

Unravelling the Patenting of Biotechnology Inventions

The European Perspective

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1. The Legal Basis: The EU-Biotech-Directive and the EPC

1.1. The EU-Biotech Directive and the EPC

Inventions in the field of biotechnology are often related to biological material. One of the reasons for the high expectations from biotech – the possibility to "play" with self-reproducing systems and to use these processes for industrial, especially medical uses - is at the same time one of the major challenges in patenting inventions relating to such systems. Moreover, the high flexibility that nature seems to provide to those systems requires very individual claim drafting strategies for such inventions.

Due to the speed and easiness which biotechnological techniques offer for receiving answers for scientific questions, a lot of financial and manpower input in the last 30 years resulted in a highly efficient, fast and straightforward set of biotechnological tools which enable amazing scientific and industrial projects. For bringing such projects from scientific promises to industrial profitability patents are regarded as one of the tools which are essentially necessary (but - of course – not sufficient) both, by the established industry (in the case of biotech "Big Pharma" and agrarian industries) and by (venture capital) investors for (small) biotech start-ups.

In the US, the relevant bodies (US-PTO, Congress and even the US Supreme Court) have immediately addressed many questions with regard to patenting of biotechnological questions mainly in favour for general patentability of such inventions in the early 1970ies. Despite an ambivalent opinion towards biotech in the general public in Europe, the EU Commission and the EU Parliament have regarded biotechnology and genetic engineering as "certainly [being] of fundamental importance for the Community's industrial development" (recital 1 of the Biotech-Directive). The aforementioned ambivalent opinion towards biotech in Europe resulted in a highly controversial attitude towards patenting of biotechnological inventions throughout the countries of the EU. Although the decision practice of the EPO in the 1980ies and (early) 1990ies was not hostile against biotechnological inventions, the national bodies in some EU countries were – mostly due to public criticism - not in favour of extensive patenting of such inventions, so that enforcement of biotechnological inventions in the EU was a game of hazard for firms relying on such patents as well as for their investors. This legal uncertainty with respect to patents was – besides a controversial discussion of biotechnology in the public – regarded as one of the most prominent reasons for the low development of biotech industry in Europe in the 1980/90ies.

The European Commission therefore decided to take measures for supporting the biotech industry and initiated a harmonisation project for the patenting of biotech inventions. A "Directive on the legal protection of biotechnological inventions" was therefore planned, the initial work being already performed as early as 1988. After a lot of discussion, re-drafting and amending, a final version was proposed in 1995 to the EU parliament. The parliament rejected the Directive. After further amendments and even more discussion, the Directive was presented to the parliament again in 1998. This time the Directive passed parliament successfully and entered into force on 30 July 1998 ("Directive 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the legal protection of biotechnological inventions"). The member states were allowed to bring their national patent laws in conformity with the Directive until 30 July 2000, a date which has been met by DK and IE.

The Directive's main object is the harmonisation of protection and enforcement of biotechnological inventions in the EU both, with respect to patentability criteria as well with respect to the scope of

protection (and exceptions thereto).

In 18 Articles preceded by 56 recitals (the relatively high number of recitals reflects the severe discussions before the final text was adopted as compromise between the various camps) the Directive regulates patentability (Articles 1 to 7), scope of protection (Articles 8 to 11), compulsory cross-licensing (Article 12) and deposit, access and re-deposit of a biological material (Articles 13 and 14). Articles 15 to 18 are „Final Provisions“ relating to the period for compliance with the Directive (Article 15; „not later than 30 July 2000“), potential amendments and up-dates (Articles 16), entering into force (Article 17; 30 July 1998) and the provision that the Directive is addressed to the EU member states (Article 18).

The Directive was implemented into the „Implementing Regulations to the EPC“ („The EPC Rules“) as Rules 23b-e. These Rules contain almost identical wording as the Articles of the Directive.

PATENTABILITY:

The Directive makes clear that patenting biotechnological inventions does not necessitate the creation of a separate body of law in place of the rules of national (or regional (EPC !)) patent law (Recital 8), however, it is mentioned that patenting of such inventions has “created uncertainty“ (Recital 9) and that harmonisation is necessary to clarify this uncertainty. This is the very purpose of the Directive.

In relying on „classical“ patent law, Article 3 of the Directive stipulates:

Article 3

1. For the purposes of this Directive, inventions which are new, which involve an inventive step and which are susceptible of industrial application shall be patentable even if they concern a product consisting of or containing biological material or a process by means of which biological material is produced, processed or used.

With respect to the concepts of novelty, inventive step and industrial applicability it is therefore referred to the given European patentability concepts based on the Strasbourg Convention (“Strasbourg Convention on the Unification of Certain Points of Substantive Law on Patents for Invention” of 27 November 1963) and reflected by e.g. Articles 52(1), 54, 56 and 57 EPC:

Article 52 EPC

Patentable inventions

- (1) European patents shall be granted for any inventions which are susceptible of industrial application, which are new and which involve an inventive step.

Article 54 EPC

Novelty

- (1) An invention shall be considered to be new if it does not form part of the state of the art.
- (2) The state of the art shall be held to comprise everything made available to the public by means of a written or oral description, by use, or in any other way, before the date of filing of the European patent application.

- (3) Additionally, the content of European patent applications as filed, of which the dates of filing are prior to the date referred to in paragraph 2 and which were published under Article 93 on or after that date, shall be considered as comprised in the state of the art.
- (4) Paragraph 3 shall be applied only in so far as a Contracting State designated in respect of the later application, was also designated in respect of the earlier application as published.
- (5) The provisions of paragraphs 1 to 4 shall not exclude the patentability of any substance or composition, comprised in the state of the art, for use in a method referred to in Article 52, paragraph 4, provided that its use for any method referred to in that paragraph is not comprised in the state of the art.

Article 56 EPC

Inventive step

An invention shall be considered as involving an inventive step if, having regard to the state of the art, it is not obvious to a person skilled in the art. If the state of the art also includes documents within the meaning of Article 54, paragraph 3, these documents are not to be considered in deciding whether there has been an inventive step.

Article 57 EPC

Industrial application

An invention shall be considered as susceptible of industrial application if it can be made or used in any kind of industry, including agriculture.

The Directive does not address in its Articles the question concerning therapeutical, surgical and diagnostic methods performed on the human and animal body, therefore Art. 52(4) EPC has also to be included into the definition of industrial utility as meant by the Directive:

Article 52 EPC

Patentable inventions

(1) - (3)

(4) Methods for treatment of the human or animal body by surgery or therapy and diagnostic methods practised on the human or animal body shall not be regarded as inventions which are susceptible of industrial application within the meaning of paragraph 1. This provision shall not apply to products, in particular substances or compositions, for use in any of these methods.

To this item, only Recital 35 of the Directive reads:

- (35) Whereas this Directive shall be without prejudice to the provisions of national patent law whereby

processes for treatment of the human or animal body by surgery or therapy and diagnostic methods practised on the human or animal body are excluded from patentability;

In addition to this „classical“ concept of patentability the Directive contains a clear and positive message with respect to biotechnological inventions, insofar as this „classical“ concept is applicable „even“ if the invention is a biotechnological invention. This is also reflected in Rule 23b EPC, which also contains a reference to the Directive:

Chapter VI
Biotechnological inventions

Rule 23b EPC

General and definitions

- (1) For European patent applications and patents concerning biotechnological inventions, the relevant provisions of the Convention shall be applied and interpreted in accordance with the provisions of this chapter. Directive 98/44/EC of 6 July 1998²⁹ on the legal protection of biotechnological inventions shall be used as a supplementary means of interpretation.

and in the EPO Guidelines in Chapter C-IV

2a. Biotechnological inventions

2a.1 "Biotechnological inventions" are inventions which concern a product consisting of or containing biological material or a process by means of which biological material is produced, processed or used. "Biological material" means any material containing genetic information and capable of reproducing itself or being reproduced in a biological system.

