General Issues of Biotech Patents

Andreas Hübel

Abstract Biotechnological inventions are clearly patentable when meeting the requirements set by the patent law. These requirements are based on well-established requirements. However, unique requirements were established such that the peculiarities of biotechnological inventions can be considered. Nonetheless, it appears that certain specific regulations for obtaining patent protection for a biotechnological invention poses more burden to an applicant than seeking patent protection in other disciplines.

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1 Introduction

Humans have been using microorganisms and their metabolic products for centuries, for example when preparing food such as bread made of sour dough, cheese, wine, or other alcoholic beverages. However, it was only discovered in the mid nineteenth century that living microorganisms were responsible for such processes, and subsequently individual strains of microbes were isolated for further use. Besides, biology was a rather descriptive discipline sharing little with chemistry, physics, or engineering. Experimental biology such as the research conducted by Gregor Mendel (1822–1884) concerning genetic inheritance appeared to be an exception rather than the common approach. However, upon

A. Hübel (✉)
Patent Attorneys, Michalski Huettermann and Partner, Neuer Zollhof 2, 40221, Duesseldorf, Germany
e-mail: hl@mhpatent.de

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elucidating the double helix structure of DNA, characterizing the basic principles of how genetic information is passed and realized, i.e. the genetic code and messenger RNA, and identifying restriction endonucleases biological science evolved to a technical discipline nowadays called biotechnology.

Today, there is no doubt that molecular biology, molecular genetics, and biotechnology are disciplines that provide technical improvements and solutions for technical problems. Hence, the results provided by these disciplines are vulnerable to patent protection such that the inventors can commercialize their finding under a limited exclusivity. The latter appears to be particularly appropriate because bringing a biotechnological invention into the market is often a very developmentally intense project.

Patents are recognized as means for protecting intellectual property and inventions. Patents provide exclusivity for the inventor in commercializing his invention. By granting a patent, a state cedes some of its rights to the patentee. To allow a patentee to enforce the right that was ceded to him, the patent has to meet various criteria that are examined before the patent right can in fact be granted to the patentee. Over time those criteria became well established for technical disciplines and evolved along with the technical progress in the technical disciplines. Of course, these criteria were and have to be applied to biotechnological inventions as well. However, it turned out that some of the criteria were insufficient for appropriately protecting biotechnological inventions due to the peculiarities of this discipline. Hence, the criteria were amended, common criteria were interpreted in new ways when applied to biotechnological inventions, and new criteria were set up. Moreover, the intellectual property right for biotechnological inventions is still changing as ever new issues arise in this fairly young subject.

This chapter will illustrate and discuss the general issues of patenting biotechnological inventions, and emphasize the peculiarities in this regard. A focus is set on European patent regulations, but differences in other jurisdictions are mentioned if considered necessary by the author. All the decisions identified in this chapter can be accessed online via the database of the technical board decisions of the European Patent Office (EPO).[1]

2 General Principles

Patent law developed criteria for assessing whether an invention is patentable or not. These criteria are applied to biotechnological inventions too. These criteria are discussed and illustrated with respect to biotechnological inventions herein below.

[1] Available online under http://www.epo.org/law-practice/case-law-appeals/search_de.html.

2.1 Discovery Versus Invention

Patents shall be granted to inventions provided they are new, involve an inventive step, and are susceptible to industrial applicability. This is what basically every patent law in the world provides by one wording or another. Surprisingly, no patent law comprises a clear and unequivocal definition of what an invention in fact is. One has to rely on case law to figure out what—at least the German Supreme Court in the case "Rote Taube"[2]—regards as an invention. The red dove is a new species of doves resulting from crossing and selective breeding of already existing species. Although genetic crosses are biological processes, human selection is a technical aspect. Hence, the German Supreme Court concluded that a selective and systematic exploitation of natural forces including biological forces should not be excluded from patent protection.

The patent laws themselves do not define "invention". The patent laws may define what shall not be regarded as an invention. The EPC for example defines that discoveries, scientific theories, mathematical methods, aesthetic creations, schemes, rules and methods for performing mental acts, playing games or doing business, programs for computers, and presentation of information shall not be regarded an invention.[3] Hence, no European patent can be obtained for any of the said subjects. For example, it is a discovery if a natural ligand for a given receptor is identified. Hence, the binding of the ligand to the receptor is not patentable. However, a medicament comprising the ligand for treating a specific disease is patentable.

