahi-application, since it failed to provide any methods for preparing the claimed polypeptide.[195]

Further, Directive 98/44/EC implements the principle of non-commercialization of the human body. Art. 5(1) states that "[t]he human body, at 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" are excluded from patentability. The Implementing Regulations to the EPC, Rule 29 EPC (former 23e (1) EPC) follows this standard.[196] However, an element isolated from the human body or otherwise produced in the course of a technical process, which is industrially applicable, may be eligible as a patentable subject matter, even if the structure of that element is identical to that of a natural element. As set forth above, biological material that is isolated from its natural environment or produced in the course of a technical process may be patentable.[197] Non-isolated genes in their natural environment, by contrast, are considered mere discoveries.[198]

With regard to computerized methods of protein analysis, the exclusion of computer programs plays an important role. The question will be addressed in the course of the following case study. At this point, it has already been stressed that exclusions are only made if the listed subject matters are claimed "*as such*".[199] The former version of Art. 52(4) EPC stated that 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 susceptible to industrial application and therefore excluded from patentability.[200] The exclusion does not apply to certain products, e.g., pharmaceuticals, which are considered industrially applicable even if used for medical treatment.[201] In light of the fact that the provision was found to be systematically incor-

194 Asahi Kasei Kogyo's Application, [1991], R.P.C. 485, 486.

195 See Tumour Necrosis Factor, 2 IIC 247 (1993), particularly the comment by Rainer Moufang in the same issue who notes that in the light of the House of Lords' decision, a patent application referring to biological material anticipates later filed applications if others "under no obligation of confidentiality had access to the said material at the critical date," at 258.

196 Ahrens, Claus, Genpatente - Rechte auf Leben? Dogmatische Aspekte der Patentierbarkeit von Erbgut, GRUR 2003, 89, 91.

197 Guidelines for Substantive Examination, Part C-IV, § 2a.2 available at http://www.epo.org/patents/law/legal-texts/guidelines.html, last checked on January 21, 2008

198 Krefft, Alexander Richard, Patente auf human-genomische Erfindungen: Rechtslage in Deutschland, Europa und den USA, München 2003, 266.

199 As for the difficulties that exist with the interpretation of the term "as such", see Busse/Keukenschrijver, PatG, § 1, No. 41.

200 Busse/Keukenschrijver, PatG, § 5, No. 19.

201 Methods which are employed outside the human body (ex vivo), on a blood or other sample also do not fall under the definition of diagnostic methods practised on the human body,

rect - since methods are excluded on public interest grounds and not due to the lack of industrial patentability[202] - the 2000 revision of the EPC, put into force on December 13, 2007, cancelled the rule. What used to be the rule under Art. 52(4) EPC is now added as c) under Art. 53 EPC:

> "European patents shall not be granted in respect of: c) methods for treatment of the human or animal body by surgery or therapy and diagnostic methods practiced 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."

2. Utility and Industrial Applicability

a) U.S. (Utility)

Two statutory provisions establish the framework for analyzing the utility requirement. As recited in 35 U.S.C. § 101:

> "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title."

The second provision with regard to the utility requirement is 35 U.S.C. § 112. It is related to the disclosure the patent applicant is obliged to make. Section 112, first paragraph explicitly requires a patent specification to disclose "the manner and process of making and using [the invention]." The concrete meaning of these two phrases has largely been developed by the courts. As for chemical research, chemical scientists often develop a chemical substance without a particular purpose in mind. Often, chemical compounds are synthesized which are believed to be useful some day for something, but for which no particular use is currently known. As for biotechnology, scientists may isolate interesting genes or gene fragments whose use is not known or completely analyzed. Sometimes researchers are able to understand that genes are triggered in many diseased cells, even though the protein that the gene is encoding is yet unknown.[203]

In 1999, the office issued the Revised Utility Guidelines, as clarification of the final Utility Examination Guidelines as published in 1995.[204] These guidelines can be considered a direct reaction to public comments expressing doubts regarding the pa-

Bostyn, Sven J.R., Enabling Biotechnological Inventions in Europe and the United States: A Study of the Patentability of Proteins and DNA Sequences with Special Emphasis on the Disclosure Requirement, Munich 2001, 115.

202 EPO, Special Edition No. 4, OJ 2007, 48.

203 Merges, Robert Patrick/Duffy, John Fitzgerald, Patent Law and Policy: Cases and Materials, Newark, San Francisco, Charlottesville 2002, 229.

204 1999 Revised Utility Guidelines, 64 Fed. Reg., 71440 (Dec. 21, 1999), which were published in response to comments regarding the earlier Guidelines, published at 60 Fed. Reg. 36263 (1995).

tentability of ESTs. In particular, the PTO determined that it had received comments that the 1995 Utility Guidelines would permit the patenting of ESTs "when the sole disclosed use of an EST is to identify other nucleic acids whose utility was not known, and the function of the corresponding gene is not known."[205] The 1999 Revised Utility Guidelines also account for allegations that "PTO examination procedures would result in granting patents based on non-specific and non-substantial utilities, contrary to established case law."[206] Consequently, the 1999 Guidelines determine that a "claimed invention must have a specific and substantial utility."[207] The guidelines did not amend the rules of the 1995 Utility guidelines with regard to other aspects, such as "credibility" and "well-established" utility.

In 2001, the USPTO again issued a new version of its guidelines on utility.[208] The 2001 Utility Guidelines provide a substantial amendment of the 1995 version. Particularly, the guidelines require that utility is only created, if the utility of a patent application is "specific", "substantial", and "credible".[209] Furthermore, the 2001 Utility Guidelines determine that - if it becomes apparent that an invention bears a "well-established utility" - the claim should not be rejected due to a lack of utility. A "well-established" utility is assumed if (a) a person skilled in the art would easily be able to determine why an invention is useful due to the properties of an invention, and (b) the utility is specific, substantial, and credible.[210] As for a specific and substantial utility, the USPTO indicates that "throw-away", "insubstantial", and "non-specific" utilities, such as the use of a complex invention as landfill are excluded. With regard to credibility, the guidelines held that "[c]redibility is assessed from the perspective of one of ordinary skilled in the art in view of the disclosure and any other evidence of record (e.g. test data, affidavits or declarations from experts in the art, patents or printed publications) that is probative of the applicant's assertions."[211]

Thus, one must distinguish between applications defining an invention's specific use and those indicating an ambiguous or unsubstantiated potential use. A general statement that a compound has "useful biological" properties and might aid in the treatment of some unnamed disorders is too vague to qualify as a specific utility. A "substantial utility" should establish a "real world" use. If a "real world" context for using the invention is not reasonably apparent from the record, then the asserted utility is not substantial.[212] It is inappropriate to label certain types of inventions as incapable of having a specific and substantial utility based solely on the setting in which the invention is used, for example, inventions used in a research or laboratory setting. Many research tools used in laboratory analysis and the assessment of com-

205 1999 Revised Utility Guidelines, 64 Fed. Reg. 71440, 71441.
206 1999 Revised Utility Guidelines, 64 Fed. Reg. 71440, 71441.
207 1999 Revised Utility Guidelines, 64 Fed. Reg. 71440, 71441.
208 2001 Utility Guidelines, 66 Fed. Reg. 1092. (Jan. 5, 2001).
209 2001 Utility Guidelines, 66 Fed. Reg. 1092, 1098.
210 2001 Utility Guidelines, 66 Fed. Reg.1092, 1098.
211 2001 Utility Guidelines, 66 Fed. Reg. 1092, 1098.
212 Merges, Robert Patrick/Duffy, John Fitzgerald, Patent Law and Policy: Cases and Materials, Newark, San Francisco, Charlottesville 2002, 249.

pounds, such as gas chromatographs, screening assays, and nucleotide sequencing techniques, have a clear, specific, and substantial utility in a research or intermediate context. However, this evaluation alone does not focus on the invention's overall utility in a patent sense. Instead, it is necessary to distinguish between inventions identifying a current and specific substantial utility and those requiring additional or future research to establish or verify usefulness. In this process, applicants' use of labels such as "research tool", "intermediate," or "for research purposes" are not determinative of whether the claimed invention has a specific, substantial and credible utility.[213]

A number of cases illustrate how patent examiners and courts struggle with setting the exact threshold for the utility requirement. In *Brenner v. Manson*[214], the inventor applied for a patent on an allegedly novel process for making certain known steroids. A patent examiner denied the application, and the denial was affirmed by the Board. The ground for rejection was the failure "to disclose any utility for the chemical compound produced by the process".[215] The failure was not cured, according to the Patent Office, by the inventors reference to an scientific article revealing that steroids of a class, which included the compound in question, were undergoing screening for tumor-inhibiting effects in mice, and that a homologue adjacent to this steroid had proven effective in that role. The U.S. Supreme Court reconfirmed that one may patent only that which is "useful". The reference to the article, however, could not create utility, since the "presumption that adjacent homologues have the same utility has been challenged in the steroid field because of a greater known unpredictability of compounds in that field".[216] The court clearly stated that where the sole "utility" consists in its potential role as an object of use-testing, a practical or specific utility does not exist. A patent should be "no award for the search, but a compensation for its successful conclusion".[217]

In *In re Brana,* the applicants filed a patent application directed to compounds for use in combination with anti-tumor substances that were based on a specific chemical formula.[218] The specification stated that the given substitutions produce compounds with "better action and a better action spectrum than anti-tumor substances" established in a particular reference.[219] The reference described a computer-assisted evaluation of specific chemicals which had been screened for anti-tumor activity by testing their efficacy *in vivo*. Further, in comparing the effectiveness of the claimed compounds with structurally similar compounds, the applicants' patent specification disclosed the cytoxicity of the claimed compounds against human tumor cells, *in*

213 Kunin, Stephen G/Nagumo, Mark/Stanton, Brina/Therkorn, Linda S./Walsh, Stephen, Reach-through Claims in the Age of Biotechnology, 51 American University Law Review April 2002, 609, 623.
214 Brenner v. Manson, 383 U.S. 519 (1966).
215 Brenner v. Manson, 383 U.S. 519, 521
216 Brenner v. Manson, 383 U.S. 519, 532.
217 Brenner v. Manson, 383 U.S. 519, 536.
218 In re Brana, 51 F.3d 1560 (Fed. Cir. 1995).
219 In re Brana, 51 F.3d 1560, 1562.

vitro, and held the opinion that these tests "had a good action".[220] The Court of Appeals for the Federal Circuit concluded that the applicant's disclosure complied with the requirements of 35 U.S.C. Section 112 (1). According to the court, the disclosed tumor models represent a specific disease against which the claimed compounds are alleged to be effective. In light of the given references, the applicant's specification alleges a sufficiently specific use. Even if one skilled in the art would be convinced of the applicant's asserted utility "… applicants proffered sufficient evidence to convince one of skill in the art of the asserted utility."[221] The provided test results showed that several compounds within the scope of the claims exhibited significant anti-tumor activity and thus would have been sufficient to satisfy applicants' burden.[222]

The early Supreme Court reasoning of *Brenner* gained particular importance in the light of the patenting of cDNA sequences. Craig Venter, a scientist working at the National Institutes of Health (NIH), initiated a project involving the documentation of all cDNA sequences matching the mRNA for each gene in the active, protein-encoding DNA sequences in a human brain. The c in cDNA refers to "complementary". A complementary DNA sequence is defined as the sequence matching the "genetic messenger" carrying the encoded information for a particular gene, the messenger RNA or mRNA.[223] Since only the exons of a DNA strand are translated into protein, the RNA only consists of the complementary information of the exons themselves. The cDNA thus must be considered as the complement of the translated exons and consequently is distinguishable from the original DNA. Before Venter initiated his work, libraries of cDNA fragments had been documented, but no one had obtained detailed base pair sequences for each fragment. Venter had only to sequence a portion of the cDNA segments, and with that portion the gene sequence itself, the actual gene, could be identified or reconstructed. He named the partial sequences "expressed sequence tags" or "ESTs". In a patent application, he claimed each of the ESTs he had produced. The U.S. National Institutes of Health (NIH) requested a legal opinion on the validity of the patent application. The opinion denied validity, reasoning in light of *Brenner*:

> "Use of the ESTs as probes to obtain full cDNA sequences has no practical benefit unless and until the full sequences themselves may be used for some purpose beyond research. Subsequent research may well prove some of the genes useful for diagnosis or therapeutic purposes, but the information disclosed in the specification fails to identify which of the genes will be useful, or for which purposes. Practical utility of the sequences awaits determination of the function of the genes they are associated with …"[224]

220 In re Brana, 51 F.3d 1560, 1563.
221 In re Brana, 51 F.3d 1560, 1567.
222 In re Brana, 51 F.3d 1560, 1567.
223 Merges, Robert Patrick/Duffy, John Fitzgerald, Patent Law and Policy: Cases and Materials, Newark, San Francisco, Charlottesville 2002, 250.
224 Eisenberg S. Rebecca; Merges,/Merges, Robert P., Opinion Letter as to the Patentability of Certain Inventions Associated with the Identification of Partial cDNA Sequences, 23 American Intellectual Property Law Association Q. J. 1995, 16-19.

Based on the opinion, Venter's patent application was ultimately dropped by NIH after having created a storm of controversy.[225] The demonstrated case law was finally summarized in the U.S. utility guidelines, which had been issued in 1995 in response to criticism of pervasive utility rejections involving biotechnology and therapeutic method claims.[226]

In *In re Fisher,* the patent applicant attempted to claim five ESTs that coded for parts of certain proteins in maize plants.[227] At the time Fisher filed the patent application, he "did not know the precise structure or function of either the genes or the proteins encoded for by those genes". The application encompassed seven uses of the claimed ESTs in an attempt to satisfy the utility requirement. The Federal Circuit concluded that "none of Fisher's seven asserted uses meets the utility requirement of § 101."[228] The court clearly determined that an "application must show that an invention is useful to the public as disclosed in its current form, not that it may prove useful at some future date after further research," and "must disclose a use which is not so vague as to be meaningless."[229] EST's coding parts of proteins with unknown function were seen as merely "objects upon which scientific research could be performed with no assurance that anything useful will be discovered in the end."[230] The court found that Fisher had not actually used gene fragments for any of the listed uses in the real world.[231] Consequently, Fisher's invention lacks "substantial" utility.[232] Fisher's patent application also does not have a "specific" utility, because "[a]ny EST transcribed from any gene in the maize genome has the potential to perform any one of the alleged uses." Therefore, "nothing about Fisher's seven alleged uses" makes the five claimed ESTs different from "any EST derived from any organism."[233]

b) Europe (Industrial Applicability)

According to Art. 57 EPC, a patent must be susceptible to industrial application, which means that it can be made or used in any type of industry, including agriculture. In compliance with the guidelines of the EPO, "industry" is construed in its

225 Merges, Robert Patrick/Duffy, John Fitzgerald, Patent Law and Policy: Cases and Materials, Newark, San Francisco, Charlottesville 2002, 253, Straus, Joseph, Patenting Human Genes in Europe - Past Developments and Prospects for the Future, 26 IIC 920, 934 (1995).
226 USPTO, Utility Examination Guidelines, 60 Fed. Reg. 36, 263 (1995).
227 In re Fisher, 421 F.3d. 1365, 1372 (Fed. Cir. 2005).
228 In re Fisher, 421 F.3d. 1365, 1370.
229 In re Fisher, 421 F.3d. 1365, I371.
230 In re Fisher, 421 F.3d. 1365, 1373.
231 In re Fisher, 421 F.3d 1365, 1374.
232 In re Fisher, 421 F.3d 1365, 1374.
233 The court emphasized that "[t]he claimed ESTs themselves are not an end of Fisher's research effort, but only tools to be used along the way in the search for a practical utility." In re Fisher, 421 F.3d 1365, 1374.

broad sense as including any physical activity of "technical character", and a useful or practical art rather than an aesthetic art.[234] The guidelines provide a list of industrially applicable inventions. Generally, they state that an invention not corresponding to the listed inventions will not be considered industrially applicable.[235] The Implementing Regulations to the EPC have incorporated the EU-Directive and require that the industrial application must be disclosed in patent applications for partial sequences of genes, Rule 29 (former Rule 23e(3)).

The European patent system reacted also to the development that large numbers of ESTs and Single Nucleotide Polymorphisms (SNPS) in the U.S. were filed for patentability.[236] The 'Biotechnology Directive' set forth in Recital 23 that a mere DNA sequence without the indication of a given function does not provide any technical information and therefore lacks industrial applicability. "Function" in this context must be understood as any function causing a technically applicable result, such as use as a diagnostic marker or screening tool. In the cases in which a sequence or partial sequence is used to produce a protein or part of a protein, the industrial applicability is only established if the patent application indicates which protein or part of a protein is produced or what function it serves (Recital 24). The EPO adopted this requirement in the Implementing Regulations to the EPC, Rules 26-29 EPC (former Rules 23b-23e EPC) and the case law of the Opposition Division approved the new established principles. In *Novel V28 seven transmembrane receptor,*[237] the division had to examine whether the requirement of industrial application was satisfied. The patentee argued that pursuant to Art. 57 EPC the requirement of industrial application of an invention is satisfied "if it can be made or used in any kind of industry". Thus, he alleged that the disclosure of how to make and to use a protein would be sufficient. The Opposition Division disagreed, maintaining that such disclosure does not provide a credible function of a DNA sequence encoding a protein and thus rejected the patent based on a lack of industrial application. With regard to the application of the Biotechnology Directive, the division stated:

> "The requirements of industrial application of biotechnology inventions are set by Rules 23b-23e EPC which concern European patent application and patents. Thus, the provisions of said rule apply to the present procedure and the recitals of European Directive 98/44/EC are applicable as supplementary means of interpretation. In view of the requirement of industrial application as set in Art. 57 in conjunction with Rule 23b-e EPC, the invention cannot be acknowl-

234 Industrially requires that the invention as such can be manufactured industrially or used in any sort of industrial field, see Busse/Keukenschrijver, PatG, § 5, No. 8.