In principle, biotechnological inventions are patentable under the EPC. For European patent applications and patents concerning biotechnological inventions, the relevant provisions of the Convention are to be applied and interpreted in accordance with the provisions of Rules 23b-e. European Union Directive 98/44/EC of 6 July 1998 on the legal protection of biotechnological inventions (OJ 2/1999, 101) is to be used as a supplementary means of interpretation. In particular the recitals (EU Dir. 98/44/EC, rec.) preceding the provisions of the Directive are also to be taken into account.

One of the major items of the Directive is the concept that – although biological material occurs in nature (including the human body) – the patentability of biological material is possible if this material is isolated from its natural environment or produced by a technological process. With respect to this point Art. 52(2)a and Art. 52(3) EPC is often cited which regards discoveries as such as non-patentable subject matter:

Patentability

Article 52 EPC

Patentable inventions

- (1) ...
- (2) The following in particular shall not be regarded as inventions within the meaning of paragraph 1:
 - (a) discoveries, scientific theories and mathematical methods;
 - (b) - (d) ...
- (3) The provisions of paragraph 2 shall exclude patentability of the subject-matter or activities referred to in that provision only to the extent to which a European patent application or European patent relates to such subject-matter or activities as such.

The fact that the patentability of biological material isolated from its natural environment is accepted may be regarded as a further development of the decisions in the 60ies and 70ies with regard to patentability of naturally occurring (chemical) substances (Article 3.2 and Recital 20 of the Directive).

Article 3

1.
2. Biological material which is isolated from its natural environment or produced by means of a technical process may be the subject of an invention even if it previously occurred in nature.

In the Directive, always a clear distinction is made between the isolated form of such biological material and the material being in its natural environment, especially as part of the human body (Article 5 and Recital 20 of the Directive).

Article 5

1. The human body, at the various stages of its formation and development, and the simple discovery of one of its elements, including the sequence or partial sequence of a gene, cannot constitute patentable inventions.
2. An element isolated from the human body or otherwise produced by means of a technical process, including the sequence or partial sequence of a gene, may constitute a patentable invention, even if the structure of that element is identical to that of a natural element.
3. The industrial application of a sequence or a partial sequence of a gene must be disclosed in the patent application.

Recital (20)

- (20) Whereas, therefore, it should be made clear that an invention based on an element isolated from the human body or otherwise produced by means of a technical process, which is susceptible of industrial application, is not excluded from patentability, even where the structure of that element is identical to that of a natural element, given that the rights conferred by the patent do not extend to

the human body and its elements in their natural environment;

The „hottest“ (political) topic in this complex is the patentability of (human) genes. This is why Art. 5.2 and 5.3 addressed this question specifically. In trying to provide a compromise between the various (political) opinions between the different interesting circles, the patentability of human genes or parts thereof was generally accepted, however, in trying to exclude „pure“ sequence patenting (i.e. patenting (partial) nucleic acid sequences (as well as the polypeptides being encoded by these sequences) which have been found by automated sequencing robots with the help of bioinformatics), the Directive stipulates that patent applications drawn to sequences or partial sequences of a gene have to disclose the industrial application (Art. 5.3; see also: Rule 23e EPC). It is remarkable that for all other inventions filed as European patent applications, the industrial application has to be explicitly stated only in cases where this is not self-evident (and this prerequisite is practically not examined thoroughly at the EPO even for e.g. (organic) chemistry inventions), whereas for biological inventions this is mandatory (Recital 22 of the Directive).

(22) Whereas the discussion on the patentability of sequences or partial sequences of genes is controversial; whereas, according to this Directive, the granting of a patent for inventions which concern such sequences or partial sequences should be subject to the same criteria of patentability as in all other areas of technology: novelty, inventive step and industrial application; whereas the industrial application of a sequence or partial sequence must be disclosed in the patent application as filed;

As outlined below, the current practice at the EPO is even stricter than required by the Directive (see below).

Moreover, the Directive also stipulates (although not in the Articles, but in the Recitals) that an industrial application for a gene is only given, if the „function“ of this gene is disclosed in the patent application as filed (Recitals 23 and 24 of the Directive):

(23) Whereas a mere DNA sequence without indication of a function does not contain any technical information and is therefore not a patentable invention;

(24) Whereas, in order to comply with the industrial application criterion it is necessary in cases where a sequence or partial sequence of a gene is used to produce a protein or part of a protein, to specify which protein or part of a protein is produced or what function it performs;

This is also reflected in the EPO Guidelines (C-II, 4.12 and C-IV, 4.6):

4.12...

Also, in relation to certain biotechnological inventions, i.e. sequences and partial sequences of genes, the industrial application is not self-evident. The industrial application of such sequences must be disclosed in the patent application (see IV, 4.6).

4.6 In general it is required that the description of a European patent application should, where this is not self-evident, indicate the way in which the invention is capable

of exploitation in industry. In relation to sequences and partial sequences of genes this general requirement is given specific form in that the industrial application of a sequence or a partial sequence of a gene must be disclosed in the patent application. A mere nucleic acid sequence without indication of a function is not a patentable invention (EU Dir. 98/44/EC, rec. 23). In cases where a sequence or partial sequence of a gene is used to produce a protein or a part of a protein, it is necessary to specify which protein or part of protein is produced and what function this protein or part of protein performs. Alternatively, when a nucleotide sequence is not used to produce a protein or part of a protein, the function to be indicated could e.g. be that the sequence exhibits a certain transcription promotor activity.

EXCEPTIONS TO PATENTABILITY:

Another major aspect of the Directive is a clarification with respect to the exceptions to patentability in the field of biotechnology. The basis for this clarification is of course, Article 53 EPC and Article 27(2) and (3) TRIPs:

Article 53 EPC

Exceptions to patentability

European patents shall not be granted in respect of:

(a) inventions the publication or exploitation of which would be contrary to “ordre public” or morality, provided that the exploitation shall not be deemed to be so contrary merely because it is prohibited by law or regulation in some or all of the Contracting States;

(b) plant or animal varieties or essentially biological processes for the production of plants or animals; this provision does not apply to microbiological processes or the products thereof.

Article 27 TRIPs

Patentable Subject Matter

(1)

(2) Members may exclude from patentability inventions, the prevention within their territory of the commercial exploitation of which is necessary to protect ordre public or morality, including to protect human, animal or plant life or health or to avoid serious prejudice to the environment, provided that such exclusion is not made merely because the exploitation is prohibited by their law.

(3) Members may also exclude from patentability:

- (a) diagnostic, therapeutic and surgical methods for the treatment of humans or animals;
- (b) plants and animals other than microorganisms, and essentially biological processes for the production of plants and animals other than non-biological and microbiological processes. However, Members shall provide for the protection of plant varieties either by patents or by an effective sui generis system or by any combination thereof. The provisions of this subparagraph shall be reviewed four years after the date of entry into force of the WTO agreement.

The topic of „immoral inventions“ according to Art.53a is reflected in Article 6 of the Directive, which also gives four specific examples for such inventions, i.a. processes for human cloning or

uses of human embryos for industrial purposes:

Article 6

1. Inventions shall be considered unpatentable where their commercial exploitation would be contrary to ordre public or morality; however, exploitation shall not be deemed to be so contrary merely because it is prohibited by law or regulation.