In addition, it is provided that European patents shall not be granted for inventions, the commercial exploitation of which would be contrary to "ordre public" or morality, plants, or animal varieties, essentially biological processes for the production of plants or animals, and methods for treating the human or animal body by surgery or therapy, as well as diagnostic methods practiced on the human or animal body.[4] One such example are human embryonic stem cells which require destruction of a blastocyst which in turn is considered as "human embryo."[5]

2.2 Novelty

For an invention to be patentable, it has to be novel. To be novel in the meaning of patent laws means that the invention shall not have been disclosed in any way prior to the first filing of the application for a patent. The invention shall not form part of the state of the art, i.e. the knowledge to mankind. State of the art in turn is everything made available to the public before the date of filing the patent

[2] GRUR 1969, 672.

[3] Article 52(1) EPC.

[4] Article 53 EPC.

[5] Decision G 2/06 of Enlarged Board of Appeals of EPA, Decision of ECJ in case C-34/10.

application. It does not matter at all, who made something available to the public (the applicant, the inventor, or any third party), and how it was made public (written description, oral presentation, use, or any other way). Thus, pursuant to the European understanding, novelty is absolute. The sole question is how to prove that the invention is novel or not.

While examining a patent application, the patent office conducts a literature search. In other disciplines, the vast majority of knowledge is present in published patent applications and patents. Hence, hardly any other literature than published patent applications are cited by a patent office when the said patent office questions novelty of the claimed invention, and/or its inventiveness. For mainly historical reasons, a lot of general information and knowledge concerning biotechnological information has been published in scientific journals. Hence, much more knowledge pertaining to biotechnology is present in other documents than in published patent applications compared to other technical disciplines. Thus, all parties involved in patenting a biotechnological invention are much more concerned with scientific literature than the parties involved in patenting other inventions. Nonetheless, a claimed invention is deemed to lack novelty if said invention is disclosed in a single document[6] in a direct, unambiguous and explicit manner. The claimed invention may to some extent also be disclosed in an implicit manner. When an explicit cross reference is made in a single document to another document, the disclosure is also considered as novelty destroying. Hence, scientific literature has to be considered routinely if patentability of a biotechnological invention shall be assessed prior to filing a patent application. Moreover, it is necessary for a company who wants to protect its IP by patents to have any other manuscript, in particular manuscripts for scientific journals which include sufficient technical details, reviewed for their content, and to assess whether the technical details disclosed therein would affect a patent application. Thus, filing and publication of (i) patent applications and (ii) scientific articles have to be coordinated to avoid disadvantages for the applicant.

To prove that a claimed invention is not novel is fairly easy, if the invention is disclosed in a single written document. However, oral descriptions such as presentations on conferences will destroy the novelty of a claimed invention in a patent application as well, if the oral presentation is made prior to the filing date of the patent application. Since it is more difficult to prove whether an oral presentation is novelty destroying for a claimed invention, it has to be established (i) at which date the alleged oral disclosure occurred, (ii) exactly what was said, and (iii) under which circumstances the alleged oral disclosure occurred. In this regard, it is to be noted that making a disclosure publicly available does not mean that the entire public must have been notified. It is sufficient if a non-restricted group of persons had the chance of becoming informed about the invention. It is not necessary to prove that a certain number of persons were indeed informed. Anyhow, establishing the above-mentioned criteria is not an easy task. But nonetheless,

[6] EPO Technical Board decision T 466/96, EPO Board of appeal decisions database.

inventors and applicants should be cautious about what to present at an oral presentation when they want to file a patent application covering the invention but not having done yet.

As an example with respect to novelty, a claimed nucleic acid molecule is novel if its sequence has not been published prior to the filing of the patent application claiming a nucleic acid molecule having a particular nucleotide sequence. This includes that the nucleic acid molecule should not have been deposited in a database from where it could be retrieved by an undisclosed number of persons. A claimed nucleic acid molecule whose nucleotide sequence deviates from the nucleotide sequence of a known nucleic acid molecule renders the claims of nucleic acid molecule novel over the known nucleic acid molecule. It does not matter whether the deviation is the absence of a single nucleotide at one of the nucleic acid's ends, the presence of a single additional nucleotide at the 5′ end or 3′ end of the nucleic acid molecule, or a nucleotide substitution.