235 Guidelines for Examination in the EPO, Part C-IV, 4, available at http://www.epo.org/patents/law/legal-texts/guidelines.html, last checked on January 21, 2008.

236 The European, Japanese and United States Patent Offices conducted a Trilateral study on the patenting of EST (Trilateral Project B3b on "The Patentability of DNA Fragments). For an analysis of their approaches see, Howlett, Melanie J./Christie, Andrew F., An analysis of the approach of the European, Japanese and United States Patent office to Patenting Partial DNA Sequences (ESTs), 34 IIC 581 (2003).

237 Decision of the Opposition Division of June 21, 2001, V28 receptor/Icos, OJ 2002, 293-308.

edged as industrially applicable because industrial applications are not disclosed in the patent application (Rule 23e(3)EPC)."[238]

3. Novelty

In the case of proteomic inventions, a major question which emerges is whether the three dimensional structure is sufficient to fulfill the novelty requirement. For such a classification, patent law principles related to the field of chemistry are of particular interest, because chemistry provides a comparable field of research. Stereochemistry is referred to as the study of the three-dimensional shape of molecules.[239] With regard to patent law, the novelty of diastereomers and enantiomers[240]is a frequently discussed issue.[241] The precise details will be demonstrated in the course of the proteomic-related case study below. At this point, the general statutory background as to novelty will be illustrated. To illustrate the entire legal terrain which proteomic inventions must face, the principles applicable to biochemistry and particularly classical protein research are also presented.

a) U.S.

Under 35 U.S.C. § 101, an invention must be "new."[242] In compliance with Section 102(a), it lacks novelty if it is "known or used by others" in the United States, or "patented or described in a printed publication" in the US or a foreign country.[243]

238 Decision of the Opposition Division of June 21, 2001, V28 receptor/Icos, OJ 2002, 293-308, 303.

239 For an introduction into the field of stereochemistry, see Alworth, William L., John Wiley & Sons, Inc., Stereochemistry and Its Application to Biochemistry, New York 1972.

240 Isomers are compounds bearing the same atomic compositions, but different physical and/or chemical properties. Stereoisomers are isomers consisting of atoms that differ only by their orientation in space. Diasteromers are stereoisomers that are non-superimposable, but are not mirror images. Enantiomers are stereoisomers that are non-superimposable mirror images. See IUPAC Compendium of Chemical Terminology, available at http://www.iupac.org/publications/compendium/index.html, last checked on January 21, 2008.

241 See particularly T12/81 Diastereomere, OJ 1982, 296; T990/96, N. Publ.(EPO 1998); T296/87 Enantionmers/Hoechst, OJ 1990, 195; T1048/92, N. Publ.(EPO 1994); T600/95, N. Publ.(EPO 1996); T1048/92, N. Publ.(EPO 1994). As for the U.S. patent law practice, see In re Doyle, 293 F.3d 1355 (Fed. Cir. 2002), also Domeij, Bengt, Pharmaceutical Patents in Europe, Stockholm 2000, 146.

242 For a brief summary on the novelty requirement, see also Rader/Adelman, Cases and Materials on Patent Law, 248-249.

243 As explained by Chisum, the meaning of the novelty requirement is further determined in Section 102(e) which „bars a patent on an invention described in a patent application published under Section 122(b) or a patent by another filed in the United States before the invention thereof by the applicant for patent. In addition, "Section 102(g) bars a patent on an in-

The distinction between the different paragraphs of 35 U.S.C. § 102 requires careful examination. Subsection (f) can be interpreted as the requirement that the patent applicant has actually invented the subject matter. It is prohibited to derive or steal it from others. Furthermore, the provision covers two major aspects: the novelty requirement as such and statutory bar subsections. Both requirements refer to timing issues. The novelty subsections are directed only to events that take part prior to the time of invention:

> § 102 (a): "before the invention thereof by the applicant", (e) (same expression), and (g): "before such person's inventions thereof".

In contrast, the statutory bar subsections may be matched by events occurring after the invention. For instance, § 102(b) prohibits the granting of a patent if the invented subject matter was disclosed in a printed publication more than one year prior to filing for a patent. Likewise, subsections (c) and (d) are also triggered by events (abandonment, foreign filing by the applicant) that takes place after the applicant's invention.[244]

In sum, novelty requires the inventor to comply with subsections (a), (e) and (g). The inventor's right to obtain a patent, however, will be lost if any event matches up with one of the statutory bars found in subsections (b) – (d). Therefore, the statutory bars are called "loss of right to patent". It is thus important to note that the U.S. defines novelty according to the date of invention. In contrast, Europe measures novelty as of the filing date.[245] The requirement that all elements of the claimed invention must be identically described in a single prior art reference ("All Elements Rule"), however, is valid in Europe as well as in the U.S. Accordingly, anticipation requires that every feature of the claimed invention must be taught - explicitly, implicitly or by incorporation by reference - in a single piece of prior art.[246] There are no specific guidelines regarding the novelty examination practice of the USPTO.

As for biological products, the "All Elements" rule often results in the question of how a given prior reference is distinguishable from a slightly modified recombinant form. In *Scripps Clinic & Research Foundation v. Genentech, Inc.*,[247] the defendant held that the alleged invention related to a recombinant product was anticipated by a published dissertation and three declarations by its author. The cited dissertation, however, differed from the "fingerprint" identification of the invention (a VIII:C

vention that before [a person's] invention therof ... was made in this country by another inventor who had not abandoned, suppressed, or concealed it."[citation omitted], see Chisum, Donald, Chisum on Patents, Volume 1, § 3.01.

244 Merges, Robert Patrick/Duffy, John Fitzgerald, Patent Law and Policy: Cases and Materials, Newark, San Francisco, Charlottesville 2002, 363.

245 Merges, Robert Patrick/Duffy, John Fitzgerald, Patent Law and Policy: Cases and Materials, Newark, San Francisco, Charlottesville 2002, 363.

246 Scripps Clinic & Research Found. v. Genentech, Inc. 927 F.2 d 1565, 1576 (Fed. Cir. 1991); Amgen, Inc. v. Hoechst Marion Roussel, Inc., 126 F.Supp. 2d 69, 91 (D.Ma.2001) Put simply, anticipation requires that every element of the claimed invention be previously described in a single reference.

247 Scripps Clinic & Research Found. v. Genentech, Inc. 927 F.2d 1565.

Factor) obtained by the patentee. The Court of Appeals for the Federal Circuit concluded that the given prior art reference did not establish anticipation, in that it did not identically demonstrate each element of the claimed invention. Accordingly, the Court remanded the case for trial to determine whether there were differences between the "fingerprint" factor (human factor VIII:C) derived from plasma and that produced by recombinant technology, such as purity, specific activities, stability, and formulations.[248]

Anticipation will be avoided if a claimed composition is of increased purity, in contrast to its unpurified appearance occurring in nature. In *In re Bergstrom* the invention was related to two chemical compounds (PGE(2) and PGE(3)).[249] The claims at issue were rejected due to the lack of novelty. The USPTO stated that the specification gave references indicating that the claimed compounds naturally occurred in natural glandular material, or in a variety of fractions and liquors derived from the glandular material. The Court concluded that novelty existed, finding that the claimed compounds exhibited a higher purity than those occurring in nature and stated that "[p]ure materials necessarily differ from less pure or impure materials and, if the latter are the only ones existing and available as a standard of reference, as seems to be the situation here, perforce the 'pure' materials are 'new' with respect to them."[250] The court, however, emphasized that

> "[w]hether the claimed pure materials have the same usefulness or assortment of properties as the impure materials of the prior art … is a question having no bearing on the factual and legal matter whether pure materials are new vis-à-vis impure materials within the meaning of § 101, although it is but one of the factors to be considered in determining their obviousness under 35 U.S.C. § 103."[251]

Accordingly, the court did not examine whether the purer compound is sufficiently different to constitute a "new and useful … manufacture, or composition of the matter, as required in 35 U.S.C. § 101"[252] Section 101 is rather equated with the standard of novelty under § 101 and a more pure compound is considered to meet the

248 Scripps Clinic & Research Found. v. Genentech, Inc. 927 F.2d 1565, 1576-1578, (Fed. Cir. 1991). A number of further Federal Circuit decisions affirm that a prior art publication must be enabling in order to anticipate an invention, see Chisum, Donald, Chisum on Patents, Volume 1, § 3.04 [1][b][iii], FN 19, citing, for instance, Transclean Corp. v. Bridgewood Services, Inc. 290 F.3d 1364, 1362 (Fed. Cir. 2002); Bristol-Myers Squbb Co. v. Ben Venue Laboratories, Inc. 246 F.3d 1368, 1374 (Fed. Cir. 2002).

249 In re Bergstrom , 427 F. 2d 1394 (C.C.P.A. 1970).

250 In re Bergstrom , 427 F. 2d 1394, 1402.

251 In re Bergstrom , 427 F. 2d 1394, 1402.

252 The approach to the purity problem taken by the Court of Customs and Patent Appeals was fundamentally different than the approach taken in earlier cases. In, for instance, Parke-Davis & Co. v. H.K. Mulford & Co. (1911), 189 F.95 (S.D.N.Y. 1911), aff'd 196 F.496, (2d. Cir. 1912), a compound was considered as new only if it differs "in kind" from the old compound. Such a difference "in kind" will normally be found only if the new pure compound has an entirely new utility from the old one. See also Merck & Co. v. Olin Mathieson Chem. Corp., 253 F.2d 156, 164 (4th Cir. 1958), Chisum, Donald, Chisum on Patents, Volume 1, § 1.02[9].

standard of novelty under § 102(a). Patentability of the compound, however, is decided under the question of non-obviousness.[253]

The question of purity is treated differently with regard to the patenting of a metabolite of a new drug. In *Schering Corp. v. Geneva Pharmaceuticals, Inc.*[254], the patent claimed a metabolite of a known drug (loratadine). The prior art disclosed this drug teaching that it could be administered to a human subject. It did not, however, disclose the later-patented metabolite. The Federal Circuit found that the claim to the metabolite was invalid, because of anticipation by inherency. The court, however, stated that a "proper" claim to the metabolite in synthetic or purified form would have had established novelty. The court explained that "[a] skilled patent drafter … might fashion a claim to cover the metabolite in a way that avoids anticipation. For example, the metabolite may be claimed in its pure and isolated form."[255]

Pursuant to Section 102(g), a patent is anticipated if "before the applicant's invention thereof the invention was made in this country by another who had not abandoned, suppressed, or concealed it." This provision is of a particular interest when parallel research is carried out by competing teams of invention entities.[256] In *Amgen, Inc. v. Chugai Pharmaceutical Co.*,[257] the claim to a purified and isolated DNA sequence expressing human erythropoietin was questioned to be anticipated by the previous work of others who had initially developed a probing strategy. Without the probing method, the isolation of the gene would not have been possible. However, the knowledge of the specific amino acid sequence of erythropoietin was necessary for isolating the gene. At the time the alleged prior invention was made, the specific amino acid sequence was still unknown. The Federal Circuit concluded that the prior disclosed probing method itself did not defeat novelty, because it did not disclose how to obtain the "purified and isolated DNA sequence". The court determined that for an "adequate conception" of the invention, the inventor must be able to "describe his invention with particularity." This requires both "(1) the idea of the invention's structure and (2) possession of an operative method of making it"[258] In contrast to the earlier invention, the claim at issue to the specific DNA probes provided all ne-

253 See, for instance, Ex Parte Gray, 10 USPQ2d 1922, 1927 (Bd. Pat. App. & Int'f 1989). The approach taken to the issue of "more pure compounds" in earlier cases continues the standard applied by the courts in more recent cases, see, for instance, Glaxo Group Ltd. v. Apotex, Inc., 376 F.3d.1339 at 1349 (Fed. Cir. 2004) (Patents claiming antibiotic drug and method of preparing such drug were not anticipated by prior art patent, despite testimony of expert that he was able to use prior art patent to create claimed formulation, in view of expert's admitted deviation from relevant example of prior art patent and his reading of one patent at issue prior to conducting his experiments.).

254 Schering Corp. v. Geneva Pharmaceuticals, Inc., 339 F.3d 1373 (Fed. Cir. 2003).

255 Schering Corp. v. Geneva Pharmaceuticals, Inc., 339 F.3d 1373, 1381.

256 Chisum, Donald, Chisum on Patents, Volume 1, § 3.05[4].

257 Amgen, Inc. v. Chugai Pharmaceutical Co. 927 F. 2d 1200 (Fed. Cir. 1991), cert. denied, 112 S. Ct. 169 (1991).

258 Amgen, Inc. v. Chugai Pharmaceutical Co. 927 F. 2d 1200, 1206.

cessary information. Therefore, the court concluded that novelty was not destroyed under § 102(g) by the prior invention of the other researchers.[259]

Similarly, the questioned claim of *Fiers v. Sugano*[260] was directed to "a DNA which consists essentially of a DNA which codes for a human fibroblast interferon-beta polypeptide."[261] The court reasoned that the DNA could be obtained by the knowledge of its specific nucleotide sequence. The mere knowledge of how to prepare the DNA would not serve as a conception of the compound. The court stressed that anticipation "does not occur unless one has a mental picture of the structure of the chemical, or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it".[262] Accordingly, a mere determination of the DNA by its principal biological property was not sufficient. In contrast, "a precise definition, such as by structure, formula, chemical name, or physical properties" would be necessary in order to provide sufficient identification.[263]

b) Europe

Pursuant to Art. 54(a) EPC "an invention shall be considered to be new if it does not form part of the state of the art". The state of the art, for the purpose of considering novelty, comprises "everything made available to the public by means of written or oral description, by use, or in any other way, before the date of the filing of the European patent application" (Art. 54(2) EPC).[264] In addition, "the content of European

259 Amgen, Inc. v. Chugai Pharmaceutical Co. 927 F. 2d 1200, 1205-1207. The rule that another inventor must have had an "adequate conception" of a new technology for anticipation was confirmed by Invitrogen Corp. v. Clonetech Laboratories, 429 F.3d 1052 (Fed. Cir. 2005) ("competitor did not show by clear and convincing evidence that researcher conceived of genetically engineered reverse transcriptase enzyme with no RNase H activity, but having DNA polymerase activity, before critical date"). The prior inventor must be diligent in reducing the invention to practice, see Monsanto Comp. v. Myogen Plant Science, 261 F.3d 1356, 1370 (Fed. Cir. 2001) ("The evidence is sufficient … to support presumed jury findings that Agracetus was diligent throughout the entire critical period in creating and testing the modified Bt genes")

260 Fiers v. Sugano, 984 F.2d 1164 (Fed. Cir. 1993).

261 Fiers v. Sugano, 984 F.2d 1164, 1166.

262 Fiers v. Sugano, 984 F.2d 1164, 1168.

263 Fiers v. Sugano , 984 F.2d 1164, 1171. A patent interference is an administrative proceeding pursuant to 35 U.S.C. §§ 102(g) and 135(a). During such a proceeding the Board is authorized to determine not only priority of invention but also to redetermine patentability. 35 U.S.C. § 6(b), see Capon v. Eshhar, 418 F.3d 1349, 1351, 1358 (Fed. Cir. 2005) (the Federal Circuit during interference examined the written description requirement, stating that an invention must not be "fully presented," if the claimed subject matter is known).

264 A detailed description of what belongs to the state of the art is provided by the EPO decision EBA1/92, Availability to the public, OJ 1993, 277-280. (The Enlarged Board of Appeals held that "the chemical composition of a product is state of the art when the product as such is available to the public and can be analysed and reproduced by the skilled person, irrespec-

patent applications as filed, of which the dates of filing are prior to the date referred to in paragraph 2 and which were published under Art. 93 on or after that date shall be comprised in the state of the art" (Art. 54(3) EPC. Thus, the EPC distinguishes between a real and a fictitious state of the art.[265] The real state of the art comprises all knowledge made available to the public by means of written or oral description, other means such as video recording, sound recording, or the Internet.[266] In order to preclude double patenting, the fictitious state of the art includes prior not disclosed patent applications, given that they have been published on or after the date of the more recent application (Art. 93 EPC) and that they are still effective, e.g. have not been withdrawn or otherwise become invalid.[267] Hence, inventions that are already subject of another European patent are not patentable.[268]

The Examination guidelines of the EPO instruct examiners to classify an invention as novel provided that it differs from what is known in the prior art.[269] Examiners consider prior art documents as of the effective date of the document. It is not permissible to combine separate items of prior art together, each document must be compared in isolation.[270] This differs from what is considered in the context of the inventive step requirement. Pursuant to Article 56 EPC "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." Thus, not the single document but the whole prior art is considered.[271] Art. 54(2) EPC states that the relevant date for the determination of the state of the art is the filing date of the European Patent application. Pursuant to Art. 89 EPC, the date of filing can be replaced by the date of priority.[272] Unlike American patent law, European law requires absolute novelty (Art. 54(1) EPC).