2. On the basis of paragraph 1, the following, in particular, shall be considered unpatentable:

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

In addressing this topic, the Recitals 38 to 45 further explain these items; Recital 38 of the Directive specifically clarifies that this list is not exhaustive:

- (38) Whereas the operative part of this Directive should also include an illustrative list of inventions excluded from patentability so as to provide national courts and patent offices with a general guide to interpreting the reference to ordre public and morality; whereas this list obviously cannot presume to be exhaustive; whereas processes, the use of which offend against human dignity, such as processes to produce chimeras from germ cells or totipotent cells of humans and animals, are obviously also excluded from patentability;

The Commission's European Groups on Ethics in Science and New Technologies is – according to Art.7 of the Directive – responsible for evaluating all ethical aspects of biotechnology; this should also include amendments to the list of Art. 6.2 of the Directive. The list of „immoral inventions“ is also reflected in Rule 23d EPC.

Art. 53b EPC is reflected in Article 4 of the Directive and further explained in Recitals 29 to 33. As further outlined below, these stipulations are also reflected in the decision G 1/98 (OJ EPO 3/2000, 111) and in Rule 23c EPC:

Article 4

1. The following shall not be patentable:

- (a) plant and animal varieties;
- (b) essentially biological processes for the production of plants or animals.

2. Inventions which concern plants or animals shall be

patentable if the technical feasibility of the invention is not confined to a particular plant or animal variety.

3. Paragraph 1(b) shall be without prejudice to the patentability of inventions which concern a microbiological or other technical process or a product obtained by means of such a process.

(29) Whereas this Directive is without prejudice to the exclusion of plant and animal varieties from patentability; whereas on the other hand inventions which concern plants or animals are patentable provided that the application of the invention is not technically confined to a single plant or animal variety;

(30) Whereas the concept ‘plant variety’ is defined by the legislation protecting new varieties, pursuant to which a variety is defined by its whole genome and therefore possesses individuality and is clearly distinguishable from other varieties;

(31) Whereas a plant grouping which is characterised by a particular gene (and not its whole genome) is not covered by the protection of new varieties and is therefore not excluded from patentability even if it comprises new varieties of plants;

(32) Whereas, however, if an invention consists only in genetically modifying a particular plant variety, and if a new plant variety is bred, it will still be excluded from patentability even if the genetic modification is the result not of an essentially biological process but of a biotechnological process;

(33) Whereas it is necessary to define for the purposes of this Directive when a process for the breeding of plants and animals is essentially biological;

SCOPE OF PROTECTION:

Under this item, two major aspects are dealt with in the Directive: 1.: that the patent protection extends to any biological material derived from the patented material by propagation or multiplication, as long as the derived material has the same (patented) characterising features which are reflected in the claims. Art. 8, 9 and 10 (together with Recital 46) of the Directive stipulate:

CHAPTER II

Scope of protection

Article 8

1. The protection conferred by a patent on a biological material possessing specific characteristics as a result of the invention shall extend to any biological material derived from that biological material through propagation or multiplication in an identical or divergent form and possessing those same characteristics.
2. The protection conferred by a patent on a process

that enables a biological material to be produced possessing specific characteristics as a result of the invention shall extend to biological material directly obtained through that process and to any other biological material derived from the directly obtained biological material through propagation or multiplication in an identical or divergent form and possessing those same characteristics.

Article 9

The protection conferred by a patent on a product containing or consisting of genetic information shall extend to all material, save as provided in Article 5(1), in which the product is incorporated and in which the genetic information is contained and performs its function.

Article 10

The protection referred to in Articles 8 and 9 shall not extend to biological material obtained from the propagation or multiplication of biological material placed on the market in the territory of a Member State by the holder of the patent or with his consent, where the multiplication or propagation necessarily results from the application for which the biological material was marketed, provided that the material obtained is not subsequently used for other propagation or multiplication.

Recital 46

(46) Whereas, in view of the fact that the function of a patent is to reward the inventor for his creative efforts by granting an exclusive but time-bound right, and thereby encourage inventive activities, the holder of the patent should be entitled to prohibit the use of patented self-reproducing material in situations analogous to those where it would be permitted to prohibit the use of patented, non-self-reproducing products, that is to say the production of the patented product itself;

In the second relevant point concerning the scope of protection the Directive addresses the „Farmer's Privilege“. It may be pointed out that this is perhaps – from a legal point of view – the stipulation in the Directive which necessitates the most amendments in current law. In Articles 10 and 11 of the Directive two exceptions from the effect of patent protection are defined: first, a farmer may use the product of his harvest for propagation or multiplication by him on his own farm; second, a farmer may make an animal or other animal reproductive material available for the purposes of pursuing his agricultural activity (but not for commercial reproduction activities)(see also Recitals 46-51):

Article 11

1. By way of derogation from Articles 8 and 9, the sale or other form of commercialisation of plant propagating material to a farmer by the holder of the patent or with his consent for agricultural use implies authorisation for the farmer to use the product of his harvest for propagation or multiplication by him on his own farm, the extent and conditions of this derogation corresponding to those under Article 14 of Regulation (EC) No 2100/94.

2. By way of derogation from Articles 8 and 9, the sale or any other form of commercialisation of breeding stock or other animal reproductive material to a farmer by the holder of the patent or with his consent implies authorisation for the farmer to use the protected livestock for an agricultural purpose. This includes making the animal or other animal reproductive material available for the purposes of pursuing his agricultural activity but not sale within the framework or for the purpose of a commercial reproduction activity.
3. The extent and the conditions of the derogation provided for in paragraph 2 shall be determined by national laws, regulations and practices.

A further Article of the Directive which specifically addresses „Farmer's Privilege“ is Article 12 which stipulates the prerequisites under which circumstances a farmer may get a compulsory license; these stipulations; however, seem to be consistent with the stipulations of Art. 31 TRIPs (“Other Use Without Authorization of the Right Holder”):

CHAPTER III

Compulsory cross-licensing

Article 12

1. Where a breeder cannot acquire or exploit a plant variety right without infringing a prior patent, he may apply for a compulsory licence for non-exclusive use of the invention protected by the patent inasmuch as the licence is necessary for the exploitation of the plant variety to be protected, subject to payment of an appropriate royalty. Member States shall provide that, where such a licence is granted, the holder of the patent will be entitled to a cross-licence on reasonable terms to use the protected variety.
2. Where the holder of a patent concerning a biotechnological invention cannot exploit it without infringing a prior plant variety right, he may apply for a compulsory licence for non-exclusive use of the plant variety protected by that right, subject to payment of an appropriate royalty. Member States shall provide that, where such a licence is granted, the holder of the variety right will be entitled to a cross-licence on reasonable terms to use the protected invention.
3. Applicants for the licences referred to in paragraphs 1 and 2 must demonstrate that:
 - (a) they have applied unsuccessfully to the holder of the patent or of the plant variety right to obtain a contractual licence;
 - (b) the plant variety or the invention constitutes significant technical progress of considerable economic interest compared with the invention claimed in the patent or the protected plant variety.

Interestingly it seems that in many countries, which have currently not introduced the Directive in their law, this (Articles 10 and 11) of the Directive is the only item where the current law (in

defining the effect of a patent) is in contradiction to the Directive, whereas for the other items of the Directive the given stipulations in the national laws may at least be interpreted in the sense of the Directive.

ENABLING DISCLOSURE

Since it is the major aim of patents to promote innovation, one of the main prerequisites of a patent is that the invention to be protected has to be described in a way which allows reproduction of the invention for any third person after the protection period. Therefore, the patent (application) has to contain a disclosure of the invention which enables the skilled man in the art to carry out the invention. Art.83 EPC therefore stipulates:

Article 83 EPC

Disclosure of the invention

The 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.