The absolute novelty is not absolute, because a couple of exceptions exist, which prevent that disclosing an invention is novelty destroying for the subject matter of a subsequently filed patent application concerning the said invention. One such exception is the presentation of the invention on particular, official exhibition. Another example is the misuse of the invention by a third party who filed a patent application concerning the invention the said third party is not entitled to.

2.3 Inventive Step

An invention has to involve an inventive step in order to be patentable. Involving an inventive step means that the invention was not obvious to a person skilled in the art at the time the claimed invention was filed for obtaining a patent. This legal provision shall prevent—for example—simple alternatives from becoming patented. Thus, the requirement of inventive step can be considered as a qualitative measure preventing the patent system from being clogged by trivialities.

Whether or not a claimed invention is based on an inventive step is by far more difficult to judge than whether it is novel, because the answer to that question is at least to some extent subjective. For example, it has to be considered who the person skilled in the art is and what knowledge the person may have. The more knowledgeable a person skilled in the art is considered, the more inventions are likely to be deemed obvious. For the field of biotechnology, the consensus skilled artisan is not a Nobel Prize laureate,[7] not a highly skilled laboratory technician[8] nor the inventor.[9] The skilled artisan would consider means that were successfully

[7] EPO Technical Board decision T 60/89, EPO Board of appeal decisions database.

[8] EPO Technical Board decision T 412/93, EPO Board of appeal decisions database.

[9] EPO Technical Board decision T 5/81, EPO Board of appeal decisions database.

applied in a very close neighboring area,[10] but the skilled artisan does not possess any inventive capability[11] nor would he enter into unexplored areas[12] or even perform any scientific research in these areas.[13] Hence, the consensus skilled artisan in biotechnology is a team of cautious PhD bench molecular biologists including their laboratory assistants which are capable of practically applying methods in the art, which are aware of the disclosure of pertinent prior art documents, which have the necessary manual dexterity and lack of fatigue. However, they would not question established prejudices nor would they try to enter into sacrosanct of unpredictable areas.[14]

Attempting to render the examination of inventiveness more reliable and comprehensible, the EPO established the technical "problem–solution approach" including the "could/would approach". In this approach, the person skilled in the art is defined, and the closest prior art is identified. Usually the closest prior art is that single reference disclosing the combination of features which constitutes the most promising starting point for a development leading to the claimed invention. In doing so, the purpose is considered or the effect of the invention. Very often, the closest prior art reference is the reference disclosing the maximum number of technical features of the claimed invention compared to all other prior art references. Subsequently, the difference of the claimed invention and the prior art in terms of structural or functional features is identified, and the technical effect resulting from the distinguishing features are assessed which in turn is used to formulate the technical problem that shall be solved by the claimed invention. This technical problem is the "objective technical problem" and may be different from the technical problem the inventor wanted to have solved when he made his invention. Then the question to be answered is whether there is any teaching in the prior art as a whole, i.e. not necessarily in the same document, but in any other prior art document that would have prompted the skilled person to modify the known closest prior art to arrive at the claimed solution. This approach recognized that it is not sufficient that the prior art could have prompted the skilled person, but beyond that has to comprise some information which would have motivated the skilled artisan to do so. Practically, this means that the combination of two or at the utmost three prior art documents has to disclose all features of the claimed invention, and that at least one of the prior art documents has to include a suggestion for combining the technical features with a reasonable expectation of success. Whether an invention is based on an inventive step is a decision on a case-by-case basis.

[10] EPO Technical Board decision T 455/91, T 387/94, EPO Board of appeal decisions database.

[11] EPO Technical Board decision T 39/93, EPO Board of appeal decisions database.

[12] EPO Technical Board decision T 296/93, EPO Board of appeal decisions database.

[13] EPO Technical Board decision T 500/91, EPO Board of appeal decisions database.

[14] EPO Technical Board decision T 455/91, EPO Board of appeal decisions database.