With regard to 3-D protein structures, a crucial question is whether the description of the tertiary structure is sufficient to establish novelty in cases in which the primary structure has already been disclosed. To answer this question, the case law

tive of whether or not particular reasons can be identified for analyzing the composition"). Id. at 280. See also Cornish, William/Llewelyn, David, Intellectual Property: Patents, Copyright, Trade Marks and Allied Rights, 6th ed., London 2007, 181-82.

265 Benkard/Melullis, EPÜ, Art. 54 Nos. 202-203.

266 Benkard/Melullis, EPÜ, Art. 54, Nos. 33-51.

267 Benkard/Melullis, EPÜ, Art. 54 No. 203; Straus, Joseph, Neuheit, ältere Anmeldungen und unschädliche Offenbarungen im europäischen und deutschen Patentrecht, GRUR Int. 1994, 89, 94.

268 Benkard/Melullis, EPÜ, Art. 54 No. 5. Prior PCT applications for which the EPO acts as the designated Office have the same effect if they have been translated into one of the official languages and the national fee has been paid, Art. 150(3) in conjunction with Art. 150(1), Art. 158(2) EPC, Singer/Stauder/Spangenberg, EPC – Vol. 1, No. 87.

269 Guidelines for Examination in the EPO, Part C-IV, 7.1.

270 Guidelines for Examination in the EPO, Part C-IV, 7.1.

271 For mosaic consideration of prior art and the question of enablement, not merely the single document but all documents in combination are relevant, see Guidelines for Examination in the EPO, Part C-IV, 9.8.

272 Singer/Stauder/Spangenberg, EPC, Vol. 1, Art. 54, No. 12; Rogge, Rüdiger, The concept of Novelty with Particular Regard to Conflicting Patent Applications, 28 IIC, 794 (1997).

related to classical protein research will be considered. In classical protein research (mostly related to the analysis of primary structure), a patent to a protein invention was considered to be novel pursuant to the following rules.[273] The disclosure of the complete amino acid sequence destroyed the novelty of a protein. The majority of protein inventions, however, cannot be classified that easily. In some, the biological activity of a protein is known without any knowledge of the enzymatic complex causing that activity. In others, some characteristics of the enzyme-substrate complex are disclosed, e.g. through determination of certain physical and chemical parameters of a partial purified protein. The question then is to determine whether the disclosure of an amino acid sequence, which was previously not known, is still sufficient to establish novelty. For a classification of the above-mentioned cases, certain rules are applicable. The first principle is one of a series of principles developed by the German Federal Supreme Court regarding the characterization of macromolecular substances through process parameters. In *Trioxane,*[274] the court stated that a description of a substance is only sufficient if it clearly identifies and distinguishes the substance from others. Accordingly, the information provided by prior art is only novelty destroying if it is sufficient for clear identification. The same standard is applied by the EPO. In *T51/95 Mature leukocyte interferons/Hoffmann-La-Roche*[275] novelty was acknowledged, since the claimed interferon molecule had not been unambiguously characterized in the prior art. Thus, the patent – covering a human bacterial-produced leukocyte interferon – was granted.[276]

aa) The principle of unambiguous parameters

The application of a new parameter for the identification of a substance already clearly identified by a previously established parameter does not create novelty. Consequently, the disclosure of new characteristics of the same substance, e.g. the disclosure of the formula, biological activity or certain physical effect will not create novelty in such a case.[277] If, however, a previously established parameter does not provide sufficient information for the clear identification of a substance, the disclo-

273 A detailed overview of the EPO's decisions on novelty for protein inventions is provided by Jaenichen, Hans-Rainer/Mcdonell, Leslie A./Haley, James F., Jr., From Clones to Claims, Cologne, Berlin, Bonn, Munich 2002, 257-267.

274 BGH, 3 IIC 226 (1972) - Trioxane.

275 T51/95 Mature leukocyte interferons/Hoffmann-La-Roche, N. Publ.

276 T51/95 Mature leukocyte interferons/Hoffmann-La-Roche, N. Publ., No. of the Reasons 19-24; see also T 71/95 Immunoassay/Amersham International plc, N. Publ., No. of the Reasons 8 (for finding lack of novelty a direct and unambiguous disclosure in the prior art is necessary).

277 Benkard/Melullis, EPÜ, Art. 54, No. 176. A new parameter, however, is sufficient for the description of a substance that differs from the already disclosed substance, if it clearly indicates on what the difference is based, see Schulte/Moufang, PatG mit EPÜ, § 1, No. 348.

sure of further properties may still establish novelty.[278] For instance, if only the biological activity of the protein is known in the prior art, the first isolation of the carrier responsible for such activity is enough for establishing novelty. Even though the biological activity of a protein may be considered substantial information about such protein, it cannot be considered a sufficient parameter for its identification.[279] In the case that all disclosed parameters can be combined and therefore establish sufficient and unambiguous substance identification, the disclosure of any further parameter does not create novelty.[280] Due to the high number of similarities between different protein groups, many parameters, however, cannot be used for such accurate determination. Thus, it is more likely that a parameter will prove that the knowledge included in the prior art is not providing the necessary information for identification. This has the following consequences. If the number of known parameters, e.g., molecular weight, statistical density, or melting point data of a compound[281]is high, the likelihood of novelty is low. If a variety of parameters and structural characteristics of a protein are already known in the prior art, it is not likely that this protein is patentable in terms of novelty at this stage. Even the characterization of the amino acid sequence is not sufficient for compliance with the novelty requirement if the protein is already determined accurately enough so that an unambiguous identification had been possible. Therefore, the description of a patent must not be considered incomplete for the sole reason that specific parameters are not included. The same principle applies with regard to the amino acid sequence. The disclosure of a complete or incomplete amino acid sequence is not a necessary requirement of an unambiguous identification of a protein. [282]

In addition, the level of purification has been an important characteristic of identification in a number of chemical related cases decided by the European Patent Office.[283] In *Interleukin-1/Immunes Corporation,* the opponents alleged that the claimed protein is no more purified than the protein disclosed by the state of the art.[284] The Board acknowledged novelty, however, since there was no evidence that the protein preparation disclosed in the cited documents exhibited features of earlier disclosed inventions, reasoning that it would have been the opponent's burden of proof to provide any corroborating evidence. The proffered unsubstantiated allegations, the Board found, were not based on a comparative analysis and had to be dis-

278 Benkard/Melullis, EPÜ, Art. 54, No. 162-163; Busse/Keukenschrijver, § 3 PateG No. 128.
279 Rauh, Peter A./Jaenichen, Hans-Rainer, Neuheit und erfinderische Tätigkeit bei Erfindungen, deren Gegenstand Protein oder DNA-Sequenzen sind -- Volker Vossius zum 60. Geburtstag, GRUR 1987, 753, 755f.
280 Benkard/Melullis, EPÜ, Art. 54, No. 162-163; Busse/Keukenschrijver, § 3 PateG No. 128.
281 BGH, 3 IIC 226, 235 (1972) – Trioxane.
282 Rauh, Peter A./Jaenichen, Hans-Rainer, Neuheit und erfinderische Tätigkeit bei Erfindungen, deren Gegenstand Protein oder DNA-Sequenzen sind -- Volker Vossius zum 60. Geburtstag, GRUR 1987, 753, 755f.
283 Singer/Stauder, EPC, Vol 1, Art. 54 No. 63.
284 T767/95 Interleukin-1/Immunes Corporation, N. Publ., No. of the Reasons 6.

regarded.[285] In *Vinylester-Crotonsäure/Hoechst,* the Technical Board stated that "a known product does not necessarily acquire novelty merely by virtue of the fact that it is prepared in a purer form", because the prove of novelty "cannot involve properties which are not attributable to the substance parameters of the product itself, i.e. which are not inherent in it.[286] In *Pure terfinadine/Albany* ,[287] the patent applicant attempted to argue that the claimed compound differed from the substances disclosed by the prior art, because it could not be achieved by conventional methods. The Board of Appeals, however, concluded that the applicant did not provide sufficient evidence to support his assertions. In particular, the Board found that the prior art already included small amounts of the substance which were achieved by well-established conventional methods.[288]

If the invention consists of the modification of a known protein, the amended amino acid is considered to satisfy the novelty requirement.[289] The question then arises whether the scope of the patent involving the original protein covers the modified protein. The issue of scope of protection is thoroughly discussed in Part IV of this study.[290] Moreover, the publication of a protein in a protein database is only novelty destroying in the event that the provided information enables a skilled person to isolate such a protein.[291] The same is true for *in silico* screening methods or written formula descriptions.[292]

As reconfirmed by the English House of Lords in *Kirin-Amgen v. TKT*, the new manufacture of a known product is not enough to satisfy the novelty requirement.[293] Here, one of the issues to be resolved was whether the recombinant 'Epo' produced by Amgen was novel or identical to the 'Epo' already part of the state of art, in particular the 'uEpo' which others had purified from urine.[294] Amgen alleged that their recombinant product had a glycosylation pattern differing from the known 'uEpo'. The court, however, denied such assertion, concluding that there was no clear dis-

285 T767/95 Interleukin-1/Immunes Corporation, N. Publ., No. of the Reasons 6-7.

286 T205/83 Vinylester-Crotonsäure Copolymerisate/Hoechst, OJ 1985, 363, 369.

287 T728/98 Pure terfinadine/Albany, OJ 2001, 319. The patent applicant particularly based his arguments on the earlier decision of T990/96 Erythro-compounds/Novartis, OJ 1998, 489.

288 T728/98 Pure terfenandine/ALBANY, OJ 2001, 335; see also Benkard/Melullis, EPÜ, Art. 54, No. 177.

289 T 1208/97 Analogs/AMGEN, N. Publ., No. of the Reasons IX, where the patentee defended novelty based on the argument that the claim feature "has been modified," which"necessarily implied a difference vis-à-vis the natural products."

290 Chapter 4 C IV 1.

291 Benkard/Melullis, EPÜ, Art. 54, No. 164.

292 T1165/06 Il-17 related polypeptide/Schering, N. Publ., No. of the Reasons 21.

293 Kirin-Amgen Inc. and Others v. Hoechst Marion Roussel Limited and Others, [2005] R.P.C. 9; as for the application of this principle in Germany, see Rauh, Peter A./Jaenichen, Hans-Rainer, Neuheit und erfinderische Tätigkeit bei Erfindungen, deren Gegenstand Protein oder DNA-Sequenzen sind -- Volker Vossius zum 60. Geburtstag, GRUR 1987, 753, 756.

294 Kirin-Amgen Inc. and Others v. Hoechst Marion Roussel Limited and Others, [2005] R.P.C. 9, No. 87. The U.S. court decided on this subject in Amgen v. Hoechst Marion Roussel, Inc., 126 F. Supp.2d 69 (D. Mass. 2001), see Welch, Andreas, Der Patentstreit um Erythropoietin, GRURInt. 2003, 579, 593.

tinction between 'uEpo' and the recombinant 'Epo'.[295] Following the approach taken by the EPO that "a new process is not enough to make the product new," the House of Lords concluded that a difference in the method of manufacturing an identical product does not make it novel. Consequently, the House of Lords declared Amgen's claim 26, which defined Epo as the product of recombinant gene expression invalid on the grounds of anticipation.[296]

The decision can be considered a landmark for two reasons. First, it revoked Amgen's claim 26 to recombinant Epo, a product, which had been very successful and powerful on the market for many years. In addition, the House of Lords changed a long existing English practice, which treated a product made by a new process as sufficient to distinguish it from an identical product which was already disclosed in the prior art.[297] Thus, the case demonstrates how national legal principles are given up in favour of standards set forth by the EPO. As stated in the Technical Board decision of *Anspruchskategorien/IFF*, claims to a product defined in terms of a process are only permissible if the product cannot be satisfactorily defined by reference to its composition, structure or other parameter. Otherwise, product-by-process claims are not allowed.[298] Art. 64(2) EPC, however, enables a patentee to rely directly on his process claim to allege infringement of a product made by this process, which is - as concluded by the House of Lords in *Amgen* - "any practical argument for allowing [any other] product-by process claims is removed."[299] Thus, only if Amgen had been capable of proving that their 'Epo' was for the first time produced in a glycols form, the case would have been solved differently. Even though a person skilled in the art would have been able to generally develop a glycols form out of a non-glycols form with the knowledge being included in the state of the art, the glycols form of 'Epo' had not been anticipated. In sum, *Kirin-Amgen v. Hoechst Marion* can be considered an important step towards a harmonization of European patent law.

295 Kirin-Amgen v. Hoechst Marion Roussel, [2005] R.P.C. 9, No. 95.

296 Kirin-Amgen v. Hoechst Marion Roussel, [2005] R.P.C. 9, No. 101.

297 As stated by Lord Hoffman in Kirin-Amgen v. Hoechst Marion Roussel, [2005] R.P.C. 9, No. 88.

298 Anspruchskategorien/IFF, OJ EPO 1984, 309; Benkard/Melullis, EPÜ, Art. 52 No. 119; T 150/82, N. Publ.The House of Lords referred to the European law in Kirin-Amgen v. Hoechst Marion Roussel, [2005] R.P.C. 9, No. 89.

299 Kirin-Amgen v. Hoechst Marion Roussel, [2005] R.P.C. 9, 90; Art. 64(2) EPC states that "[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." See also Benkard/Mellulis, EPÜ, Art. 54 No. 174, Benkard/Jestaedt, EPÜ, Art. 64, No. 20.

bb) The principles of second and further medical indications

The development of first and second medical indications for pharmaceuticals by the Enlarged European Board of Appeal of the European Patent office[300] are of major interest for proteomic inventions, since many of these patents may be directed to the treatment of diseases. The following discussion attempts to briefly present the underlying theoretical structure of how novelty is derived from medical indications, keeping in mind the question of whether the principles are transferable to the field of proteomics.[301]

The 2000 EPC revision, put into force on December 13, 2007, led to the amendment of the law related to medical indications.[302] As already mentioned, what used to be the rule under Art. 52 (4) EPC is now added as c) under Art. 53 EPC.[303] Furthermore, the conference established a new version of Art. 54 EPC, including the content of Art. 54 (5) EPC regarding the purpose-related substance protection for the first medical indication in Art. 54 (4). Finally, the provision was extended by a new paragraph (Art. 54(5) EPC), allowing claims for second and further medical indications, and reading as follows:

> "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 any method referred to in Art. 53(c), provided that such use is not comprised in the state of the art."[304]

Several patents are available for pharmaceuticals under the EPC. Generally, a product patent may be obtained for a substance that provides absolute novelty and matches all further patentability requirements. Absolute novelty requires that the substance be not disclosed in any field of the art. Novelty is established, moreover, if the substance is clearly distinguishable from any known substance by at least a single technical characteristic.[305] In addition, already-known substances are patentable as pharmaceutical means if they were not previously known as agents for treatment or diagnosis. Unlike the U.S., under the EPC, novelty of such a claim, however, cannot be established by method for treatment claims, because Art. 53(c) (former Art. 52(4) EPC) declares methods of treatment and diagnosis practiced on the hu-

300 EBA 1/83, Second medical indication/Bayer, OJ 1985, 60; EBA 5/83, Second medical indication/Eisai, OJ 1985, 64; EBA 6/83, Second medical indication/Pharmuka, OJ 1985, 64; A detailed description is provided by Utermann, Jasper, Der zweckgebundene Verfahrensanspruch für Arzneimittel - Zwei Lösungen für die zweite Indikation, GRUR 1985, 813.

301 As for the scope of protection provided for medical indications, see De Lacroix, Stefan Féaux, Auslegung von Zweckansprüchen in Verfahrenansprüchen - Zweite nichtmedizinische Indikation, GRUR 2003, 282.

302 Nack, Ralph/Phélip, Bruno, Diplomatic Conference fort the Revision of the European Patent Convention. Munich 20 – 29 November 2000, 32 IIC 200 (2001).

303 Chapter 3 A II 1 a) bb).

304 EPO, Special Edition No. 4, OJ 2007, 54; Nack, Ralph/Phélip, Bruno, Diplomatic Conference for the Revision of the European Patent Convention. Munich 20 – 29 November 2000, 32 IIC 200, 204 (2001), Schulte/Moufang, PatG mit EPÜ, §3 Nos. 7-8.