Due to the complex nature of biological material, the necessity of providing an enabling disclosure was always one of the most challenging issues in the present field. In the 1950ies and 60ies the first decisions were issued in Europe and in the US which accepted the deposition of microorganisms at a scientific depository as a substitute for sufficient written disclosure. The Budapest Treaty of 1977 ("Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purpose of Patent Procedure" of 28 April 1977) finally formed the legal framework for mutual international acceptance of such a deposition.

One of the prerequisite of a sufficient deposition is the provision that there is a possibility for third persons to get samples of such microorganisms for e.g. testing the claimed invention. The EPC has – in its implementing regulations – stipulated the requirements in Rules 28 and 28a. These stipulations have been the basis of Articles 13 and 14 of the Directive. According to these stipulations, a deposition of biological material at a recognised depository authority may substitute for a written disclosure, if the material was deposited no later than the filing date of the patent application. The patent application has to contain the details of the deposition (depository institution, accession number) which allows third persons to get samples of such material. Such samples are provided to any third person after the publication of the application, unless the applicant has requested the so-called „expert solution“: According to this “expert solution”, a sample requested between publication of the application and the grant of the patent is only delivered to a nominated independent expert upon request of a third party. This independent expert then carries out the requested tests and studies (Article 13.2b of the Directive; Rule 28(4) EPC). After the grant of the patent, the „expert solution“ is not applicable any more. The samples are only provided to third persons which have undertaken undertaken vis-à-vis the applicant for or proprietor of the patent not to make the biological material or any biological material derived therefrom available to any third party and to use that material for experimental purposes only (Article 13.3 of the Directive; Rule 28(3) EPC).

If the deposited material ceases to be available (if it has lost viability) the deposition has to be repeated again (Article 14 Directive; Rule 28a EPC).

Rule 28 EPC

Deposit of biological material

- (1) If an invention involves the use of or concerns biological material which is not available to the public and

which cannot be described in the European patent application in such a manner as to enable the invention to be carried out by a person skilled in the art, the invention shall only be regarded as being disclosed as prescribed in Article 83 if:

(a) a sample of the biological material has been deposited with a recognised depositary institution not later than the date of filing of the application;

(b) the application as filed gives such relevant information as is available to the applicant on the characteristics of the biological material;

(c) the depositary institution and the accession number of the deposited biological material are stated in the application, and

(d) where the biological material has been deposited by a person other than the applicant, the name and address of the depositor are stated in the application and a document is submitted satisfying the European Patent Office that the latter has authorised the applicant to refer to the deposited biological material in the application and has given his unreserved and irrevocable consent to the deposited material being made available to the public in accordance with this Rule.

(2) The information referred to in paragraph 1(c) and, where applicable, (d) may be submitted

(a) within a period of sixteen months after the date of filing of the application or, if priority is claimed, after the priority date, this time limit being deemed to have been met if the information is communicated before completion of the technical preparations for publication of the European patent application;

(b) up to the date of submission of a request for early publication of the application;

(c) within one month after the European Patent Office has communicated to the applicant that a right to inspect the files pursuant to Article 128, paragraph 2, exists.

The ruling period shall be the one which is the first to expire. The communication of this information shall be considered as constituting the unreserved and irrevocable consent of the applicant to the deposited biological material being made available to the public in accordance with this Rule.

(3) The deposited biological material shall be available upon request to any person from the date of publication of the European patent application and to any person having the right to inspect the files pursuant to Article 128, paragraph 2, prior to that date. Subject to paragraph 4, such availability shall be effected by the issue of a sample of the biological material to the person making the request (hereinafter referred to as “the requester”). Said issue shall be made only if the requester has undertaken vis-à-vis the applicant for or proprietor of the patent not to make the biological material or any biological material derived therefrom available to any third party and to use that material for experimental purposes only, until such time as the patent application is refused or withdrawn or deemed to be withdrawn, or before the

expiry of the patent in the designated State in which it last expires, unless the applicant for or proprietor of the patent expressly waives such an undertaking.

The undertaking to use the biological material for experimental purposes only shall not apply in so far as the requester is using that material under a compulsory licence. The term “compulsory licence” shall be construed as including *ex officio* licences and the right to use patented inventions in the public interest.

(4) Until completion of the technical preparations for publication of the application, the applicant may inform the European Patent Office that

- (a) until the publication of the mention of the grant of the European patent or, where applicable,
- (b) for twenty years from the date of filing if the application has been refused or withdrawn or deemed to be withdrawn,

the availability referred to in paragraph 3 shall be effected only by the issue of a sample to an expert nominated by the requester.

(5) The following may be nominated as an expert:

- (a) any natural person provided that the requester furnishes evidence, when filing the request, that the nomination has the approval of the applicant;
- (b) any natural person recognised as an expert by the President of the European Patent Office.

The nomination shall be accompanied by a declaration from the expert *vis-à-vis* the applicant in which he enters into the undertaking given pursuant to paragraph 3 until either the date on which the patent expires in all the designated States or, where the application has been refused, withdrawn or deemed to be withdrawn, until the date referred to in paragraph 4(b), the requester being regarded as a third party.

(6) For the purposes of paragraph 3, derived biological material shall mean any material which still exhibits those characteristics of the deposited material which are essential to carrying out the invention. The undertaking referred to in paragraph 3 shall not impede any deposit of derived biological material necessary for the purpose of patent procedure.

(7) The request provided for in paragraph 3 shall be submitted to the European Patent Office on a form recognised by that Office. The European Patent Office shall certify on the form that a European patent application referring to the deposit of the biological material has been filed, and that the requester or the expert nominated by him is entitled to the issue of a sample of that material. After grant of the European patent, the request shall also be submitted to the European Patent Office.

(8) The European Patent Office shall transmit a copy of the request, with the certification provided for in paragraph 7, to the depositary institution as well as to the applicant for or the proprietor of the patent.

(9) The President of the European Patent Office shall publish in the Official Journal of the European Patent Office the list of depositary institutions and experts

recognised for the purpose of this Rule.

Rule 28a EPC

New deposit of biological material

(1) If biological material deposited in accordance with Rule 28, paragraph 1, ceases to be available from the institution with which it was deposited because:

- (a) the biological material is no longer viable, or
- (b) for any other reason the depositary institution is unable to supply samples,

and if no sample of the biological material has been transferred to another depositary institution recognised for the purposes of Rule 28, from which it continues to be available, an interruption in availability shall be deemed not to have occurred if a new deposit of the biological material originally deposited is made within a period of three months from the date on which the depositor was notified of the interruption by the depositary institution and if a copy of the receipt of the deposit issued by the institution is forwarded to the European Patent Office within four months from the date of the new deposit stating the number of the application or of the European patent.

(2) In the case provided for in paragraph 1(a), the new deposit shall be made with the depositary institution with which the original deposit was made; in the cases provided for in paragraph 1(b), it may be made with another depositary institution recognised for the purposes of Rule 28.

(3) Where the institution with which the original deposit was made ceases to be recognised for the purposes of Rule 28, either entirely or for the kind of biological material to which the deposited sample belongs, or where that institution discontinues, temporarily or definitively, the performance of its functions as regards deposited biological material, and the notification referred to in paragraph 1 from the depositary institution is not received within six months from the date of such event, the three-month period referred to in paragraph 1 shall begin on the date on which this event is announced in the Official Journal of the European Patent Office.

(4) Any new deposit shall be accompanied by a statement signed by the depositor certifying that the newly deposited biological material is the same as that originally deposited.