2.4 Industrial Applicability

Legal provisions provide that an invention should have industrial applicability to be patentable. This requirement is rather broad and does not possess an undue burden, because an invention is considered to be susceptible of industrial applicability if the invention can be made or used in any kind of industry, including agriculture.[15] Biotechnology is an industry, and hence, inventions concerning or involving nucleic acids, proteins, microbiological strains, methods for producing (micro)organisms, and the like are susceptible of industrial applicability.

However, therapeutic and diagnostic methods were considered as lacking industrial applicability, because medical services were not considered to be an industry; all medical doctors should be free to choose the methods for treating their patients. Whether this presumption holds true remains to be discussed. However, Article 53(c) EPC provides that European patents shall not be granted for methods for treatment of the human or animal body by surgery or treatment and diagnostic methods plasticized on the human or animal body.[16] Hence, therapeutic and diagnostic methods as such are not patentable nowadays, regardless of whether they will be considered applicable in an industry or not.

The prohibition of patenting therapeutic or diagnostic methods does not apply to products for use in these methods.[17] Thus, biological molecules such as peptide hormones, antibodies, nucleic acid molecules which may be used in therapy can be patented.

For a sequence of a gene or a partial sequence of a gene, its industrial application has to be disclosed in the patent application.[18] Thereby, it is acknowledged in the EPC that even a partial sequence of a gene can have industrial applicability. However, the industrial applicability has to be disclosed in the patent application. Whether or not this disclosure requirement also affects the scope of a patent claim concerning a nucleic acid molecule will be discussed herein below.

2.5 Unity

A patent application shall relate to one invention only, or to a group of inventions so linked as to form a single general inventive concept.[19] Such a single inventive concept can be seen in a common technical feature of the different subject matters that are claimed in an application. Although a nucleic acid molecule may encode a specific protein which in turn can fulfill a specific function, the nucleic acid

[15] Article 57 EPC.
[16] Article 53(c) EPC.
[17] Article 53(c) EPC.
[18] Rule 29(3) EPC.
[19] Article 82 EPC.

molecule is not part of the polypeptide. Thus, it appears that a nucleic acid molecule and a polypeptide which is encoded by the nucleic acid molecule do not share a common technical feature. The polypeptide and the nucleic acid sequence encoding the polypeptide are two distinct molecules with different features and utilities. Hence, it appears that claims within a single application can be construed as lacking unity, if they are directed to a nucleic acid molecule encoding a polypeptide, and to the polypeptide encoded by the nucleic acid molecule when the claims are drafted too broadly.

The same consideration may apply to claims directed to a nucleic acid molecule which is characterized by different features such as (i) its nucleotides sequence, (ii) its hybridization properties, and (iii) its similarity to a given nucleic acid sequence. Although apparent from the skilled artisan that all these subject matters are linked to one another by a single technical concept, such a single technical concept may not be sufficient to support unity of the invention by means of patent law. In such cases, the applicant may file one or more divisional applications to pursue his interest in all embodiments of the invention. However, the applicant has to face significant costs for the divisional applications as all fees due for the parent application have to be paid for each divisional application too.

3 Specific Regulations

This section provides information about specific regulations which were introduced into patent law for addressing peculiarities of biotechnological inventions. Although these regulations are reasonable, it appears that fulfilling the requirements provided by these regulations require more attention by those seeking patent protection for their biotechnological invention, more effort, and have to be considered in strategic considerations.

3.1 Biological Material

When a biotechnological invention concerns biological material, it may be difficult to describe the biological material in a sufficiently clear and precise manner in writing, for example when the invention concerns microbes. Anyhow, the invention has to be disclosed in the patent application in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art at the filing date or priority date.[20] To overcome the conflict of not being able to clearly describe an invention concerning microbial strains and the requirement of doing so, it is possible to deposit the biological material in order to supplement the written description of the invention. With respect to the EPC, the EPO is a member

[20] Article 83 EPC.

"state" of the Budapest Treaty; the formal requirements are set out in Rule 31 of the Implementing Regulations.