305 Schulte/Moufang, PatG mit EPÜ, § 1, Nos. 250-251.

man or animal body as being excluded from patentability.[306] If previously known substances are useful for methods of treatment and diagnosis, their novelty is rather derived under the principles of first and further medical indications. In this respect, two Enlarged Board of Appeal decisions – still related to the rules valid before the 2000 EPC Revision - must be considered landmarks[307]:

In *Second medical indication/Eisai*[308], the Enlarged Board of Appeals had to decide whether a patent with claims directed to the use of a substance of composition for the treatment of human or animal bodies could be granted. The Board made a distinction between a claim directed to the "use of a substance or composition for the treatment for the human or animal body by therapy" and "a claim directed to the manufacture of substances or compositions for use in any methods for treatment of the human or animal body". The first claim, the Board concluded, does not essentially differ from a claim directed to "a method of treatment of the human or animal body by therapy with the substance or composition" and therefore is clearly in conflict with Art. 52(4) EPC. On the other hand, the latter claim involves without doubt inventions that satisfy the requirement of industrial applicability under Art. 52(1) EPC. The Board emphasized that this is essentially made clear in Art. 52(4) EPC, last sentence, but also can be derived from the definition of "susceptible of industrial application" in Art. 57 EPC, particularly because inventions "can be made or used in any kind of industry, including agriculture". Furthermore, the Board argued with Art. 54(5), according to which the provisions relating to novelty shall not prohibit the patentability of any substance or compositions, comprised in the state of the art, for use in a method referred to in Art. 52(4), provided that its use for any such method is not comprised in the state of the art. Patent protection for such "first medical indication" would be available as a purpose-limited – covering, however, all medical uses, product protection.[309] In a second step, the Board carefully considered the possibility of protecting second and further medical indications by means of a claim directed to the use of a substance or composition for the manufacture of a medicament for a specified (new) therapeutic application.[310] Accepting the practice of the Swiss

306 As for the rational behind former Art. 52(4) EPC that is still applicable to the new Art. 53(c) EPC, see Jaenichen, Hans-Rainer/Mcdonell, Leslie A./Haley, James F., Jr., From Clones to Claims, Cologne, Berlin, Bonn, Munich 2002, 22. The policy behind the exclusion of Art. 52(4) EPC is to ensure that those who carry out surgical, therapeutic, or diagnostic methods as part of the medical treatment of humans or animals should not be hampered by exclusive rights of others; Ricker, Mathias, The exclusion of diagnostic methods from patentability by the EPC: a case for review? 22 Nature Biotechnology 2004, 1167, 1167.

307 As landmark decision of the Technical Board of Appeals of the European Patent office T 385/86, N. Publ., can be considered. Furthermore, the diverging decision T964/99, N. Publ., applies a significantly broader view, Ricker, Mathias, The exclusion of diagnostic methods from patentability by the EPC: a case for review?, Nature Biotechnology, 22 Nature Biotechnology 2004, 1167, 1167.

308 EBA 5/83, Second medical indication/Eisai, OJ 1985, 64.

309 EBA 5/83, Second medical indication/Eisai, OJ 1985, 64, 64-66.

310 EBA 5/83, Second medical indication/Eisai, OJ 1985, 64, 66.

Federal Intellectual Property Office, the Enlarged Board acknowledged patent protection for such claims.

The decision *Second medical indication/Bayer*[311] corresponds to the case law reported above. The Enlarged Board had to decide whether to grant a use patent for a substance of which a therapeutic use had already been included in the prior art. The board rejected the claim directed to the use of a known compound X for the treatment of disease Y, reasoning that such a claim falls under the exclusion from patentability of "methods for treatment of the human or animal body" according to Art. 52(4) EPC. However, it accepted the patent claim directed to the "use of a substance X for the manufacture of a medicament for therapeutic application Y", concluding that novelty of a so-called "Swiss-claim" is determined through the new pharmaceutical use of that known substance.[312] Thus, according to the Enlarged Board, the interpretation of the EPC does not result in general exclusion of second and further medical indications from patentability.

Thus, claims directed to the use of a substance or composition for the design of a new drug with new and inventive therapeutic application are legally accepted. Novelty exists due to the new therapeutic use. The inventive step (Art. 56 EPC) is established if a person skilled in the art was not able to suggest such new therapeutic use.[313] In sum, the following patents are available for medical compositions under the EPC:

- A product patent: Pursuant to 54(1)(2) EPC in combination with Art. 53(c) EPC (former Art. 52 (4) EPC), substances or compositions are patentable, even if they are used in diagnostic methods or methods for treatment, provided that they are new and inventive.[314]

- Purpose-related product patent: The provision that indicates the form of claim permissible for a *first* medical indication is Art. 54 (4) EPC (former Art. 54(5) EPC). Accordingly, in the case of a first medical use, i.e., when the invention results in the finding that a certain substance can be used pharmaceutically, a broad claim to a pharmaceutical composition containing the substance is allowed without restriction to the actual identified medical use (first medical indication).[315]

311 EBA 1/83, Second medical indication/Bayer, OJ 1985, 60.

312 Utermann, Jasper, Der zweckgebundene Verfahrensanspruch für Arzneimittel - Zwei Lösungen für die zweite Indikation, GRUR 1985, 813, 813.

313 In T 0254/93 Ortho Pharmaceutical, N. Publ. (EPA 1997) the invention was rejected on grounds of the inventive step requirement, because it merely suggested that the combined administration of two known substancees causes the avoidance of "skinnatropie".

314 Singer/Stauder, EPC, Vol. 1, Art. 52, Nos. 82-87; see also Schulte/Moufang, PatG mit EPÜ, § 1 Nos. 248, 250-252.

315 Singer/Stauder, EPC – Vol. 1, Art. 54, Nos. 96-99; Schulte/Moufang, PatG mit EPÜ, § 1 Nos. 248, 254, noting that the principle of first medical indications should provide incentives

- Use patent: When a further medical use of a substance already known to be pharmaceutically useful is identified, the EPC allows so-called second medical use claims in the Swiss-type format. These claims relate to the new use of an already known substance (second and further medical indication, incorporated in Art. 54(5) EPC).[316]

4. Nonobviousness and Inventive Step

a) U.S. (Nonobviousness)

According to 35 U.S.C. § 103, a patent claim is rejected "if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains".[317] A patent application fails when, at the time the invention was made, the prior art revealed sufficient information for one skilled in the art to produce the invention with "a reasonable expectation of success."[318]Even though obviousness is treated as a

for potential inventors of pharmaceuticals, whose inventive activity does not depend on whether the pharmaceutically used substance was absolutely new or merely new in the field of medicine.

316 The principle of second and further medical indications determine how a known drug for the treatment of a particular disease can achieve patent protection for the treatment of other diseases, see Singer/Stauder/Spangenberg, EPC – Vol 1, Art. 54 No. 101.

317 For a detailed overview of the requirement of obviousness and applying case law, see Chisum, Donald, Chisum on Patents, Volume 2, Chapter 5, for an introduction, see particularly § 5.01 As for the perspective of the skilled person of art on nonobviousness, see Eisenberg, Rebecca, "Obvious to whom? Evaluating Inventions from the Perspective of PHOSITA", 19 Berkeley Technology L. J. 885 (2004), with regard to the the Historical Development of the nonobviousness requirement, see Duffy, John F., Rethinking the Prospect Theory of Patents" U.Chi.L.Rev. 439 (2004), see also Velander v. Garner, 348 F.3d 1359, 1363 (Fed. Cir. 2003) (The obviousness requirement is based on "(1) the scope and content of the prior art; (2) the level of ordinary skill in the prior art; and (3) the differences between the claimed invention and the prior art.")

318 Medichem, S.A. v. Rolabo, S.L., 437 F.3d 1157, 1165 (Fed. Cir. 2006) (To be sure, "to have a reasonable expectation of success, one must be motivated to do more than merely to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful" (citation omitted).

question of law,[319] the question of whether the claimed subject matter would have been obvious includes factual findings as "relevant secondary considerations".[320]

Relevant secondary considerations are (1) the scope and content of prior art; (2) the level of ordinary skill in the art; (3) the differences between the claimed subject matter and the prior art; and (4) significant, objective evidence of nonobviousness, such as long-felt need in the art, mercantile success, failure of others, copying, and unexpected results.[321] Secondary considerations must be examined whenever they are present and must be given the same weight as to the primary considerations. The initial burden is on the examiner to mount a *prima facie* case of obviousness based on three criteria: 1) the suggestion or motivation in the reference or common general knowledge to modify the reference; 2) the reasonable expectation of success; and 3) the prior art reference suggesting all the claim limitations. Once the examiner establishes a *prima facie* case, the onus shifts to the applicant to demonstrate that the claimed invention is not obvious.[322] The question of obviousness requires the evaluation of the entire prior art. This is in contrast to the novelty factor, where each element is considered separately. Regarding a claim to a DNA or cDNA molecule, the prior art must disclose a teaching of a specific, structurally definable compound that provides the obvious motivation or suggestion to alter the known compound. Accordingly, *prima facie* obviousness exists, if the prior art at least gives a reasonable expectation of success. This includes guidance, which is sufficiently specific to draw

319 Richardson-Vicks Inc. v. Upjohn Co., 122 F.3d 1476, 1479 (Fed. Cir. 1997) (The ultimate conclusion of whether a claimed invention would have been obvious is a question of law reviewed de novo based on underlying findings of fact reviewed for clear error.)

320 Pfizer v. Apotex, 480 F.3d 1348, 1372 (Fed. Cir. 2007), ("Although secondary considerations must be taken into account, they do not necessarily control the obviousness conclusion." (citation omitted)); Eli Lilly and Co. v. Zenith Goldline Pharmaceuticals, Inc., 471 F.3d 1369, 1380 (Fed. Cir. 2006) ("Among other things, Lilly proved extensive secondary considerations to rebut obviousness").

321 Syntex (U.S.A.) LLC v. Apotex, Inc., 407 F.3d 1371, 1378 (Fed. Cir. 2005), (the secondary consideration of commercial success exists largely to provide a means for patentees to show in close cases that subject matter that appears obvious is in law unobvious because a high degree of commercial success permits the inference that others have tried and failed to reach a solution (citation omitted); Graham v. John Deere Company of Kansas City, 383 U.S. 1, 17-18 (U.S. Supreme Court 1966), ("Such secondary considerations as commercial success, long felt but unsolved needs, failure of others, etc., might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented. As indicia of obviousness or nonobviousness, these inquiries may have relevancy."). See also Chisum, Donald, Chisum on Patents, Volume 2, § 5.05[1] (Long-Felt Need - Failure to Others), [2] (Commercial Success), [5](Copying).

322 In re Kumar, 418 F.3d 1361, 1366 (Fed. Cir. 2005) („In patent examination context, the prima facie case is a procedural tool requiring that examiner initially produce evidence sufficient to support a ruling of obviousness, after which burden shifts to applicant to come forward with evidence or argument in rebuttal."); In re Harris, 409 F.3d 1339, 1343 (Fed. Cir. 2005) („When the PTO shows prima facie obviousness, the burden then shifts to the applicant to rebut.") (citation omitted); See also Howlett, Melanie J./Christie, Andrew F., An analysis of the approach of the European, Japanese and United States Patent office to Patenting Partial DNA Sequences (ESTs), 34 IIC 581, 590f (2003).

the attention of someone ordinary skilled in the art to the selection of parameters and choices necessary to obtain the invention, without undue experimentation. Consequently, the prior art that provides the necessary motivation to produce the invention must enable an ordinary skilled person to do so.[323]

Under 35 U.S.C. Section 102(e), a patent is precluded when the "invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant." In *Hazeltine Research, Inc.,* the Supreme Court determined that Section 102(e) is considered a source of prior art under Section 103.[324] Accordingly, the content adequately described in an issued United States patent is fully effective as a reference as of the date when the application for the patent was filed. Thus, *Hazeltine* views material as prior art for the purposes of determining obviousness at the time when the material is not available to the public and is still secret.[325] The decision further developed an earlier established doctrine that "delays of the patent office ought not to cut down the effect of what has been done"[326] The Supreme Court in *Hazeltine* concluded that this rationale extended to the determination of prior art pursuant to § 103 as well as for anticipation.[327] The court explained that the prior applicant has "done what he could to add his disclosure to the prior art."[328] *In re Bartfeld*[329] further made clear that "[t]hough not anticipatory, a reference that would otherwise qualify as prior art under 35 U.S.C. § 102(e) may form the basis of an obviousness rejection under § 103; hence, §102(e)/§ 103 rejections."[330]

Furthermore, two major decisions concerning the obviousness standard are *Hybritech, Inc. v. Monoclonal Antibodies*[331] and *In re O'Farrell*[332]. The first suggested a

323 In re Inland Steel Co., 265 F.3d 1354, 1364 (Fed. Cir. 2001) (the prior art references identify a common problem … and give explicit guidance tying that parameter to the key parameter of another reference).

324 Hazeltine Research, Inc. v. Brenner, 382 U.S. 252 (1965). See also Eli Lilly and Co. v. Aradigm Corp., 376 F.3d 1352, 1367 (Fed. Circ. 2004) (The examiner rejected all of the claims in Lilly's patent application stating that they were anticipated by, under section 102(e), or in the alternative obvious under section 103(a) with respect to a co-pending patent application claiming the same subject matter.)

325 Hazeltine Research, Inc. v. Brenner, 382 U.S. 252, 254. Compare Riverwood International Corp. v. R.A. Jones & Co., 324 F.3d 1346, 1355-56, 66 (Fed. Cir. 2003).

326 As established in Alexander Milburn Co. v. Davis Bournville, 270 U.S. 390 (1926).

327 Hazeltine Research, Inc. v. Brenner, 382 U.S. 252, 256.

328 Hazeltine Research, Inc. v. Brenner, 382 U.S. 252, 256; see also Chisum, Donald, Chisum on Patents, Volume 2, § 5.03[3][b].

329 In re Bartfeld, 925 F.2d 1450 (Fed. Cir. 1991).

330 In re Bartfeld, 925 F.2d 1450, 1451 n.4 (Fed. Cir. 1991), see also Purdue Pharma L.P. v. Boehringer Ingelheim GmbH, 98 F. Supp.2d 362, 392 (S.D. N.Y. 2000), aff'd, 237 f.3d 1359 (Fed. Cir. 2001) (citing Bartfeld; "a terminal disclaimer is incapable of overcoming a rejection on grounds of obviousness pursuant to 35 U.S.C. §§ 102(e) and 103."); Chisum, Donald, Chisum on Patents, Volume 5, § 5.03[3][b].

331 Hybritech, Inc. v. Monoclonal Antibodies, 802 F.2d 1367 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987)

332 In re O'Farrell, 853 F.2d 894 (Fed. Cir. 1988).

milder approach toward the validity of the claims than the latter.[333] In *Hybritech*, a process patent on a "sandwich assay" for detecting the presence of antigenic substances in fluid samples using monoclonal antibodies was challenged.[334] The district court rejected the claim due to obviousness, relying on prior art disclosing methods to prepare monoclonal antibodies and describing similar assays using conventional polyclonal antibodies.[335] The Federal Court reversed the judgment of invalidity, emphasizing that prior art did not disclose more than "invitations to try monoclonal antibodies in immunoassays" that "do not suggest how that end might be accomplished."[336]

In contrast, the Court in *In re O'Farrell* affirmed the rejection of claims due to obviousness.[337] The claimed invention consisted of a method for producing proteins in bacterial host cells. It involved the insertion of the target gene in a plasmid in the DNA of a bacterial protein, followed by transfer of the protein into the bacterial host. In order to produce the gene for the bacterial protein, the host was prepared to "read through" and to express the target gene. In a further step, the expressed gene encoded a protein consisting of the amino acids derived from the genetic information.[338] The USPTO rejected the patent application under 35 U.S.C. § 103, reasoning that the prior art disclosed so much information regarding the claimed method that the latter would have been obvious to a person skilled in art.[339] The inventor argued that the given prior art would not have rendered the claimed method obvious, given the significant unpredictability in this field of molecular biology. He alleged that the standard given was only a standard of "obvious to try", which would not be sufficient for a rejection.[340] The Court of Appeal for the Federal Circuit agreed that "obvious to try" was not the standard being examined under Section 103. Nevertheless, the court stated, the claim at issue should be considered as obvious, since obviousness does not require absolute predictability of success. The existing possibility of unexpected success would not be sufficient to create nonobviousness.[341]

333 Eisenberg, Rebecca, Patenting the Human Genome, 39 Emory Law Journal 1990, 721-745, 731.

334 Hybritech, Inc. v. Monoclonal Antibodies, 802 F.2d 1367, 1368-69.

335 Hybritech, Inc. v. Monoclonal Antibodies, 802 F.2d 1367, 1371.

336 Hybritech, Inc. v. Monoclonal Antibodies, 802 F.2d 1367, 1380. Disagreement recognized by Singh v. Brake, 222 F.3d 1362, 1369 (Fed. Cir. 2000) ("While the witnessing of the laboratory notebooks fell far short of ideal, we do not agree that the belated witnessing undermines all corroborative value that these entries may possess. Under a "rule of reason" analysis, the fact that a notebook entry has not been promptly witnessed does not necessarily disqualify it in serving as corroboration of conception.")

337 In re O'Farrell, 853 F.2d 894.

338 In re O'Farrell, 853 F.2d 894, 895, for a summary, see Eisenberg, Rebecca, Patenting the Human Genome, 39 Emory Law Journal 1990, 721-745, 732.