(5) If the new deposit has been made under the provisions of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure of 28 April 1977, the provisions of that Treaty shall prevail.

further information : see EPO Guidelines, C-II, 6 (“Inventions relating to biological material”)

DIRECTIVE CHAPTER IV

Deposit, access and re-deposit of a biological material

Article 13

1. Where an invention involves the use of or concerns biological material which is not available to the public and which cannot be described in a patent application in such a manner as to enable the invention to be reproduced by a person skilled in the art, the description shall be considered inadequate for the purposes of patent law unless:

- (a) the biological material has been deposited no later than the date on which the patent application was filed with a recognised depository institution. At least the international depository authorities which acquired this status by virtue of Article 7 of the Budapest Treaty of 28 April 1977 on the international recognition of the deposit of micro-organisms for the purposes of patent procedure, hereinafter referred to as the 'Budapest Treaty', shall be recognised;
- (b) the application as filed contains such relevant information as is available to the applicant on the characteristics of the biological material deposited;
- (c) the patent application states the name of the depository institution and the accession number.

2. Access to the deposited biological material shall be provided through the supply of a sample:

- (a) up to the first publication of the patent application, only to those persons who are authorised under national patent law;
- (b) between the first publication of the application and the granting of the patent, to anyone requesting it or, if the applicant so requests, only to an independent expert;
- (c) after the patent has been granted, and notwithstanding revocation or cancellation of the patent, to anyone requesting it.

3. The sample shall be supplied only if the person requesting it undertakes, for the term during which the patent is in force:

- (a) not to make it or any material derived from it available to third parties; and
- (b) not to use it or any material derived from it except for experimental purposes, unless the applicant for or proprietor of the patent, as applicable, expressly waives such an undertaking.

4. At the applicant's request, where an application is refused or withdrawn, access to the deposited material shall be limited to an independent expert for 20 years from the date on which the patent application was filed. In that case, paragraph 3 shall apply.

5. The applicant's requests referred to in point (b) of

paragraph 2 and in paragraph 4 may only be made up to the date on which the technical preparations for publishing the patent application are deemed to have been completed.

Article 14

1. If the biological material deposited in accordance with Article 13 ceases to be available from the recognised depositary institution, a new deposit of the material shall be permitted on the same terms as those laid down in the Budapest Treaty.

2. Any new deposit shall be accompanied by a statement signed by the depositor certifying that the newly deposited biological material is the same as that originally deposited.

A further specificity of inventions concerning nucleic acid and polypeptide sequences is that patent applications which disclose such sequences have to contain a sequence listing (see Rule 27a EPC). This sequence listing has to be provided according to a certain standard (currently: WIPO Standard ST. 25) in written and in electronic form together with a statement that the information recorded on the data carrier is identical to the sequence listing. This electronic sequence listing is used by the examiners to search through their electronic sequence data libraries. The EPO has developed (together with the USPTO) a computer program called „PatentIn“ which is freely available and may be downloaded from the EPO home page.

CLARITY OF CLAIMS:

Due to the specificities of biotechnological inventions the wording of the claims for a given invention is very critical for providing an adequate protection for this invention. Although the flow of genetic information into polypeptidic structure is known in principle, many issues in this pathway may occur in the connection with certain inventions (e.g. post-translational modifications of the polypeptide, interaction with other polypeptides (or di- or multimerisation of the single polypeptide) to form active principle,...). Moreover, it is known that whereas it is possible to introduce even significant changes in some regions of a sequence without affecting the overall function to a major extent, minor changes in specific points of the sequences may indeed have significant impact on structure and function of a given polypeptide. Often, an invention, although being exemplified by a single experiment, has a large scope of application and may easily be specifically adjusted to many ways of performing the invention. Therefore, claims of biotechnological inventions usually contain a lot of so-called „functional language“, wherein the invention is – apart from the structural information given e.g. by a sequence – defined in a functional way. These circumstances can cause a lack of clarity of claims (see below), because Article 84 EPC stipulates that the claims must be clear and supported by the description.

Article 84 EPC

The claims

The claims shall define the matter for which protection is sought. They shall be clear and concise and be supported by the description.

INFORMED CONSENT:

The Directive also contains stipulations in its Recitals which address the question of informed consent. In Recital 26 it is mentioned that for inventions which are based on biological material of human origin an opportunity of expressing free and informed consent has to be given to the donor

of the material. According to Recital 27 information on the geographical origin should be added for inventions based on biological material of plant and animal origin, where appropriate.

(26) Whereas if an invention is based on biological material of human origin or if it uses such material, where a patent application is filed, the person from whose body the material is taken must have had an opportunity of expressing free and informed consent thereto, in accordance with national law;

(27) Whereas if an invention is based on biological material of plant or animal origin or if it uses such material, the patent application should, where appropriate, include information on the geographical origin of such material, if known; whereas this is without prejudice to the processing of patent applications or the validity of rights arising from granted patents;

The Directive does not address any sanctions for not complying with these stipulations, which are therefore to be treated according to national law. Non-compliance with these stipulations, however, should not lead to lack of patentability or lack of enforceability.

1.2. ECJ-Decision concerning the Directive (Case C-377/98)

Shortly after the issuance of the Directive, on 19 October 1998, NL filed an application for annulment of this Directive. By 3 May 1999 IT and NO intervened in support of NL. The application was based on six pleas:

a) that the Directive does not fall within the definition of measures for approximation of the provisions laid down by law, regulation or administrative action in Member States which have as their object the establishment and functioning of the internal market, and was incorrectly adopted on the basis of Article 100a of the Treaty

b) that the Directive breaches the principle of subsidiarity laid down by Article 3b of the EC Treaty (now Article 5 EC) and, in the alternative, that it does not state sufficient reasons to establish that this requirement was taken into account

c) that, rather than helping to remove the legal ambiguities described in the recitals, the Directive tends to exacerbate them, thus breaching the principle of legal certainty

d) that the obligations created by the Directive for Member States are incompatible with those resulting from their international undertakings, even though, according to Article 1(2) of the Directive, it does not affect obligations under international agreements, in particular, the Directive breaches the Agreement on TRIPs, the Agreement on Technical Barriers to Trade (the TBT Agreement), the EPC and the Convention on Biological Diversity (CBD),

e) that the patentability of isolated parts of the human body provided for by Article 5(2) of the Directive reduces living human matter to a means to an end, undermining human dignity and that the absence of a provision requiring verification of the consent of the donor or recipient of products obtained by biotechnological means undermines the right to self-determination,

f) that the Directive is vitiated by breach of procedural rules in that it gives no indication that the Commission's proposal was adopted by a college of members on the basis of a text available in all the official languages.

The ECJ in its final decision of 9 October 2001 followed the Opinion of the Advocate General of 14 June 2001 dismissed the application for annulment in all six points. Whereas the items a), b) and f) are of rather formal nature, the other items, especially items c) and e) relate to topics of particular practical interest for patenting biotechnological matter.

Item c)

With respect to the mentioned legal uncertainties, mainly two issues have been addressed by the NL: First, it was argued that the Directive gives the national authorities a discretion in applying concepts expressed in general and ambiguous terms, such as ordre public and morality which appear in Article 6 of the Directive. Second, it was asserted by the NL that there are unclear provisions whose relationship with one another is ambiguous existing side by side in the Directive, particularly as regards the patentability of plant varieties.

The ECJ stated that Article 6 of the Directive (which rules out the patentability of inventions whose commercial exploitation would be contrary to ordre public or morality) should – by its purpose allow the administrative authorities and courts of the Member States a wide scope for manoeuvre in applying this exclusion. Even though this issue is highly dependent on social and ethical questions which are changing in time, the ECJ acknowledges that the Directive limits the concepts in question, both by stating that commercial exploitation is not to be deemed to be contrary to ordre public or morality merely because it is prohibited by law or regulation, and by giving four examples of processes or uses which are not patentable. Thus, the ECJ followed that the Directive gives guidelines for applying the concepts at issue which do not otherwise exist in the general law on patents. Therefore the Directive lessens the legal uncertainty in this field of law rather than exacerbating them as alleged by the NL.