It is noteworthy that US patent practice allows depositing microorganisms before grant of the patent, whereas the EPC requires that the deposition has to be made by the European filing date at the latest. Thus, claiming priority of a US patent application which refers to biological material which was not deposited at the filing date of said US patent application in a subsequent European patent application affects the claimed priority.

From the date the European patent application has been published, the deposited biological material must be available to any person or at least to an expert who has been nominated by the requester.[21] The deposited biological material is part of the application's disclosure. As the application is made public 18 months after its priority date, such that its disclosure becomes available to the public, the deposited material should also become publicly available. Therefore, it is prescribed that the applicant identifies the designation of the biological material, the deposition number, date of deposition, and has to identify the institution where the deposition was made.

From the day, the patent application has been published, any one may request a sample of the biological material, provided that the requester confirmed that he will not make available the said biological material to others, and will use for experimental purposes only, until the application has been withdrawn, is deemed to be withdrawn, or the patent has lapsed in all states.

The applicant does not have to fear that anyone can request obtaining a sample of the biological material from the institution of deposition. The applicant can restrict the public availability of the deposited biological material in choosing the "expert solution". This means that the applicant can request that a sample of the biological material shall only be provided to an expert who has been named by the applicant. The technical expert may then be the one assessing whether the deposited biological material indeed has the features disclosed in the application.

3.2 Nucleotide Sequences/Amino Acid Sequences

For inventions concerning nucleic acids or polypeptides, an applicant has to file a sequence listing which constitutes part of the application's disclosure.[22] The sequence listing has to be filed in written and a copy of the sequence listing has to be provided in computer-readable format also, such that the nucleotide sequences and amino acid sequences can be deposited in a database, and can be used for searching databases by the patent office to figure out, whether the relevant sequences are novel.

The sequence listing has to meet multiple formal requirements which render a sequence listing error prone such that it has to be corrected during the subsequent

[21] Rule 33(1) EPC

[22] Rule 30 EPC

prosecution. For the applicants' convenience the software PatentIn is provided, and can be downloaded from the internet pages of—for example—the EPO and the USPTO. An alternative software (BiSSAP) is available from the EPO too. The use of this computer program for preparing the sequence listing is highly recommended to reduce errors.

It became necessary for an applicant to identify the utility of the claimed nucleic acid in the description of the application. Back in the early days of genome sequencing, a tremendous number of ESTs were identified, and the nucleotide sequences were claimed in applications although the applicant did not have a clue to what protein an EST encodes and what the function of the said protein is. Hence, having an EST identified is rather a discovery than an invention. To render an EST becoming an invention, patent law was amended in that it became mandatory to identify the utility of the nucleic acid in the application text.

Interestingly enough, recent opinions demonstrate that the patenting of nucleic acids becomes more and more restricted to purpose-bound protection. One example is the recent ruling issued by the European Court of Justice (ECJ) against Monsanto, in which it was decided that patent claims related to genetic sequences are restricted, in their scope, to those embodiments in which the genetic information performs its function. The ECJ deemed that this was not the case for refined soybean meal comprising a claimed DNA providing herbicide resistance to the growing soybean plant.[23]

3.3 Stem Cells

Stem cells are a hot topic, not just in medical sciences, but in ethic discussions as well as with respect to intellectual property rights. With respect to intellectual property rights concerning pluripotent stem cells, the ECJ is concerned with the task of providing a definition of the human embryo for the needs of the protection of biotechnological inventions.[24] Article 6(1) of Directive 98/44/EC provides that inventions must be considered unpatentable where their commercial exploitation would be contrary to *ordre public* or morality. Article 6(2)(c) of the directive cites the use of human embryos for industrial or commercial purposes as an example of inventions which are considered unpatentable.

The ECJ considered that the concept of a human embryo applies from the fertilisation of an ovum by a sperm via the initial totipotent cells and to the entire ensuing process of the development and formation of the human body. As totipotent cells represent the first stage of the human body which they will become, they have to be legally categorised as embryos. It is irrelevant whether that categorisation must be recognised from before or only after nidation and whether fertilization occurred

[23] Case C-428/08 (Monsanto vs. Cefetra), published on the website of the European Court of Justice (http://curia.europa.eu).