339 In re O'Farrell, 853 F.2d 894, 901.

340 In re O'Farrell, 853 F.2d 894, 902.

341 In re O'Farrell, 853 F.2d 894, 903-904; Pfizer v. Apotex, 480 F.3d 1348, 1366 (Fed. Cir. 2007) ("Although we recognize some degree of unpredictability of salt formation, the mere possibility that some salts may not form does not demand a conclusion that those that do are necessarily non-obvious." (citation omitted)); Abbott Laboratories v. Andrx Pharmaceuti-

This reasoning was confirmed in *In re Deuel*[342], which involved a patent application referring to DNA and cDNA molecules encoding a protein that stimulates cell division.[343] The Federal Circuit held that the prior art, which included the encoded amino acid and an enabling method for isolating and purifying the DNA, was insufficient to render a claim directed to DNA or cDNA *prima facie* obvious. The court concluded that prior art disclosure of the amino acid sequence of a protein would not automatically make particular DNA molecules encoding the protein obvious because "the redundancy of the genetic code permits one to hypothesize an enormous number of DNA sequences coding for the protein."[344]

The readjustment of the nonobviousness requirement relating to the patenting of DNA process patents is of particular interest for inventions related to the proteomic sector, since it demonstrates how traditional legal standards can be readjusted in order to cope with new technologies such as genomics. Based on the Biotechnological Process Patents Act of 1995, Section 103 was amended, with the result that the *prima facie* obviousness evidence was significantly simplified. The amendment was the final solution of a dilemma that started with the application of principles developed in the field of chemical inventions. In *In re Durden,*[345] a process patent claim concerning a chemical process had been rejected by the USPTO. The patent applicant argued on appeal that while individual process steps were obvious, the use of a novel and nonobvious starting material and the production of a new and nonobvious product implied that the process should be patentable. The Court held that the use of a new starting material and the development of a patented product did not automatically establish the nonobviousness of a process or the grant of a process patent. The Court argued that if every process using a new or novel material was granted a patent, then simple processes such as dissolving or heating would be patentable when using a new compound. This principle however, created a major problem for inventors of a patentable composition of matter who wanted to apply for a biotechnological processes patent making use of the (patented) composition of matter. Inventors of patentable compositions of matter used in a biotechnological process were unable to receive process patents for the use of the patentable composition. This resulted in

cals, Inc., 452 F.3d 1331, 1352 ("The court concluded that they were not so similar as to be interchangeable in the context of polymers like HPMC, correctly rejecting the argument that "obvious to try" can establish obviousness.")

342 In re Deuel, 51 F.3d 1552 (Fed. Cir. 1995).

343 In re Deuel, 51 F.3d 1552, 1554 (Fed. Cir. 1995).

344 In re Deuel, 51 F.3d 1552, 1560. Not followed as dicta in Regents of University of Cal. v. Monsanto Co., 2005 WL 3454107 (N.D.Cal. 2005) ("It is true that one might argue that the cases leave open the question whether disclosure of the complete amino acid sequence of a protein--where specified by unique codons or otherwise described in such a way that knowledge of outside genetic methods could be shown to identify all DNA sequences encoding the protein--can render claims to generic DNA sequences for that protein obvious. Nonetheless, such statements are dictum in both cases, and do not control the decision here."); see also Hoscheid, Dale H./Hemmendinger, Lisa M., Biotechnology and the Federal Circuit, Washington D.C. 2000, 33.

345 In re Durden, 763 F.2d 1406 (Fed. Cir. 1985).

the problem that "unless a patent on the process is obtained (or a patent on the final product), the final product could be prepared overseas and imported back into the U.S. for sale without infringing the patent on the materials used in the process".

For this reason, the U.S. Congress significantly amended Section 103. The revised subsection provides that where a composition of matter meets the novel and nonobvious requirement under main section (103 a), a "biotechnological process" using or resulting in the patentable composition of matter must also be treated as nonobvious if the following five conditions are met.[346]

- The biotechnological process and composition of matter be contained in the same application, separate applications, or separate applications having the same effective filing date;
- both the biotechnological process and composition of matter are owned or subject to an assignment to the same person at the time the process was invented;
- a patent issued on the process also contains the claims to the composition of matter used in or made by the process, or, if the process and composition of matter are in different patents, the patents expire on the same date;
- the biotechnological process falls within the definition set forth in 103(b); and
- a timely election proceeds under the provision of 103(b).[347]

The amendment had a deep impact on the whole field of biotechnological patents. Its effects extend far beyond the process of examination. It establishes absolute protection from the defense in infringement litigation that qualifying biotechnological process claims are construed to be invalid for obviousness.

Another characteristic of the nonobviousness requirement is significant for inventors of protein structures. The application of a strict obviousness standard significantly decreases the risk of permanent and harmful monopoly positions of gene patent holders. Although the USPTO issued several DNA patents based on the general requirements set forth above, it does not imply that the successful identification of a DNA sequence in a gene of interest will remain a nonobvious procedure. Specifically, scientific advances in biotechnology and related fields (such as improved cloning and identification techniques) will likely make future DNA sequences obvious as of the time they are identified. Moreover, advances in protein chemistry have facilitated to an increasing degree the separation, purification, and amino acid sequencing of proteins. Consequently, the cloning and sequencing of genes corresponding to these proteins may become a trivial scientific achievement well established as within the ordinary skill of biotechnological researchers. Claims to newly purified chemicals have often been challenged in the past as obvious relative to naturally existing

346 USPTO Notice, Guidance on Treatment of Product and Process Claims in Light of In re Ochiai, In re Brwouwer and 35 U.S.C. § 103(b), available at http://www.uspto.gov/go/og/con/files/cons104.htm, last checked on January 21, 2008.

347 USPTO Notice, Guidance on Treatment of Product and Process Claims in Light of In re Ochiai, In re Brwouwer and 35 U.S.C. § 103(b), available at http://www.uspto.gov/go/og/con/files/cons104.htm, last checked on January 21, 2008.

impure products. In response, courts upheld the validity of those claims, concluding that nonobviousness was established by the fact that the inventor had shown the difficulty and unpredictability of synthesizing the desired gene. It is, however, likely that patent examiners in the near future will reject any claims to the protein-encoding DNA sequence, provided sufficient information is available regarding the protein corresponding to the gene to enable its synthesis in pure form.[348]

In *Teleflex v. KSR*[349]*,* Teleflex sued KSR arguing that one of KSR's products infringed Teleflex's patent involving an adjustable vehicle control pedal connected to an electronic throttle control. KSR assessed that the connection of the two elements was obvious, and the claim was therefore invalid. The district court ruled in favor of KSR, but the Court of Appeals for the Federal Circuit reversed the judgment.[350]

The Supreme Court reversed the Federal Circuit holding, stating that claim 4 of the patent was obvious under the threshold of 35 U.S.C. §103. The Court found that in "rejecting the District Court's rulings, the Court of Appeals analyzed the issue in a narrow, rigid manner inconsistent with §103 and our precedents," referring to the Federal Circuit's application of a "teaching, suggestion, or motivation" (TSM) test, under which "a patent claim is only proved obvious if the prior art, the problem's nature, or the knowledge of a person having ordinary skill in the art reveals some motivation or suggestion to combine the prior art teachings."[351]

The Supreme Court made clear that "[a] person of ordinary skill is also a person of ordinary creativity, not an automaton."[352] The judge acknowledged that his definition of a person having ordinary skill in the art does not necessarily conflict with other Federal Circuit cases that described a skilled person as having "common sense" and whose incentive was based on "implicitly in the prior art."[353] The judge emphasized that his opinion had the purpose of correcting the "errors of law made by the Court of Appeals in this case" and does not necessarily overturn all other Federal Circuit rulings.[354]

348 Eisenberg, Rebecca, Patenting the Human Genome, 39 Emory Law Journal 1990, 721-745, 730-731.
349 Teleflex, Inc. v. KSR International, 127 S. Ct. 1727 (Fed. Cir. 2007).
350 Teleflex, Inc. v. KSR International, 127 S. Ct. 1727, 1727.
351 Teleflex, Inc. v. KSR International, 127 S. Ct. 1727, 1729.
352 Teleflex, Inc. v. KSR International, 127 S. Ct. 1727, 1742.
353 Teleflex, Inc. v. KSR International, 127 S. Ct. 1727, 1743.
354 Teleflex, Inc. v. KSR International, 127 S. Ct. 1727, 1743.

With regard to a general standard of obviousness, the Court ruled:

> "One of the ways in which a patent's subject matter can be proved obvious is by noting that there existed at the time of invention a known problem for which there was an obvious solution encompassed by the patent's claims."[355]

When the requirements for obviousness were applied to the question at issue, however the Court stated:

> "ordinary skill, facing the wide range of needs created by developments in the field of endeavor, would have seen a benefit to upgrading [the technology disclosed by the prior art] with a sensor.[356] "

Hence, the court defined the recognition of a benefit as the crucial factor for any obviousness evaluation. This is, however, a different approach than asking whether someone had been motivated to make a chance, a threshold applied in earlier decisions.

The decision started an intense debate over the impact on the TSM test and the earlier used "obvious to try" standard. This was particularly because, even though the Supreme Court did not reject the TSM test in general, it had referred to it with some critical language. More specifically, the judge found that obviousness

> "must not be confined within a test or formulation too constrained to serve its purpose."[357]

Generally, *KSR* ruled against the approach restricting the use of a "common sense", denying "rigid preventatives rules that deny factfinders recourse to common sense".[358]

The judge, however, made clear that the TSM test remains applicable to the question of obviousness, emphazising, however, that the manner in which the test is to be applied is newly instrued."[359]

In *Leapfrog Enterprises, Inc. v. Fisher-Price, Inc.*, (Fed. Cir. May 9, 2007), the Federal Circuit interpreted the *KSR* case, holding the patent under review was invalid for being obvious.[360] Accordingly, even though *Teflex* did not suddenly make all inventions obvious, *Leapfrog* shows that the *Teflex* approach is the now applied standard for defining obviousness.

b) Europe (Inventive Step)

Pursuant to Art. 56 EPC, 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

355 Teleflex, Inc. v. KSR International, 127 S. Ct. 1727, 1742.
356 Teleflex, Inc. v. KSR International, 127 S. Ct. 1727, 1744.
357 Teleflex, Inc. v. KSR International, 127 S. Ct. 1727, 1746.
358 Teleflex, Inc. v. KSR International, 127 S. Ct. 1727, 1742-1743.
359 Teleflex, Inc. v. KSR International, 127 S. Ct. 1727, 1741.
360 Leapfrog Enterprises, Inc. v. Fisher-Price, Inc., 485 F.3d. 1157 (Fed. Cir. 2007).

art. In this respect, the prior art is considered as a whole, i.e., the teachings of separate prior art documents are combined together.[361]

Several tests are used to determine inventive activity, such as the problem-solution approach[362] and the "could/would" test[363]. Indications for inventive activity include commercial success, surmounting of difficulties, disbelief and scepticism of experts, satisfaction of long existing needs and the finding of new and unexpected results.[364] The relevant moment for determination is the filing/priority date and no *ex post facto* judgement is allowed.[365]

The finding of unexpected results often occurs in the field of chemicals or pharmaceuticals, where surprising effects or characteristics of substances are the outcome of experimentation.[366] Such surprising characteristics can include, for example, reduced side effects, improved resorption and stability of the new protein. Even if the isolation as such is not inventive, the surprising effect is sufficient to establish inventiveness.[367]

In the field of chemical inventions, *Triazole/Agrevo*[368] can be considered a major decision, in which the problem-solution-approach of the EPO was defended and approved against the appellant's allegation that Art. 56 EPC did not expressly require that the subject matter of a patent application had to solve a technical problem. The Board of Appeals defined the "problem-solution-approach" as a "generally accepted legal principle" and held that the technical effect of the claimed invention is inherently connected to the determination of inventive step. The Board stated that what the skilled person would have done depends on the technical result they set out to achieve rather than "idle curiosity". Lacking the solution to a technical problem, an

361 Benkard/Jestaedt, EPÜ, Art. 56, No. 1. This differs from the examination of novelty, where it is not permissible to combine separate prior art documents together, see Chapter 3 A II 3 b); T 153/85, OJ 1988, 1 "Alternative Claims".

362 The test asks whether a person skilled in the art not only theoretically "could" have prepared the claimed compounds, but whether he "would" have done so in view of the state of the art; Szabo, George S. A , The Problem and Solution Approach in the European Patent Office, 26 IIC 457 (1995).

363 T 513/90, Geschäumte Körper/Japan Styrene, OJ 1994, 154, 160f.; T 455/91 Expression in Yeast/Genentech, OJ 1995, 684, 730f; Guidelines for Examination in the EPO, Part C-IV, 9.10.2.

364 Kraßer, Rudolf, Patentrecht: ein Lehr- und Handbuch zum deutschen Patent- und Gebrauchsmusterrecht, europäischen und internationalen Patentrecht, 5. Aufl., München 2004, 325-332.

365 The desisive question is whether the person skilled in the art had been able to carry out the invention on the priority date without any inventive activity, see Busse/Keukenschrijver, PatG, § 4, No. 24.

366 Busse/Keukenschrijver, PatG, § 4, No. 16, emphasize that an element is interpreted as a very strong sign for inventive activity.

367 T 181/82 Spiroverbindungen/Ciba-Geigy, OJ 1984, 401, 409; T 57/84 Tolylfluanid/Bayer, OJ 1987, 53; T 939/92; OJ 1996, 309, 317. The fact that a chemical substance's property was distinct from other chemical substances had been surprising for a person skilled in the art may be sufficient to establish inventive activity, see Busse/Keukenschrijver, PatG, § 4, 89.

368 T 939/92, Triazone/Agrevo, OJ 1996, 309, 317.

invention would probably not involve any inventive step. The case dealt with claims for chemical compounds. The Board held that an arbitrary selection of chemical compounds that were structurally similar to the closest prior art could not involve any inventive step. For the assessment of the inventive step, the examiner must study the claim, the closest prior art, and the difference in terms of features of the claim and the closest prior art. Then the examiner must determine whether the conclusion of all of the closest prior art documents would prompt the skilled person, faced with the technical problem, to adapt the closest prior art to arrive at something within the terms of the claim. The inventive step criteria must be examined in relation to all aspects of the claimed invention, including the underlying problem, the insight upon which the solution relies, the means constituting the solution, and the effect or results obtained. The ruling clearly describes the method of the "problem-solution-approach", describing the three main stages: e.g., determining the "closest prior art"; establishing the "objective technical problem" to be solved; and considering whether or not the claimed invention, starting from the closest prior art and the objective technical problem, would have been obvious to the skilled person.[369]

With regard to the recombinant production of proteins, *Human beta-interferon/BIOGEN*[370] is an example of how the requirement of inventive step is analyzed. The Board of Appeal rejected a claim to a recombinant produced polypeptide displaying the immunological or biological activity of human beta-interferon (β-IFN) for lack of an inventive step. The examiners concluded that the construction of the β-IFN expression vector *per se* does not require more than routine effort from the average skilled person. A skilled person could have reasonably expected the beta-IFN cDNA to be expressed in the recombinant host as an active protein. Thus, the known properties of the human β-IFN contained a clear and obvious suggestion as to how to produce it.[371]

In *Milk production/MONSANTO*[372], the EPO adopted the U.S. standards of analyzing the obviousness requirement that had been established in *In re O'Farrell*. As in *In re O'Farrell*, the appellant alleged that a standard of "obvious to try" would not be sufficient for a rejection. The court followed the U.S. patent law by stating that obviousness does not require absolute predictability of success. The court clarified that the need of experimentally confirming a reasonably expected result does not render an invention unobvious, determining that, in the case at issue, an average skilled person was provided "with a clear hint from the prior art pointing him in the direction of the claimed method."[373]

In sum, the European inventive step requirement is very similar to the U.S. law on obviousness: a patent claim lacks inventive activity if every element of the claim is included or suggested by the state of the art. The state of the art as such must pro-

369 T 939/92, Triazone/Agrevo, OJ 1996, 2.4 – 2. 7.
370 T 207/94 Human beta-interferon/BIOGEN, N. Publ.
371 T 207/94 Human beta-interferon/BIOGEN, N. Publ., No. of the Reasons, 22-44.
372 T 249/88, Milk production/MONSANTO, N. Publ.
373 T 249/88, Milk production/MONSANTO, N. Publ., No. of the Reasons, 8.

vide the motivation to combine several references to meet the claims. In the U.S., the decision of *In re Deuel*, however, made clear that prior art does not render a claim obvious, if the skilled person is permitted "to hypothesize an enormous number" of possibilities to carry out the invention.[374]

5. Written description/patent description and sufficient disclosure

Compared to other patentability requirements, the need to provide a written description fulfilling certain minimum standards (in the case of the U.S.) and to suffciently disclose the invention (in the case of Europe) has long been considered an issue of a somewhat lower importance. This has changed in recent years, not least as a consequence of the increasing complexity of explaining and demonstrating the nature and scope of biotechnological patents.

a). U.S.

In particular in the U.S., a controversial debate about whether and in what form patent law princples imply a "seperate" written description requirement has emerged. A review of this debate offers important lessons, not only for inventors of proteomic structures. Before going through the arguments that have dominated the discussion, the following section will first outline the basic statutory background, focusing on cases with a biotechnological subject matter.

aa) Basic statuatory background

Pursuant to Section 35 U.S.C. § 112(1), a patent application shall

> "contain a written description of the invention, and of the manner and process of making and using it in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention."