Item d)

With respect to the TRIPs agreement the NL argued under item d) that Article 27(3)(b) of the TRIPs Agreement allows Member States not to grant a patent for plants and animals other than micro-organisms, whereas the Directive does not allow Member States that possibility. The ECJ held that, while the Directive does deprive the Member States of the choice which the TRIPs Agreement offers the parties to that agreement as regards the patentability of plants and animals, the option taken in Article 4 of the Directive is in itself compatible with the Agreement, which, moreover, does not prevent certain party States adopting a common position with a view to its application. The joint selection of an option offered by an international instrument to which the Member States are parties was regarded by the ECJ as an act that falls within the approximation of laws provided for by Article 100a of the EC Treaty.

Regarding the TBT Agreement, the ECJ held that the Directive does not in any event contain any technical regulations within the meaning of the TBT Agreement, such a regulation being defined in Annex I to the WTO Agreement as a document which lays down product characteristics or their related processes and production methods. It was therefore regarded as not being necessary to rule on the extent to which the legal protection of biotechnological inventions might fall within the scope of the TBT Agreement.

Regarding the EPC it was first emphasized by the ECJ that the EPC does not create obligations for the EU, since it is not a party to it. The NL submitted that Article 6(1) of the Directive, which rules out the patentability of inventions “whose commercial exploitation would be contrary to ordre public or morality, is incompatible with Article 53 of the EPC, which excludes from patentability “inventions the publication or exploitation of which would be contrary to ordre public or morality. Although the ECJ noticed the difference in the terms used in the Directive and in the EPC, the ECJ held that the NL „in no way“ indicated in what respect the slightly different wording used by the Directive on that point, inspired by the wording of Article 27(3) of the TRIPs Agreement, requires Member States to breach their obligations under the EPC in order to comply with their obligations under the Directive. In the absence of specific examples to the contrary, it seemed reasonable to the ECJ to suppose that a breach of ordre public and morality as regards a specific invention could be equally well established by reference to its publication, exploitation or commercial exploitation.

Regarding the CBD, especially NO argued that the very purpose of the Directive, which is to make biotechnological inventions patentable in all the Member States, runs counter to the principle of equitable sharing of the benefits arising out of the utilization of genetic resources, which is one of the objectives of the CBD. Due to the hypothetical description of the potential risks and due to the fact that these risks are not regarded as being derived directly from the provisions of the Directive but, at the very most, from the use which might be made of them, the ECJ did not accept this argumentation. It was held that, in the absence of evidence, which was lacking in this case, it cannot be assumed that the mere protection of biotechnological inventions by patent would result in depriving developing countries of the ability to monitor their biological resources and to make use of their traditional knowledge, any more than it would result in promoting single-crop farming or in discouraging national and international efforts to preserve biodiversity. Moreover, in pointing to the objective of the CBD (the fair and equitable sharing of the benefits arising out of the utilization of genetic resources, including by appropriate access to genetic resources and by appropriate transfer of relevant technologies), the ECJ noted that the CBD specifies that this sharing of benefits must be done taking into account all rights over those resources and technologies. It was emphasized that there is no provision of the CBD which requires that the conditions for the grant of a patent for biotechnological inventions should include the consideration of the interests of the country from which the genetic resource originates or the existence of measures for transferring technology.

Item e)

Under this plea, the NL submitted that the patentability of isolated parts of the human body provided for by Article 5(2) of the Directive reduces living human matter to a means to an end, undermining human dignity, and that the absence of a provision requiring verification of the consent of the donor or recipient of products obtained by biotechnological means undermines the right to self-determination („informed consent“).

In analysing the question concerning respect for human dignity, the ECJ held that this is guaranteed in principle by Article 5(1) of the Directive which provides that the human body at the various stages of its formation and development cannot constitute a patentable invention. Moreover, it was pointed out that the elements of the human body are patentable in themselves and that their discovery cannot be the subject of protection. According to the Directive, only inventions which combine a natural element with a technical process enabling it to be isolated or produced for an industrial application can be the subject of an application for a patent. In pointing to the twentieth and twenty-first recitals of the preamble to the Directive, the ECJ stressed that an element of the human body may be part of a product which is patentable but it may not, in its natural environment, be appropriated. In applying this distinction to work on the sequence or partial sequence of human genes, the ECJ found that the result of such work can give rise to the grant of a patent only if the application is accompanied by both a description of the original method of sequencing which led to the invention and an explanation of the industrial application to which the work is to lead, as required by Article 5(3) of the Directive. In case of a mere discovery of a DNA sequence, which would not be patentable as such, there would be no invention.

It was confirmed that the protection envisaged by the Directive covers only the result of inventive, scientific or technical work, and extends to biological data existing in their natural state in human beings only where necessary for the achievement and exploitation of a particular industrial application. As an additional security the ECJ pointed to Article 6 of the Directive, which cites as contrary to ordre public and morality, and therefore excluded from patentability, processes for cloning human beings, processes for modifying the germ line genetic identity of human beings and uses of human embryos for industrial or commercial purposes. The thirty-eighth recital of the preamble to the Directive states that this list is not exhaustive and that all processes the use of which offend against human dignity are also excluded from patentability. According to the ECJ, it

is clear from those provisions that, as regards living matter of human origin, the Directive frames the law on patents in a manner sufficiently rigorous to ensure that the human body effectively remains unavailable and inalienable and that human dignity is thus safeguarded.

In analysing the question of free and informed consent of the donor and recipient, the ECJ argued that such reliance on this fundamental right was clearly misplaced as against a directive which concerns only the grant of patents and whose scope does not therefore extend to activities before and after that grant, whether they involve research or the use of the patented products. The ECJ held that the grant of a patent does not preclude legal limitations or prohibitions applying to research into patentable products or the exploitation of patented products, as the fourteenth recital of the preamble to the Directive points out. It was stated that the purpose of the Directive is not to replace the restrictive provisions which guarantee, outside the scope of the Directive, compliance with certain ethical rules which include the right to self-determination by informed consent.

2. The (current) European Practice

Although the EPO is not a patent office falling under the direct effect of the Directive, the EPO incorporated – as mentioned above – the main stipulations of the Directive in the Implementing Regulations of the EPC (the „Rules“ as Rules 23b-e.

The EPO has granted patents to nucleic acid sequences, polypeptides, vectors, cells, viruses and other biological material in the past (before the Directive). This practice was also accepted by the Technical Boards of Appeal in numerous decisions. Indeed, many aspects contained in these decisions of the EPO Boards of Appeal (BoA), including the Enlarged Board of Appeal (EBo), found their way into the Directive (e.g. T 19/90 concerning the „Oncomouse“ (Art.6.2.c and Art.4.2 of the Directive) or G1/98 (Art 4.2 of the Directive)).

PATENTABILITY

As mentioned above, patentability of biological inventions was accepted by the BoA already in decisions in the early 80ies (e.g. T 292/85 „Polypeptide expression/GENENTECH; OJ EPA 1989, 275); however, the question whether (human) DNA may be patentable in principle (either because this is intrinsically unethical or because this may be regarded as a discovery) was addressed in the „Relaxin“ decision (OJ EPO 1995, 388). This is a decision from the Opposition Division (OD) of the EPO concerning a patent which relates to the DNA of relaxin, a polypeptide which is present in serum of pregnant women and is responsible for raising the flexibility (i.e. relaxing) of the pubic bone joint thereby allowing shorter birth times and lesser stillbirths. It is clear that providing relaxin as a drug is highly efficient for pregnant women having too low or missing relaxin concentrations in their blood.