[24] Case C-34/10

naturally or in vitro. The blastocyst is the product of the totipotent cell's capacity for development at a certain moment. The blastocyst is therefore one stage in the development of the human body. Accordingly, a blastocyst has to be categorised as an embryo, like any stage before or after that development.

Embryonic stem cells are not capable of resuming the development of the human body when they have been removed from the blastocyst. As pluripotent cells they cannot lead to a complete human being. Thus, embryonic stem cells, taken in isolation, cannot be categorised as human embryos. However, when pluripotent stem cells are removed from the blastocyst, the blastocyst will be destroyed by the said removal. As the blastocyst itself is categorized as an embryo, the removal of the pluripotent stem sells destroys the embryo they are removed from.

The ECJ considers that an invention has to be excluded from patentability, where the application of the technical process for which the patent is filed necessitates the prior destruction of human embryos or their use as base material, even if the description of that process does not contain any reference to the use of human embryos.

The proposal of the Advocate General is in line with the decision G 2/06 ("Stem cells/WARF") issued by the Enlarged Board of Appeal of the EPO, wherein the board ruled that claims directed to products which could be prepared exclusively by a method which necessarily involved the destruction of the human embryos from which the products are derived is excluded from patentability under EPC, even if the method is not part of the claims.

Thus, totipotent stem cells will not be patentable in Europe. Pluripotent stem cells may be patentable if they were not obtained from a blastocyst by destructing an embryo.

3.4 Antibodies

Antibodies are the fastest growing group of protein therapeutics. Hence, antibodies are among the molecules most often found in patent applications in Biotechnology. The desired protection may involve the antibody itself and the methods of generating/producing the antibodies. For the former, claims are drafted wherein the antibody is characterized by its amino acid sequence, by its binding properties, or by the deposition of the cell line producing the antibody. Antibodies may also be claimed by the process of how they are made.

Some kind of protection may also be obtained for already existing antibodies, for example by claiming a different medical use of the antibody than known, or as means of combination therapy with another compound. In the latter case superior efficacy has to be proven by the applicant in order to demonstrate inventiveness.

However, as antibody generation and selection processes become more and more straightforward and automatized, patent prosecution for antibodies thus produced will become more difficult.

3.5 Breeding Technologies for Plants

The European Patent Convention provides that no patent shall be granted for "essentially biological processes for the production of animals or plants". However, it has not been defined what an "essentially biological process" is, or what renders a process "essentially biological". These questions of law were referred to the enlarged Board of Appeals which answered that a non-microbiological process for the production of plants which contains or consists of the steps of sexually crossing the whole genomes of plants and of subsequently selecting plants is in principle excluded from patentability as being "essentially biological" within the meaning of Article 53(b) EPC. Such a process does not escape the exclusion of Article 53(b) EPC only because it contains, as a further step or as a part of any of the steps of crossing and selection, a step of a technical nature which serves to enable or assist the performance of the steps of sexually crossing the whole genomes of plants or of subsequently selecting plants. If, however, such a process contains within the steps of sexually crossing and selecting an additional step of a technical nature, which step by itself introduces a trait into the genome or modifies a trait into the genome or modifies a trait in the genome of the plant produced, so that the introduction or modification of the trait is not the result of the mixing of the genes of the plants chosen for sexual crossing, then the process is not excluded from patentability under Article 53(b) EPC. In the context of examining of whether such a process is excluded from patentability as being "essentially biological" within the meaning of Article 53(b) EPC, it is not relevant whether a step of a technical nature is a new or known measure, whether it is trivial or a fundamental alteration of a known process, whether it does or could occur in nature or whether the essence of the invention lies in it.

Providing this decision, the Enlarged Board of Appeal of the EPO provided clarity for applicants on what may be patentable, and on what is definitely not patentable as being considered to be an "essentially biological process". However, plants obtainable by an essentially biological process remain patentable if the remaining patentability requirements are met.

4 Conclusion

Biotechnological inventions are clearly patentable when meeting the requirements set by the patent law. These requirements are based on well-established requirements. However, unique requirements had to be established such that the peculiarities of biotechnological inventions can be considered. Nonetheless, it appears that certain specific regulations for obtaining patent protection for a biotechnological invention poses more burden to an applicant than seeking patent protection in other disciplines.