The provision can be seen as containing four individual requirements, usually denominated as: (1) written description, (2) enablement, (3) best mode and (4) definiteness[375]. However, as discussed in detail below, the Federal Circuit has not decisively clarified whether the written description requirement must be considered separately from enablement and best mode.

374 In re Deuel, 51 F.3d 1552, 1560. See Chapter 3 A II 4 a).

375 See Guidelines for Examination of Patent Applications under the 35 U.S.C. § 112, 1, "Written description" Requirement, 66 Fed. Reg. 1099, 1014 (Jan. 5, 2001) [hereinafter Written Description Guidelines].

The requirement of enablement demands that the applicant's specification provides sufficient disclosure about the invention. Generally, the specification must provide enough instruction so that a person skilled in the art would not have to exercise any "undue experimentation"[376] to make and use the full scope of the claimed invention.

In re Wands set forth the details of enabling.[377] In this decision, a patent application, referring to the disclosure of immunoassay methods for detecting the hepatitis B virus using high-affinity immunoglobulins, was rejected. The court stated that the application did not enable one to make and use the claimed invention. On appeal to the CAFC, the patentee argued that the application in fact was enabling because a DNA encoding the high-affinity immunoglobulin had been deposited with the American Type Culture Collection (ATCC) and was accessible to the public. Consequently, a person skilled in the art would not have had to perform undue experimentation to make the antibodies necessary for the claimed invention. The CAFC agreed that the patent application was complying with the enablement factor. In the decision, the court stressed the factors that should be considered when determining whether undue experimentation would be required to practice a claimed invention. The so-called *Wands factors* include:

- The quantity of experimentation necessary to practice the claimed invention;
- the amount of direction or guidance presented in the specification;
- the presence or absence of working examples in the specification;
- the nature of the invention;
- the state of the prior art
- the relative skill of those of ordinary skill in the art
- the predictability or unpredictability of the art; and
- the breadth of the claims.[378]

Amgen, Inc. v. Chugai Pharm. Co. shows how the Federal Circuit applies the patent jurisprudence relating to chemical compounds to biotechnology, and provides a framework for the treatment of enablement in cases involving nucleic acid sequences.[379] Amgen was the owner of a patent to a purified and isolated DNA sequence encoding the human erythropoietin ('Epo') gene. The district court invalidated a claim covering a "potentially enormous" number of 'Epo' analogs for lack

376 In re Wands, 858 F.2d 731, 731 (Fed. Cir. 1988). See also Kunin, Stephen G/ Nagumo, Mark/ Stanton, Brinaet al., Reach-through claims in the age of biotechnology, 51 American University Law Review April 2002, 609-638, 630.

377 In re Wands, 858 F.2d 731 (Fed. Cir. 1988).

378 In re Wands, 858 F.2d 731, 731.

379 Amgen, Inc. v. Chugai Pharm. Co., 927 F.2d 1200, 1206, 1212. (Fed. Cir. 1996) ("A gene is a chemical compound, albeit a complex one, and it is well established in our law that conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials, and to describe how to obtain it.")

of enablement.[380] The Federal Circuit confirmed that the claims were not enabled, but instead based its conclusion on the lack of enablement of the underlying DNA sequences. The court explained:

> "It is not necessary that a patent applicant test all the embodiements of this invention; what is necessary is that he provides a disclosure sufficient to enable one skilled in the art to carry out the invention commensurate with the scope of the claims. For DNA sequences, that meant disclosing how to make and use enough sequences to justify grant of the claims sought. Amgen had not done that here."[381]

In *In re Fisher*,[382] the Federal Circuit confirmed the rejection of enablement, "because the claimed ESTs were not disclosed as having a specific and substantial utility."[383] According to the court "it is well established that the enablement requirement of § 112 incorporates the utility requirement of § 101."[384]

In *Falko-Gunter Falkner v. Inglis*,[385] the patent application claimed a novel type of vaccine production applicable to various types of "vector viruses", such as adenoviruses, herpesviruses, poxviruses and retroviruses. In vaccinations using vector viruses, immunity against the target virus is achieved by exposing the immune system to harmless fragments of the target virus. To prevent infections through the viral vector itself, genes that cause a vector's harmful effects have to be inactivated, traditionally by deleting an *inessential* gene from the respective genome. By devising a method in the course of which an *essential* gene is inactivated, the inventors claimed to have discovered a substantially safer way of vaccine production. Moreover, the new method offered a solution to a fundamental problem of vaccine production. By growing vaccines in cells that were complementarily modified to produce the absent essential viral gene product "on behalf of" the vector virus, the difficulty of growing an inhibited or "attenuated" version of a virus was effectively circumvented.

While being applicable to the various viruses mentioned above, the patented invention dealt specifically with vaccines in which the vector virus is a *poxvirus*.[386] The specification, however, provided a detailed example of an embodiment that comprised herpes virus, not poxvirus, including identity of deleted essential se-

380 Amgen, Inc. v. Chugai Pharm. Co., 927 F.2d 1200, 1204.
381 Amgen, Inc. v. Chugai Pharm. Co., 927 F.2d 1200, 1212.
382 In re Fisher, 421 F.3d 1365 (Fed. Cir. 2005). For a summary of the factual background and the court's ruling regarding the utility requirement, see Chapter 3 A II 2a.
383 In re Fisher, 421 F.3d 1365, 1378.
384 In re Fisher, 421 F.3d 1365, 1378, (citations omitted); see also In re Kirk, 376 F.2d, 936, 942 (C.C.P.A. 1967) ("Necessarily, compliance with § 112 requires a description of how to use presently useful inventions, otherwise an applicant would anomalously be required to teach how to use a useless invention."); In re Brana, 51 F.3d 1560, 1564 (Fed. Cir. 1995) ("Obviously, if a claimed invention does not have utility, the specification cannot enable one to use it.").
385 Falko-Gunter Falkner v. Inglis, 448 F.3d 1357 (Fed. Cir. 2006).
386 Falko-Gunter Falkner v. Inglis, 448 F.3d 1357, 1360.

quences therein. The Federal Circuit nevertheless concluded that the patent was adequately enabled, and explained:

> "[T]here is extensive disclosure of the selection of an essential gene, its deletion or inactivation and the production of a mutated virus with said deleted or inactivated gene, albeit for herpesvirus." Moreover, because the differences between the herpesviruses and poxviruses were well known, this would have aided the person of ordinary skill in the art in her application of the lessons of the herpesvirus example in the construction of poxvirus vaccines. … the mere fact that the experimentation may have been difficult and time consuming does not mandate a conclusion that such experimentation would have been considered to be 'undue' in this art. Indeed, great expenditures of time and effort were ordinary in the field of vaccine preparation."[387]

The court declared that a skilled person was clearly considered to be able "to identify the 'essential' poxvirus genes [by] relying on publications in professional journals that had disclosed the DNA sequence of the poxvirus genome along with the locations of the 'essential regions,'… since a patent need not teach, and preferably omits, what is well known in the art."[388]

bb) Deposit requirements

In order to overcome the difficulty of providing a detailed written description sufficient to permit the production of complex living organisms, the courts accepted as a substitute the deposit of living material with a public depository. Public access to the deposited material was determined to be sufficient to satisfy Section 112, first paragraph.[389] This solution was established in *In re Argoudelis.*[390] The United States Court of Customs and Patent Appeals (CCPA) assumed that "there can be no description in words alone of how to obtain the microorganism from nature".

A deposit was sufficient to satisfy the enablement requirement of Section 112, first paragraph, if (1) a public depository was used, (2) the deposit was made prior to the filing date of the application, (3) the depository and accession number were referenced in the application as filed, (4) the depository was under a contractual obligation to maintain the deposited culture in the permanent collection, (5) the depository was under obligation to supply samples to persons having access to the pending application, (6) the deposited organism would be made available to the public without restriction on the issue date of the patent, and (7) the cultures were not expected to undergo any physical changes rendering them unusable.[391]

387 Falko-Gunter Falkner v. Inglis, 448 F.3d 1357, 1365.
388 Falko-Gunter Falkner v. Inglis, 448 F.3d 1357, 1365, citing Spectra-Physics, Inc. v. Coherent, Inc., 827 F.2d 1524, 1534 (Fed. Cir. 1987).
389 Monsanto Co. v. Scruggs, 459 F.3d 1328, 1337 (Fed. Cir. 2006) (The written description requirement was satisfied because the '605 patent incorporates by reference deposits with the American Type Culture Center, which are publicly available.)
390 In re Argoudelis, 434 F.2d 1390 (C.C.P.A. 1970).
391 In re Argoudelis, 434 F.2d 1390, 1394.

In *Feldman v. Aunstrup*[392], the court stated that the requirements established in *Argoudelis* were not mandatory. More specifically, a deposit in private foreign entities was deemed sufficient under Section 112. The essential criteria, the court reasoned, were that the culture was permanently available, and that access was assured. In I*n re Lundak*, the court concluded that even the "deposit" of a microorganism in the inventor's private laboratory may meet the standard of Section 112 at the time of filing, and that public depository is sufficient if it is made at any time prior to the issuance of the patent.[393] The court further held that neither the postfiling depository nor the addition of the accession number to the pending application enlarges the disclosure of the specification by the addition of new matter.[394]

cc) The debate on a separate written description requirement

i. Background to the debate

Soon after broad biotechnological claims had become standard practice, concerns were raised about their medium- and long-term effects on product innovation.[395] In the ensuing debate about how to prevent overly broad claims, proposals ranged from legislative changes to a stricter approach to patent specification requirements.[396] With respect to the latter, a number of landmark decisions of the Federal Circuit Court further attracted substantial interest. A majority of Federal Circuit judges interpreted Section 112, first paragraph of the U.S. Patent Act as imposing a "separate written description requirement". More specifically, "written description" was seen as a requirement distinct from "enablement", a view that has inspired an intense dispute over the appropriateness of alternative patent drafting strategies and the legal certainty that can be reasonably expected when possessing a patent. Due to its wide-ranging implications and its importance for the debates on the appropriate scope of protection, it is essential to review the court's decision extensively.[397]

In several cases, the majority of judges concluded that a patent serves not only to disclose to the public how to 'make and use' an invention, but also to indicate whether the inventor actually "possessed the invention" at the time the application was filed. Accordingly, an analysis pursuant to Section 112 would ask for two sepa-

392 Feldman v. Aunstrup, 517 F.2d 1351, 1352 (C.C.P.A. 1975).
393 In re Lundak, 773 F.2d 1216, 1222 (Fed. Cir. 1985).
394 In re Lundak, 773 F.2d 1216, 1223.
395 See, for example, Schiermeier, Quirin, German agencies sound alarm on risks of broad gene patents, Nature 406, 2000, 111.
396 Barton, John H., United States Law of Genomic and Post-Genomic Patens, 33 IIC 779, 782 (2002), noting that after the Ely Lilly decision it is unlikely that a gene can be patented without identification of its sequence.
397 Mull, William C., Using the Written Description Requirement to Limit Broad Patent Scope, Allow Competition, and Encourage Innovation in Biotechnology, 14 Health Matrix: Journal of Law-Medicine 2004, 393, 393ff.

rate and independent requirements. First, the applicant must describe the invention so that a person skilled in the art can recognize the claim as what has actually been invented (i.e., actually or constructively "possessed"). Second, the description has to be drafted in a way that enables the public to make and use the full scope of the invention."[398]

A minority of Federal Circuit Judges, headed by Judge Rader, strongly opposed the majority view, rejecting the appropriateness and legal consistency of a "separate written description requirement". Without regard to enablement, the content of the written description and its adequacy to support the claims should only be considered in cases related to priority, but not in the context of patentability. In the view of the minority, such a reading would be consistent with earlier rulings by the Federal Circuit, which only examined enablement and best mode under §112.[399] It would also be sufficient to accommodate Section 132, which prohibits the addition or amendment of claims subsequent to the effective filing date that would add new matter to the application.[400]

398 Amgen Inc. v. Transkaryotic Therapies, Inc., 314 F.3d 1313, 1330 (Fed. Cir. 2003). In Regents the University of California v. Eli Lilly & Co., 119 F.3d 1559 at 1566 (Fed. Cir. 1997), the Federal Circuit clearly determined that the § 112 analysis "requires a precise definition, such as by structure, formula, chemical name, or physical properties, not a mere wish or plan for obtaining the claimed … invention." In Amgen, 314 F.3d at 1332 (Fed. Cir. 2003), the threshold was narrowed down by the Federal Circuit's statement that "Eli Lilly did not hold that all functional descriptions of genetic material necessarily fail as a matter of law to meet the written description requirement, rather, the requirement may be satisfied if the knowledge of the art of the disclosed function is sufficiently correlated to a particular, known structure." Capon v. Eshhar, 418 F.3d 1349, 1360 (Federal Circuit 2005) weakened the Eli Lily doctrine much further with the statement that "[t]he predictability or unpredictability of the science is relevant to deciding how much experimental support is required to adequately describe the scope of an invention." Capon, however, fails to establish clear rules of how broad a patent specification must be drafted. Even though it states that prior art must be taken into account, more detailed information of how far this prior art consideration must be made, is missing.

399 In re Gay, 50 C.C.P.A. 725, 309 F.2d 769, 772 (C.C.P.A. 1962). Originally, courts considered claims part of the disclosure, which is why they could not lack adequate description, see In re Smith, 481 F.2d 910, 914 (C.C.P.A. 1973) ("Where the claim is an original claim, the underlying concept of insuring disclosure as of the filing date is satisfied, and the description requirement has likewise been held to be satisfied.")

400 In Enzo Biochem., Inc. v. Gen-Probe International, 323 F.3d 956 at 977 Judge Rader starts his analysis with a detailed review of the origin and history of the written description requirement ("[E]very patent system must have some provisions to prevent applicants from using the amendment process to update their disclosure (claims or specification) during their pendency before the patent office). In contrast, the judge refuses to analyse the written description in cases in which priority is not in question, Id. at 979 ("[W]ritten description does not examine the specification for 'literal support' of the claim language unless priority is in question."). Chiron v. Genentech, 963 F.3d 1247 at 1255 (Fed. Cir. 2004) also exemplifies how the written description requirement is examined in the context of priority. ("[T]he written description requirement prevents applicants from using the amendment process to update their disclosures.").

The implications of these alternative solutions are wide-ranging. In particular, a 'separate written description requirement' forces applicants to provide a much more detailed delineation of the nature, scope, and application of claims.[401] Moreover, it is likely that certain subject matter cannot be patented until a later stage of understanding of the invention and its potential embodiments. Similar to the utility requirement, an additional written description requirement may thus force inventors to delay the filing of a claim, while at the same time limiting the broadness of a claim. This is particularly relevant for biotechnological inventions, as many generic inventions may be enabled without a clear understanding of what the claim actually applies to.

ii. Development of a 'separate written description' doctrine

In *Regents of the University of California v. Eli Lilly & Co*[402], the Federal Circuit held cDNA encoding rat insulin to be an insufficient written description to support claims to cDNAs encoding vertebrate, mammalian, or human insulin, even though the application included a method to isolate those cDNAs. The court clarified that "describing a method or preparing a cDNA or even describing the protein that the cDNA encodes does not necessarily describe the cDNA itself."[403] A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, whose features constitute a substantial portion of the genus.[404] Thus, the court concluded, the § 112 analysis "requires a precise definition, such as by structure, formula, chemical name, or physical properties, not a mere wish or plan for obtaining the claimed chemical invention", but "none of those descriptions appeared in that patent."[405]

The reasoning of *Ely Lilly* was adapted in further cases. In *Carnegie Mellon v. Hoffman-La Roche*[406], a district court held that claims referring to plasmids for the controlled expression of DNA polymerase I derived from any bacterial source were invalid because the specification only described DNA polymerase I from E.coli. The court argued that the *Lilly* decision was applicable, stating that "there is nothing in the *Eli Lilly* decision to suggest that the Federal Circuit's observations about the na-

401 Under Section 112, the applicant is required to disclose what he "regards as the invention." Thus, although the disclosure may be used to help interpret the claims, the disclosure may evidence a variance from the nature of the invention that the applicant actually believed was invented (and thus was possessed at the time of filing). Although inquiry may still be made into such differences between claim meaning and the invention during prosecution, they are no longer able to be raised in litigation to challenge the validity of the claims. See Solomon v. Kimberley Clark Corp., 216 F.3d 1372, 1377 (Federal Circuit 2000).

402 Regents of the University of California v. Eli Lilly & Co., 119 F. 3d 1559 (Fed. Cir. 1997).

403 Regents of the University of California v. Eli Lilly & Co., 119 F. 3d 1559, 1567.

404 Regents of the University of California v. Eli Lilly & Co., 119 F3d. 1559, 1569.

405 Regents of the University of California v. Eli Lilly & Co, 119 F.3d 1559, 1566.

406 Carnegie Mellon v. Hoffman-La Roche, Inc.; 148 F. Supp. 2d 1004 (N.D. Cal. 2001).

ture of DNA was applicable only to novel DNA and not to any DNA sequence. A similar finding is established in *Bristol-Myers Squibb v. Rhone-Poulenc er.*[407]Here, the district court held that a generic claim must be rejected because the patentee failed to provide a copy of a scientific article by the inventors indicating that they themselves did not believe the invention could be practiced as broadly as claimed. Therefore, inventors should warrant that the extent of the claims is commensurate with the underlying science.