Members of the Green Fraction of the European Parliament have filed an opposition against this patent claiming that this patent is unethical (because in the course of delivering the DNA sequence of Relaxin, tissue samples had to be taken from a pregnant woman) and that – in general – the DNA of a given polypeptide is already present in nature and the delivery thereof only a discovery, which is per se unpatentable.

In its decision, the opposition division made it clear that

- *a DNA fragment encoding a human protein does not lack novelty by virtue of having been always present in the human body;*
- *isolation and characterisation of such a DNA fragment does not represent a discovery; and*
- *the isolation of mRNA encoding a human protein from human tissue is not immoral or intrinsically unethical, nor is the patenting of a DNA fragment.*

The decision is currently under appeal (the opponents filed a rather chaotic appeal and the EBo first had to resolve the formal issue whether an appeal (or an opposition) can be filed jointly by more than one person, the group of persons forming one party to the proceedings; this was accepted by the EBo in G3/99 (OJ EPO 2002, 347)).

The decisions of the EPO senates also clarified that living matter is not generally excluded from patentability:

“No general exclusion of inventions in the sphere of animate nature can be inferred from the EPC” (T 49/83 Propagating material/CIBA-GEIGY; OJ EPO 1984, 112

Specifically to the exclusion of plant and animal varieties the EBoA clearly stated in G1/98 (OJ EPO 2000, 111):

„A claim wherein specific plant varieties are not individually claimed is not excluded from patentability under Article 53b EPC, even though it may embrace plant varieties.“

NOVELTY

The BoA has followed the novelty assessments of the RELAXIN decision in that a DNA fragment encoding a human protein or the protein itself do not lack novelty by virtue of having been always present in the human body. However, when the claim relates to a DNA molecule or a polypeptide, produced and used in a recombinant environment, where the protein was known from biochemical isolation and characterisation, the BoA accept novelty only if the claimed recombinant product has at least one (significant) structural difference compared to the natural product described in the art. In this connection it is important to point out that one cannot obtain a patent on something that is known in the prior art, just because one explicitly states a feature in the claims which was previously unappreciated, unstated or even unknown (e.g. the formula or a biological activity of a known protein). In order to be novelty-destroying, a prior art document has to contain “a clear and unmistakable disclosure for the skilled person of the subject-matter of a claim in question”. Novelty assessment “requires consideration of both the explicit and implicit disclosure of the document. However, there must be no doubt that the prior disclosure, as read by the skilled person, unambiguously corresponds in all its technical features to the subject-matter as claimed” (T 838/97 Translational inhibition/RESEARCH FOUNDATION). In assessing novelty in practice the EPO uses the “photographic novelty approach” (although this is often disputed by the EPO). Therefore, the difference in only one nucleotide or amino acid residue is sufficient to establish novelty, see e.g. T 886/91 Hepatitis B virus/BIOGEN, wherein one of the opponents argued that the claimed DNA and amino acid sequences of a HBV serotype were anticipated by the sequences of a different serotype reported in the prior art which sequences “did not substantially differ” from the claimed sequences and “no special technical effect was shown to be linked to the reported differences”. The Board, however, did not share this opinion of the opponent:

“None of the said documents discloses sequences or fragments thereof identical with those recited in the claims at issue. The argument propounded by Appellant V that, in view of the particular nature of the field, small differences in a sequence are not sufficient to confer novelty cannot be accepted by the Board as it is well known that even a change in one amino acid can dramatically change the properties of a protein molecule.

The argument put forward by the Intervener that novelty of the claims under consideration should be affected because a comparison of the known sequences with the claimed sequences shows that they contain identical stretches is, in the Board’s opinion, merely theoretical because none of the cited documents discloses or suggests any discrete fragment of the reported sequences as an identifiable entity which could be used for a comparison.”

It was also accepted that the existence of DNA molecules containing Interferon-alpha encoding DNA sequences in a genomic DNA library which comprises size-fractionated fragments of fetal human chromosomal DNA in a phage vector does not anticipate a claim to these specific recombinant DNA molecules (T 301/87 Alpha-interferon/BIOGEN), because the mere existence of this library does not make the sequence encoding alpha-interferon available. Whether this may also be the case for an “electronic” DNA sequence library, wherein only raw sequences are contained, remains to be clarified by the BoA.

If a comparison between the prior art and the claims results in novel structural features, novelty is accepted by the BoA:

For example, in the decision T 656/94 Colony-stimulating factor/KIRIN-AMGEN” the BoA has e.g. accepted novelty of a claim drawn to

”1. An isolated polypeptide consisting only of part or all of the amino acid sequence 1-174 set forth in Table VII which:

- (a) has one or more of the biological properties typical of naturally-occurring human pluripotent granulocyte colony-stimulating factor (hpG-CSF) of the sequence set forth in Table VII,*
- (b) is a non-naturally occurring polypeptide; and*
- (c) is the product of procaryotic or eucaryotic expression of an exogenous DNA sequence.”*

as novel over a method for producing hpG-CSF from conditioned medium of a bladder carcinoma cell line or from CHU cells. It was the Board’s judgement in this special case that the known “natural” hpG-CSF always occurs as a mixture of polypeptides having 174 and 177 amino acids, whereas the recombinant form for which protection was sought for comprises only the 174 amino acid species. It were the features”isolated” and “only” which were highlighted in this connection by the Board. The Board was left in “serious doubt as to the alleged identity of the products of the prior art with the claimed products” (the opponents did not provide convincing (experimental) proofs to the contrary.

In T 767/95 Interleukin 1/IMMUNEX CORPORATION the claim

- ”1. A protein composition consisting essentially of human interleukin-1 having*
- a. a molecular weight of about 17,500 daltons as determined by SDS-PAGE;*
 - b. a pI of about 5.9-6.3 when solubilised in a buffer comprising 2% (w/v) SDS and 2% (v/v) 2-mercapto-ethanol prior to electrophoresis; and*
 - c. an amino acid sequence comprising the series Ser-Leu-Val-Met-Ser-Gly-Pro-Tyr-Glu-Leu-Lys-Ala-Leu- His-Leu-Gln-Gly-Gln-Asp-Met-Glu-Gln-Gln-Val-Val-Phe near the N-terminal portion of the protein, wherein said protein composition is detected as a single band by SDS-PAGE and silver staining, and is sufficiently homogeneous to have the above noted amino acid sequence determined by Edman degradation.”*

was regarded as novel over prior art identifying a preparation with a molecular weight of 15 ,000 daltons (or 12,300 daltons, respectively in the BoA’s interpretation) and the figures in the prior art “suggesting” (BoA) a mixture of proteins rather than a homogenous preparation of a single polypeptide species. Although the opponents (as appellants) argued that the degree of purification of the prior art was high enough to allow amino acid sequencing, the BoA held:

“8. The appellant submits that the claimed protein is no more purified than the protein disclosed in document (1). In support of his proposition, arguments are provided inter alia about a peer review of the manuscript underlying document (9) by a respondent’s scientist. In the board’s judgement, however, it is the appellant who carries the burden of proof regarding facts barring patentability. Since the appellant failed to provide any corroborating evidence, these unsubstantiated allegations must be disregarded and the patent proprietor has to be given the benefit of doubt.”

In a highly competitive field with a significant amount of academic players, such as biotechnology and genetic engineering, disclosures of the invention before the priority (or filing) date are often a critical issue. A publication of the invention in the prior art is, however only regarded as novelty or inventiveness destroying if it contains an enabling disclosure, i.e. if the skilled man in the art got enough information from this publication to work the invention and if the publication was public, i.e. if the potential addressees of this publication are not required to keep this information secret. This is especially in cases of oral disclosures difficult to prove.