Enzo Biochem v. Gen-Probe[408] is another landmark decision in which the strict written description requirement was confirmed. In the case, the CAFC considered a patent directed to three nucleic acid probes that hybridize preferentially with the DNA of the bacterium causing gonorrhea. The broader claims of the patent recited the probes as binding preferentially to the gonorrhea organism rather than a closely related one. The court argued that because the patentee had described the probes only in terms of sequence function (preferential hybridization), the written description for the claimed invention was inadequate as a matter of law. The court considered that although a "description of the ability of the claimed probe to bind to N. gonorrhoeae may describe that probe's function, it does not describe the probe itself. We reject *Enzo's* characterization of the hybridization as a distinctive 'chemical property' of the claimed sequence." Therefore, it is inadequate to describe genetic material by what it does, such as hybridizing with N. gonorrhoeae, notwithstanding the labeling of the described property as "chemical" or "functional".

In *University of Rochester v. Searle et al*.,[409] the patentee claimed a method for selectively inhibiting the activity of a particular protein by "administering a non-steroidal compound that selectively inhibits activity of that protein in a human in need of such treatment". The University of Rochester sought to enforce its patent relating to the "new generation" of pain relievers, which act selectively through the

407 Bristol-Myers Squibb v. Rhone-Poulenc Rorer, 2001 WL 1512597.

408 Enzo Biochem v. Gen-Probe, 323 F.3d 956 (Fed. Cir. 2002). The Federal Court ruled on the issue in a number of further decisions. For the direct history of the case, see Enzo Biochem, Inc. v. Gen-Probe Inc., 285 F.3d 1013, 62 (Fed. Cir. 2002). Opinion Vacated on Rehearing by Enzo Biochem, Inc. v. Gen-Probe Inc., 323 F.3d 956 (Fed. Cir. 2002). For Additional Opinion, see Enzo Biochem, Inc. v. Gen-Probe, Inc., 2002 WL 32063710, 63 U.S.P.Q.2d 1618 (Fed. Cir. 2002) AND Appeal After Remand Enzo Biochem, Inc. v. Gen-Probe Inc., 414 F.3d 1376 (Fed. Cir. 2005). Order Recalled and Vacated by Enzo Biochem, Inc. v. Gen-Probe Inc., 143 Fed. Appx. 350 (Fed. Cir. 2005) (Not selected for publication in the Federal Reporter).

409 University Of Rochester v. G.D. Searle & Co., Inc., 358 F.3d 916 (Fed.Cir. 2004). The Federal Circuit decided on the issue in a number of further decisions, see University of Rochester v. G.D. Searle & Co., Inc., 249 F.Supp.2d 216 (W.D.N.Y. 2003). Decision Affirmed by University Of Rochester v. G.D. Searle & Co., Inc., 358 F.3d 916 (Fed. Cir. 2004). Rehearing and Rehearing en banc denied by University of Rochester v. G.D. Searle & Co., Inc., 375 F.3d 1303 (Fed. Cir. 2004) AND Certiorari denied by University of Rochester v. G.D. Searle & Co., Inc., 543 U.S. 1015 (2004).

409 Warburg, Richard J./Wellman, Arthur/Buck, Todd/Ligler Schoenhard, Amy E., Patentability and Maximum Protection of Intellectual Property in Proteomics and Genomics, 22 Biotechnology Law Report 2003, 264, 269.

inhibition of COX-2. By doing so, these pain relievers achieve the desired effect (inhibition of pain) while avoiding some of the undesirable side effects (particularly stomach irritation) invoked by earlier pain relievers which inhibit both COX-2 and COX-1. The patent disclosed and claimed methods for screening compounds to identify those that selectively inhibited the COX-2 gene product while having minimal effect on COX-1 activity, and the specification identified a single compound (NS-398) which is a specific inhibitor of COX-2 activity.[410]

The district court found the claims to be invalid for lack of an adequate written description, concluding that the patent did not disclose a specific compound, and provided no guidance on how to make or obtain any compound that fell within the scope of the patent's claim." [411] On appeal, the University contested the district court's ruling that a claim drawn to a method of obtaining a biological effect in a human by administering a compound cannot, as a matter of law, satisfy the written description requirement without disclosing the identity of any such compound.[412] The Federal Circuit rejected this argument, stating that an adequate written description requirement would "describe the claimed invention so that one skilled in the art can recognize what is claimed."[413] Generalized language may be inadequate if it does not convey the detailed identity of an invention. The court explained that "[r]egardless whether a compound is claimed *per se* or a method is claimed that entails the use of the compound, the inventor cannot lay claim to that subject matter unless he can provide a description of the compound sufficient to distinguish infringing compounds from non-infringing compounds, or infringing methods from non-infringing methods."[414]

iii. The 'dissenting line'

The other line, followed by a minority of judges of the Federal Circuit, strictly denies a separate written description requirement. The opinions and arguments underlying this "dissenting line" were most clearly articulated in the cases of *Eli Lilly*[415], *Enzo I and II,* and *Rochester*[416]. For the opponents of a separate written description requirement, to make a distinction between the disclosure of how to 'make and use' an invention and a disclosure that shows that an invention has in fact been "possessed" is "contrary to logic and the statue itself." Underpinning the dissenting line

410 Warburg, Richard J./Wellman, Arthur/Buck, Todd/Ligler Schoenhard, Amy E., Patentability and Maximum Protection of Intellectual Property in Proteomics and Genomics, 22 Biotechnology Law Report 2003, 264, 269.
411 University Of Rochester v. G.D. Searle & Co., Inc., 358 F.3d 916, 919.
412 University Of Rochester v. G.D. Searle & Co., Inc., 358 F.3d 916, 920.
413 University Of Rochester v. G.D. Searle & Co., Inc., 358 F.3d 916, 922-923.
414 University Of Rochester v. G.D. Searle & Co., Inc., 358 F.3d 916, 926.
415 Regents of the Univ. of Cal. v.. Eli Lilly & Co., 119 F.3d 1559 (Fed.Cir.1997). The decision was criticized in University of Rochester v. Searle, 375 F.3d 1303, 1307 (Fed. Cir. 2004).
416 University of Rochester v. Searle, 375 F.3d 1303, 1307.

is the view that, Section 112, first paragraph requires that the patent document "enables" the invention in terms of providing information sufficient to allow one with ordinary skill in the art to make and use the invention without undue experimentation. To advocate that the written description serves a purpose over and above the enablement factor leads to the anomaly that a patent specification could apparently enable a skilled artisan to make and practice the entire invention, but still not prove that the inventor possessed the invented subject matter.[417]

Besides arguing that "a straightforward reading of the text of Section 112 suggests that the test for an adequate written description is whether it provides enough written information for others to make and use the invention,[418] Judge Rader cited Federal Circuit precedent. He reasons that the cases[419] established by the Federal Circuit's predecessor concluded that the patent claims as such satisfy the written description requirement. Hence, the specification did not necessarily have to comply with a written description requirement.[420] Moreover, Judge Rader argued that, prior to the *Eli Lilly* decision; the case law had not applied the written description requirement to questions of validity. In contrast, the application of the principle was merely restricted to questions of priority in order to determine the first inventor of the claimed subject matter. The separate written description doctrine, according to Judge Rader's view, created "enormous confusion."[421]

Affirming summary judgment in *Enzo I,* the Federal Circuit extended the reach of *Lilly*. The claims at issue were directed to nucleic acid probes which where specified for bacteria that cause gonorrhea. The patent described the binding affinity of claimed sequences, and deposited three probes that met the claim limitations.[422] The court held that reference in the specification to deposits in public depositories of nucleic acid probes whose sequences were not disclosed in the specification, but which possessed a known functionality, may not satisfy the written description requirement.[423] The court argued that the inventor's disclosure was "purely functional" because the hybridization conditions did not identify the sequences but merely described what they do.[424] Even though not binding for the court,[425] the Judges also

417 Judge Rader, dissenting from denial of en banc review, University of Rochester v. Searle, 375 F.3d 1303, 1307. (Fed. Cir. 2004).

418 Judge Rader, dissenting in Enzo (denial of en banc review), Enzo Biochem Inc. v. GenProbe Inc., 323 F.3d 956, 976 (Fed. Cir. 2002).

419 In re Gay, 50 C.C.P.A. 725, 309 F.2d 769, 772 (C.C.P.A. 1962); In re Smith, 481 F.2d 910, 914 (C.C.P.A. 1973) ("Where the claim is an original claim, the underlying concept of insuring disclosure as of the filing date is satisfied, and the description requirement has likewise been held to be satisfied.").

420 Judge Rader, dissenting from denial of en banc review, University of Rochester v. Searle, 375 F.3d 1303, 1307.

421 Judge Rader, dissenting from denial of en banc review, University of Rochester v. Searle, 375 F.3d 1303, 1308.

422 Id.

423 Enzo Biochem, Inc. v. Gen-Probe, Inc., 285 F.3d 1013 at 1020. (Fed. Cir. 2002) (Enzo I).

424 Id. at 1018.

425 Enzo I, 285 F.3d at 1019.

noted that the functional description failed to meet the written description guidelines established by the USPTO.[426] While conceding that the inventors, unlike those in *Lilly*, had achieved more than "a mere wish or a plant of obtaining the claimed invention"[427], the majority finally held that the absence of sequence information could not be cured by public deposit."[428]

Judge Dyk's dissenting opinion mainly focused on *Lilly*. In an attempt to highlight the wide-ranging implications of this in his view, misguided decision, he stated that *Lilly* "is open to serious question". Emphasizing the potentially unequal treatment of different fields of innovation and the need for a consistent extrapolation of long-held legal practices, he warns that *Lilly* imposes a "unique written description requirement in the field of biotechnology" and departs form the general rule of "possession" of the invention.[429] In addition, he harshly criticized the majority's view that sequence information could not be made public by public deposit, arguing that reference to a deposit "is an ideal way of satisfying the written description requirement."[430]

The *Enzo I* decision was intensively discussed within the legal profession, and raised serious concerns, especially within the biotech community itself.[431] Against this background, the same panel of judges had to reconsider the case.[432] Taking into account the USPTO's Written Description Guidelines, the panel partly vacated its earlier position. The major aspect of the reversed conclusion was that, in some cases and under certain conditions, a description of the function of genetic materials will be sufficient to meet the written description requirement:

> "[T]he PTO has determined that the written description requirement can be met by showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics … i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics."[433]

426 Guidelines for Examination of Patent Applications Under 35 U.S.C. 112, Para 1 "Written Description" Requirement, 66 Fed. Reg. 1099 at 1106 (Jan. 5, 2001) ("WD Guidelines").

427 Enzo I at 1018 (quoting Lilly, 119 F.3d at 1566).

428 Enzo I at 1021.

429 Id. at 1025 (dissenting opinion).

430 Id. at 1027 ("The primary purpose of the statutory written description requirement is to provide notice to comptentitors and the public of the scope of the patent claims.")

431 See, e.g., Brief of Amicus Curiae United States at 1 Enzo Biochem, Inc. v. Gen Probe, Inc., 323 F.3d 956 (Fed. Cir. 2002), cited in Judge Rader dissenting from denial of en banc review in University of Rochester v. G.D. Searle & Co., Inc., 375 F.3d 1303 ("That Enzo opinion caused an immediate firestorm").

432 Enzo Biochem, Inc. v. Gen-Prob, Inc., 323 F.3d 956 (Fed. Cir. 2002) (Enzo II).

433 Id. at 964 (citing Guidelines for Examination of Patent Applications Under 35 U.S.C. 112, Para 1 "Written Description" Requirement, 66 Fed. Reg. 1099 at 1106 (Jan. 5, 2001)). Generally, the WD Guidelines are consistent with the Federal Circuit case law, as they require an applicant "permit a person skill in the art to clearly recognize [the] applicant had possession of the claimed invention." 66 Fed. Reg. at 1105. As for nucleotide sequences, however, the Guidelines did not fully embrace the doctrine of a separate written description requirement as it was developed in Lilly.

Based on this more flexible set of principles, the court remanded the case to the district court, which was asked to determine whether the specification provided sufficient information to "demonstrate possession of the generic scope of the claims" by the inventors.[434] Emphasizing the significance of the deposits and the scope of the claims, the remand order entrusted the district court to determine whether the claimed subject matter had been sufficiently disclosed, as judged by a person skilled in the art.[435]

While providing a more flexible interpretation, the court followed its earlier view that the mere possession is not sufficient for a disclosure. Enzo had claimed that it had shown "possession" of the claimed invention sufficient to meet the requirement of § 112 because it had effectively reduced three sequences within the scope of the claims to practice, Rejecting this argument, the court held that possession is merely "ancillary to the statutory mandate". Without additional information, a claim lacks sufficient disclosure.[436]

In stark contrast to *Enzo I*, the *Enzo II* panel rejected the view that a biological deposit referred to in the specification could not be considered part of the disclosure. It explained that:

> "references in the specification to a deposit in a public depository, which makes its contents accessible to the public when it is not otherwise available in written form, constitutes an adequate description of the deposited material sufficient with the written description requirement of § 112 Para 1."[437]

In sum, the Federal Circuit allowed the rehearing of *Enzo I*, but rejected a petition to rehear the appeal *en banc*.[438] In his dissent from this denial, Judge Rader argued that outside the context of resolving priority, no statute or precedent supports an independent written description requirement.[439] Judge Lourie's concurring opinion rejected this criticism, noting that "[n]ew interpretations of old statutes in light of new fact situations occur all the time."[440] In light of the opinion, a strong written description standard will ensure that in exchange for the exclusive right to practice an in-

434 Id. at 966.
435 Id. at 967.
436 Id. at 969.
437 Enzo II, 323 F.3d 965.
438 Id. at 970.
439 Id. at 978 (dissenting opinion) ("The function of the description requirement is to ensure that the inventor had possession, as of the filing date of the application relied on, of the specific subject matter later claimed by him. In sum, WD was a new matter doctrine, a priority policeman.") (citing In re Wertheim, 541 F.2d 257, 262 (C.C.P.A.A 1976). Based on this historical genesis of the written description requirement, Judge Rader condluced that the requirement's sole purpose served the "very clear function [of] preventing new matter from creeping into the claim amendments." Id. Jdge Linn's dissenting opinion raised similar arguments. Id. at 987.
440 Id. at 971.

vention, a patentee must disclose both what the invention is and how to make and use it.[441]

Judge Rader's view is illustrated in his dissenting from denial of *en banc* review in *University of Rochester v. Searle*. For the Judge the fact that the court first "faithfully followed *Eli Lilly*" but later reversed the decision as being invalid means that the *Eli Lilly* description doctrine was misguiding.[442] With regard to the "practical problems" that an application of the *Eli Lilly* position created, Judge Rader concluded:

> "This new 1997 rule changes the established rules of claiming and disclosing inventions. Many biotechnological inventions predate *Eli Lilly*. Before the 1997 change, no inventor could have foreseen that the Federal Circuit would make a new disclosure rule. Without any way to redraft issued patents to accommodate the new rule, many patents in the field of biotechnology face serious and unavoidable validity challenges simply because the patent drafter may not have included the lengthy nucleotide sequences."[443]

Judge Rader further raises fundamental patent policy concerns:

> "Must a University or small biotech company expend scarce resources to produce every potential nucleotide sequence that exhibits their inventive functions? Perhaps more important for overall patent policy, must inventors spend their valuable time and resources fleshing out all the obvious variants of their last invention instead of pursing their next significant advance in the useful arts? Again, *Eli Lilly* and *Rochester* appear to have given little thought to these unintended consequences."[444]

Hence, the Judge is particularly concerned that the described uncertainty may affect pharmaceutical and biotechnological industries, as patent protection has been described as the industries' "lifeblood." Biotechnological drug design necessarily depends on the expenditure of both time and money. Judge Rader further argues that a separate written description requirement extends uncertainty and imposes costs to the judicial system:

> "[A] trial court, as in this case, must first ask its jury whether the specification provides sufficient information to enable one of ordinary skill in the art to make and use the invention. Then the trial court must ask the jury again to look at the same specification for information that an inventor of extraordinary skill "possessed" the invention. … Moreover, the trial court must give separate instructions and entertain separate witnesses on these inseparable patent rules to ensure adequate disclosure. Viewed in the practical terms of trial procedure and jury understanding, this 1997 doctrine unnecessarily complicates and prolongs patent enforcement."[445]

441 Id. at 971-972, 974-975. Judge Newman considered the patent description the "foundation of the patent specification."

442 Judge Rader dissenting from denial of en banc review, University of Rochester v. Searle, 375 F.3d 1303, 1308 (Fed.Cir. 2004).

443 Judge Rader dissenting from denial of en banc review, University of Rochester v. Searle,375 F.3d 1303, 1313 (Fed.Cir. 2004).

444 Judge Rader dissenting from denial of en banc review, University of Rochester v. Searle, 375 F.3d 1303, 1313 (Fed.Cir. 2004).

445 Judge Rader dissenting from denial of en banc review, University of Rochester v. Searle, 375 F.3d 1303, 1314. The judge confirmed his opinion in his dissent from the order denying rehearing en banc in Lizardtech, Inc. v. Earth Resource Mapping, 433 F.3d 1373, 1376 (Fed.

Judge Linn also dissented from the court's decision not to hear the case en banc. He agreed with Judge Rader with regard to the "confusion our precedent in *Eli Lilly* and *Enzo* has engendered in establishing 'written description' as a separate requirement on which a patent may be held invalid." *Eli Lilly*, Judge Linn stated, constituted the first time that the Federal Circuit had done so. According to Linn, the essential question of Section 112, first paragraph is whether the written description describes the invention recited in the claims – themselves part of the specification – in a sense that it is sufficient to enable a person of ordinary skill in the art to make and use the claimed invention and practice the best mode contemplated by the inventor. Hence, Judge Linn argues, *Eli Lilly* "should be overturned". According to his view, a separate written description requirement creates "an inevitable clash between the claims and the written description" as the emphasis of the application. In his eyes, only the claims "establish the bounds of the right to exclude" and "construing Section 112 to contain a separate written description requirement beyond enablement and best mode creates confusion as to where the public and the court should look to determine the scope of the patentee's right to exclude."[446]

Judge Dyk takes a midpoint between the other positions, reasoning that Section 112 contains a separate written description requirement, which applies in the context of priority and validity disputes. However, he cautions his view by stating that his vote should not be taken as an endorsement of our existing written description jurisprudence. According to his view, it is necessary that satisfactory standards be applied to all fields of technology articulated.[447]

The current dispute in the U.S. shows a high level of uncertainty surrounding a major patentability condition. But is the strict emphasis of a separate written description requirement necessary for adequate patent protection? Pursuant to claim constructing rules, the claims are the decisive element for the determination of scope. Thus, a person skilled in the art should be able to define the scope with the help of the claim language and the amendments made in the course of the patent application process. A separate weight of the written description requirement, by contrast, obliges the patent applicant to provide a precise definition of the subject matter claimed in structural terms. If he is not capable of doing so, the claim fails. Such a focus on structural features makes it almost impossible to use functional terminology in the patent claims. The inventor has rather to describe all compositions claimed by their chemical structure. Therefore, the enablement factor should be considered a sufficient means to evaluate whether the inventor does not try to claim beyond the

Cir. 2006) ("This court's written description jurisprudence has become opaque to the point of obscuring other areas of this court's law.").445

446 Judge Linn dissenting from denial of en banc review, University of Rochester v. Searle, 375 F.3d 1303, 1325.

447 Judge Dyk concurring from denial of en banc review, University of Rochester v. Searle, 375 F.3d 1303, 1327.

scope of what he has disclosed. Hence, a separate written description obligation appears unnecessary.[448]

b) Europe (Sufficient disclosure)

The European "sufficient disclosure" requirement is laid down in Articles 83 and 84 EPC, the respective Implementing Regulation as well as in the EPO Guidelines for Examination. Under Art. 83 EPC, 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." Art. 84 EPC requires that patent claims are "supported by the description." The Implementing Regulation to the EPC, Rule 42(1)(e) (former Rule 27) states that the inventor is required to "describe in detail at least one way of carrying out the invention claimed." Finally, The EPO Guidelines for Examination[449] determine that the description must disclose sufficient detail to render it apparent to the skilled person how to put the invention into practice without having to perform any undue burden or inventive activity.[450]

Consistent with the diverse nature of biotechnological inventions, there are overly restrictive rules as to how much information has to be provided in a patent application. In principle, even broad claims can be supported by disclosing merely one way of performing the claimed subject matter, provided that the invented effect can be easily achieved by the skilled person. In addition to the example provided, however, the application must contain sufficient information to enable the person skilled in the art to perform the invention over the whole area claimed.[451] In all cases, the amount of technical details to be disclosed is highly context-specific. The more difficult it is to obtain the claimed effect, the more technical features and the more examples have to be provided.

448 A different view is presented in Mull, William C., Using the Written Description Requirement to Limit Broad Patent Scope, Allow Competition, and Encourage Innovation in Biotechnology, 14 Health Matrix: Journal of Law-Medicine 2004, 393-435, 435, concluding that "[t]he Federal Circuitis correctly applying the written description requirements part of the disclosure to limit broad claim scope in biotechnology patents. The written description requirement is separate from the enablement requirement and applies to all claims."

449 Guidelines for Examination in the EPO, Part C-II, 4.9., available at http://www.epo.org/patents/law/legal-texts/guidelines.html, last checked on January 21, 2008.

450 T727/95, Weyerhaeuser Company/Ajinomoto, OJ 2001, 1; Benkard/Schäfers, EPÜ, Art. 83, No. 48.

451 See Guidelines for Examination in the EPO, Part C-II, 4.9., available http://www.epo.org/patents/law/legal-texts/guidelines.html, last checked on January 21, 2008; Benkard/Schäfers, EPÜ, Art. 83, No. 50; T435/91 Reinigungsmittel/UNILEVER, N. Publ., No. of the Reasons 4.1.2, 4.14.

As for biotechnological inventions more narrowly, a number of examination guidelines and implementing regulations are highly relevant.[452] First, if the invention is defined in terms of a parameter, the application must provide a clear description of the methods used to determine the parameter values, unless the skilled person would be knowledgeable with regard to what method to use.[453] Second, the deposit of biological material is regulated by Implementing Regulations to the EPC, Rules 33 and 34 (former Rules 28 and 28a.)[454] The deposit has to be made as of the filing date. This is contrary to U.S. patent law, where the deposit must be made at any time the patent is granted.[455] Third, the EPO, in line with other patent offices worldwide, requires a written and computer-readable sequence protocol for the sufficient disclosure of protein and gene inventions (Implementing Regulations to the EPC, Rule 30(1) (former Rule 27 a)).[456]

Large numbers of cases deal with the interpretation of Art 83 and 84 EPC. In *Polypeptide Expression/Genentech,*[457] the court ruled that an invention the claim on which prohibits from multiple uses can be enabled by disclosing a single use only. The case dealt with a patent application that had been rejected because the terms "plasmid" and "bacteria" were considered too broad, since some of them depended on yet unavailable entities. The Technical Board of Appeals, classifying the critical expressions as functional terms, approved that they were allowable 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".[458] It argued that the inclusion of yet unavailable entities resembled the protocol of using broad 'comprising-language' and had to be seen as "normal practice in many technical

452 Most of the relevant rules were released in a specific protocol, which determines how amino acid-related information should be released. See decision of the President of the EPO dated 02.10.1998 concerning the representation of nucleotide and amino acid sequences in patent applications and the filing of sequence listings, see Suppl. No. 2 to OJ EPO 11/1998, 1-68; Singer/Stauder, EPC, Vol. 1, Nos. 70-75; Meyer-Dulheuer, K.-H., Der Schutzbereich von auf Nucleotid- oder Aminosäurensequenzen gerichteten biotechnologischen Patenten, GRUR 2000, 179, 179.

453 Guidelines for Examination in the EPO, Part C-II, 4.9.

454 Singer/Stauder, EPC – Vol. 1, Nos. 76-101; Schulte/Moufang, PatG mit EPÜ, Nos. 449-516; also Straus, Joseph/Moufang, Rainer, Deposit and release of biological material for the purposes of patent procedure: industrial and tangible property issues, Baden-Baden 1990, 69. The formal deposit requirements correspond to the provisions of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure that was signed by almost all member states of the European Patent System. BGBl II 984 II 679 = BIPMZ 84, 318 = TabuDPMA Nr. 635; Schulte/Moufang, PatG mit EPÜ, No. 453; Busse/Keukenschrijver, PatG, § 34, No. 311.

455 See In re Lundak, 227 USPQ 90 (CAFC 1985).

456 See Meyer-Dulheuer, K.-H., Der Schutzbereich von auf Nucleotid- oder Aminosäurensequenzen gerichteten biotechnologischen Patenten, GRUR 2000, 179, 179. The particular amino acid sequence must be determined; it is not sufficient to merely disclose the protein's variant, see Busse/Keukenschrijver, PatG, § 34, No. 271.

457 T 292/85, Polypeptide Expression/Genentech, OJ 1989, 275.

458 T 292/85, Polypeptide Expression/Genentech, OJ 1989, 275, 283.

fields."[459] It is thus sufficient that at least one use is clearly indicated, which enables the skilled person to carry out the invention.[460]

The Technical Board of Appeals has always denied the application of an official "one way rule." Nevertheless, the analysis of their case law reveals that such a rule has been a frequently used practice.[461] For example, the Board in *Harvard* remanded the decision of the opposition division that had limited the patent scope, and decided that the patent granted was confined to rodents and no longer to non-human mammals. The Board held that, on the base of the *Genentech* ruling:

> "The description of the invention firstly ensures that the inventions can be reproduced on mice. And secondly, it may be assumed that the skilled person is aware – in the same way as in case T 0292/85 – of other suitable mammals on which the invention can likewise be successfully performed. There is thus no reason why the application should be refused."[462]

In *Fuel oils/Exxon,*[463]the Technical Board of Appeal narrowed down the potential for an overly broad interpretation of the patent description, by emphasizing that:

> "…the disclosure of one way of performing the invention is only sufficient within the meaning of Article 83 EPC if it allows the person skilled in the art to perform the invention in the whole range that is claimed."[464]

The exact way to interpret "whole range", however, remained undetermined, as the Board made clear that such determination must be made on a case-by-case-basis.[465]

In *ALSTOM Holdings/ABB Patent GmbH*[466], the European Board of Appeals determined that the person skilled in the art must be able to carry out the fundamental aspect of the technical teaching of an invention:[467]

> "[T]he disclosure in a patent application or patent must enable a person skilled in the art to carry out successfully the claimed invention in practice in the *whole range* claimed… [I]t is … of no significance whether the invention could have been carried out in the form of a variant covered by the wording of the claim … if this variant does not correspond to the fundamental aspect of the technical teaching of the invention to which the only concrete embodiment dis-

459 T 292/85, Polypeptide Expression/Genentech, OJ 1989, 275, 284.

460 T 292/85, Polypeptide Expression/Genentech, OJ 1989, 275, 284. In Biogen, the Technical Board approved the ruling of Genentech, stating that "…this provision has previously been interpreted by the Board of Appeal in decision T 292/85 … as being satisfied 'if at least one way is clearly indicated enabling the skilled person to carry out the invention'. In other words, in the Board's view, it is not necessary for the purpose of Article 83 and 100(b) EPC that the disclosure of a patent is adequate to enable the skilled man to carry out all conceivable ways of operating the invention which are embraced by the claims …" See T 0301/87, Biogen, OJ 1990, 325, 343.

461 See Bostyn, Sven J.R., A European Perspective on the Ideal Scope of Protection and the Disclosure Requirement for Biotechnological Inventions in a Harmonized Patent System, 5 The Journal of World Intellectual Property 2002, 1014, 1023-1024.

462 T 19/90, Onco-mouse/Harvard (1990), OJ 1990, 476.

463 T 409/91, Fuel oils/Exxon, OJ 1994, 653.

464 T 409/91, Fuel oils/Exxon, OJ 1994, 653, 660.

465 T 409/91, Fuel oils/Exxon, OJ 1994, 653, 660.

466 T 1173/00, ALSTOM Holdings/ABB Patent GmbH, OJ EPO 2004, 16.

467 T 1173/00, ALSTOM Holdings/ABB Patent GmbH, OJ EPO 2004, 16, 27.

closed refers… A variant which is clearly not based on the same technical effect is not suitable as a basis for generalizations of this type."[468]

Requiring that the "fundamental aspects of the technical teaching" have to be disclosed, does not imply an additional and separate written description requirement. In *Kirin-Amgen,* a case in which the claim at issue was directed to the recombinant production of Erythropoietin, the Board made clear that broad claims are generally allowed:[469]

> "…it is a fundamental principle of patent law that a claim can validly cover broad subject matter, even though the description of the relevant patent does not enable every method of arriving at the subject matter to be carried out. Otherwise no dominant patent could exist, and each developer of a new method of arriving at the subject matter would be free of earlier patents. In many cases in the field of biotechnology, patent protection would then become illusory."[470]

The Board thus made clear that patentability requirements may not be interpreted in a way that impedes the granting of broad patents.

The decision of *Production of Erythropoietin/Kirin-Amgen, Inc*[471] also exemplifies how limits are set regarding the deposit of biological material. With the mere guidance of the disclosure and without deposit of recombinant host cells, the appellants argued, the enablement of the claimed embodiments was only possible after exerting 4½ years of effort, "which was an unacceptable burden."[472] The appellees argued that "once the Epo gene was cloned and the sequence made available, it was straightforward for someone to clone and express the Epo gene."[473] In response to these arguments, the Board of Appeal stated that Art. 83 EPC only requires a deposit if others were not able to "repeat the invention at all."[474] It also made clear that undue burden could not be a rationale for requiring a deposit:

> "This concept relates more to cases where the route that the reader is to follow is so poorly marked that success is not certain. If the route is certain but long and laborious, the patentee is under no obligation to assist the disclosure by making actual physical samples, e.g. 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."[475]

In *The General Hospital Corporation,*[476] the court made clear that "undue burden" is determined from the perspective of a person skilled in the art. The case is also relevant because it directly refers to the need to disclose information that relates to the

468 T 1173/00, ALSTOM Holdings/ABB Patent GmbH, OJ EPO 2004, 16, 26.
469 Kiren-Amgen/Erythropoietin [2000] E.P.O.R. 135 (EPO 1998). See, more generally Bostyn, Sven J.R., A European Perspective on the Ideal Scope of Protection and the Disclosure Requirement for Biotechnological Inventions in a Harmonized Patent System, 5 The Journal of World Intellectual Property 2002, 1014ff, 1026.
470 Kiren-Amgen/Erythropoietin [2000] E.P.O.R. 135, 145.
471 T 412/93, Production of Erythropoietin/Kirin-Amgen, Inc., [1995] E.P.O.R. 629.
472 T 412/93, Production of Erythropoietin/Kirin-Amgen, Inc., [1995] E.P.O.R. 629, 633.
473 T 412/93, Production of Erythropoietin/Kirin-Amgen, Inc., [1995] E.P.O.R. 629, 638.
474 T 412/93, Production of Erythropoietin/Kirin-Amgen, Inc., [1995] E.P.O.R. 629, 657.
475 T 412/93, Production of Erythropoietin/Kirin-Amgen, Inc., [1995] E.P.O.R. 629, 657.
476 T 497/02, The General Hospital Corporation, N. Publ. (EPO 2004).

secondary and tertiary structure of proteins. The claim was directed to the use of a peptide in the preparation of an agent for the treatment of diabetes mellitus. The Board of Appeal rejected the claim for a lack of sufficient disclosure under Art. 83 EPC, arguing that the patent application did not provide any evidence that the cited peptides were in fact performing the required biological activity. The skilled person therefore has to perform tests and experimentations that amount to an undue burden with no certainty of success. The board explained:

> "… that the biological activity of proteins is highly dependent on their secondary and tertiary structures, resulting from their primary structure… There is no basis in the application to conclude that any of the 31 peptides involved, or, if any, how many thereof will show secondary and tertiary structures, giving them properties that make them candidates for use in the treatment of diabetes mellitus."[477]

To sum up, the European sufficient disclosure requirement is met by adequately enabling practice of the full scope of the claim and disclosing in the specification at least one method. An inventor is required to provide sufficient information to 'make and use' the invention, but not to separately describe every single element of the patented subject matter. Applicants are required to provide the information necessary for a skilled person to carry out the invention in the whole area claimed without any undue experimentation.[478]

Finally, and in contrast to the U.S. situation, it is worth noting that the cases represented above suggest that neither Art. 84 EPC nor Art. 83 EPC are used as a basis for a separate written description doctrine. This understanding is consistent with the principle that the claims, rather than the patent description are the decisive element of patent scope, a principle confirmed by further EPC provisions.[479]

III. Conclusion

The comparison of both patent systems shows that a major distinction remains because the U.S. law does not contain an explicit exclusion of patentability due to ethical concerns. In sum, however, the requirements of both systems are in many ways comparable to each other.[480] The currently discussed reform of the U.S. legal system can be understood as a further step towards harmonization.[481] The analysis in this

477 T 0497/02, The General Hospital Corporation, No. of the Reasons 18.

478 Schulte/Schulte, PatG mit EPÜ, § 34, Nos. 362, 367. It is not sufficient that the invention can be carried out generally, it is rather necessary that the skilled person is able to release the claimed invention into practice, see Busse/Keukenschrijver, PatG, § 34, No. 236.

479 Schulte/Kühnen, PatG mit EPÜ, § 14, No. 12. Terms used within the patent claims must be interpreted in accordance to the skilled person's understanding, Busse/Keukenschrijver, PatG, § 14, No. 66.

480 Kleine, Tatjana/Klingelhöfer, Thomas, Biotechnologie und Patentrecht - Ein aktueller Überblick, GRUR 2003, 1, 10.

481 The National Academies' Board on Science, Technology and Economics and the Federal Trade Commission on modernizing U.S. patent law drafted recommendations that suggest