In T 838/97 Translational inhibition/RESEARCH FOUNDATION the BoA held that any information presented at a Gordon Research Conference cannot be regarded as public disclosure:

“In the board's judgment, since the purpose of the Gordon Research Conferences is to encourage free, informal and open discussion exclusively on the latest developments among scientists from various institutions and laboratories, the restrictions which the participants are invited to accept upon registration cannot be narrowly interpreted as being limited to printed references, but have to be understood as meaning that any information presented at a Gordon Research Conference, whether in a formal talk, poster session or discussion, amounts to a private communication from the individual making the contribution and is presented with the restriction that such information is not for public use. Otherwise, the stated purpose of the conferences would fail.”

In proving the content of an oral presentation, even a statement by the presenter (in the present case “Dr. Shulman”) may not be convincing enough to the BoA, as held in T 400/97 Immunoglobulins/CELLTECH. Therein the BoA stated that

“ For the evidence to be regarded as safe and satisfactory, it must unequivocally relate to what was made available to the public at the lecture. This is not a matter which this Board considers capable of being put beyond reasonable doubt by any evidence of the lecturer alone. The lecturer will have had the knowledge prior to the lecture, and will have prepared the lecture. His or her knowledge will not change as a result of the lecture, that of the audience may. The lecturer's evidence can be taken as defining the maximum amount of knowledge that may have been conveyed to the audience, but cannot be relied on to establish even what minimum of new knowledge was necessarily conveyed to the audience. The lecturer is in a quite different position to a member of the audience, and evidence of the lecturer's intentions or impression as to what was conveyed to the audience cannot even be treated as making out a prima facie case that such information was actually made available to the public, certainly as regards to information which would have been new to the audience. Here the Board's approach differs completely from that of the Opposition Division who accepted the lecturer's evidence by itself as sufficient. This approach is also the reason why the Board declined to hear Dr. Shulman at the oral proceedings before it, as further evidence from him would not serve to make up for the lack of evidence from the audience..”

The BoA then sketches the kind of proof which would have been regarded as being acceptable and recommended especially written documents, such as handouts, scripts etc.:

“What evidence can be regarded as safely and satisfactorily establishing the information content made publicly available by a lecture will necessarily have to be judged on a case by case basis. Account must be taken of the fact that a lecture is ephemeral, so that the manner or speed of presentation may affect the comprehensibility of a lecture. Even an audio or video tape recording made of the lecture (unless themselves publicly available) would have to be treated with caution if several hearings or viewings are necessary to extract all information. Information appearing in

each of the contemporary written notes made at the lecture by at least two members of the audience can usually be regarded as sufficient, whereas information in the notes of a single member of the audience might be inadequate as reflecting the thoughts of the listener rather than solely the content of the lecture.

If the lecturer read his lecture from a typescript or manuscript, or the lecturer wrote up his lecture subsequently, and the lecture was subsequently published in this form as part of the proceedings, then the written version might be taken as some evidence of the contents of the lecture, though with some caution as there would be no guarantee that a script was completely and comprehensibly read, or that a write-up was not amplified (compare decision T 890/96, supra). Most useful would be a handout given to the public at the lecture, containing a summary of the most important parts of the lecture and copies of the slides shown.

None of these types of evidence are available for Dr Shulman's lecture: he did not prepare a complete script, no hand-out of the contents was made, and Dr Shulman did not write up his lecture and there was no subsequent publication of specifically this lecture."

The date of entry of data into a public data base may also be difficult to prove for relying on this entry as prior art. In T 91/98 Antiviral nucleosides/WELLCOME the problems associated therewith were addressed. In this case a document (document (8)) from the Lexis-Nexis data base was cited as prior art. The document was printed out in 1996, ie some ten years after the filing date of the patent in suit, 14.3.86, claiming priorities from 16.3.85. The heading of this entry reads: "10th Story of Level 1 printed in Full format. Copyright 1985 U.P.I. September 3, 1985, Tuesday AM cycle". This latter date, so the BoA, cannot be equated to the distribution date of the information and need not even be right. In trying to prove the availability date of this data base entry, the Respondents submitted several declarations, affidavits and letters that this document (8) must have been available to the public shortly after the 3 September 1985. Even the managing Editor of United Press International (U.P.I.) certified "that to the best of my knowledge, the Nexus copy of the UPI story dated Sep.3, 1985, is a true and accurate copy of the story UPI moved at that time". This, however, stil was not sufficient to convince the Board "beyond reasonable doubt":

"In the Board's judgment, this statement does not amount to a clear and unequivocal statement that the information contained in document (8) was then available to the public because it is impossible to understand what kind of action the term "moved at that time" might involve. Furthermore, there is no indication why the managing director on August 27, 1997, the date of his letter, can exactly remember the story moved at that time ie twelve years before. He gives no explanations having special circumstances to remember that very article or having found a record of the article and the date of publication in the archives of UPI. The Board is convinced that the testimony in this letter is only influenced by the date written in document (8) and is not based on true recollection. Therefore, the expression in the said letter "to my best knowledge" is merely relative and cannot be considered as a factual argument."

The Board concluded that the date at which the information contained in document (8) was made available to the public cannot be unambiguously defined and, that, in consequence, this document cannot be taken into consideration to evaluate inventive step.

CLAIMING PRIORITY

Inventions in the field of biotechnology are often made in a highly competitive environment with a high pressure for fast patenting and fast publication. In many cases, an international or European application is based on a series of priority applications. The valid claiming of priorities is often necessary to exclude publications of the invention within the priority interval from the state of the art. The European practice with respect to validly claiming priority is rather strict; according to the decision of the EBo G 2/98 Requirement for claiming priority of the "same invention" ;OJ EPO 2001, 413, it was held:

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

The requirement that the claimed subject matter is "directly and unambiguously" disclosed in the priority application may be difficult to fulfil, if the invention was defined in a (slightly) different way in the priority-claiming application than in the priority application. Care should therefore be taken with publications of the invention in the priority interval, especially for ongoing projects, for which additional data are generated in this interval which may lead to a re-definition (broadening, precision, alternative definition) of the invention.

INVENTIVE STEP

As for all other inventions the EPO also bases the assessment of inventive step on the so-called "problem-solution-approach" as outlined in the EPO guidelines C-IV, 9.5.: When assessing inventive step the examiner has first to determine the closest prior art, i.e. that combination of features derivable from one single reference that provides the best basis for considering the question of obviousness, and to define the difference between the claimed invention and the closest prior art. Second, the "objective" technical problem to be solved by the invention has to be established and it has to be clarified whether the claimed invention solves this technical problem. Third, it has to be considered whether or not the claimed invention, starting from the closest prior art and the technical problem, would have been obvious to the skilled person. The general standard is to investigate whether it was obvious to try the claimed subject matter with a reasonable expectation of success (T 60/89 Fusion proteins/HARVARD; OJ EPO 1992, 268). Thereby it is not sufficient if the skilled person "could" have applied the known teaching, but that it is necessary to show why a person "would" have applied the teaching to be examined (T 2/83 Simethicon tablet/RIDER; OJ EPO 1984, 265).

In showing non-obviousness of biotechnological inventions it is possible to rely on actual difficulties or uncertainties in arriving at the invention, e.g. in cloning the claimed DNA. In doing so it is not sufficient to address potential or hypothetical problems, it is necessary to prove the actual difficulties and that it needed an inventive step to overcome them.

Another successful strategy may be based on unexpected results, e.g. if the cloned protein has unexpected superior properties or if the combination of features show synergistic results.

Other points to be addressed: was there a technical prejudice in the prior art? Was the invention more than an obvious selection or an obvious combination of features? etc.

Since the argumentation concerning inventive step is almost always drawn to the specific case, a

comprehensive discussion of case law is not provided here. As illustrative examples the following decisions of the BoA are cited: T 301/87 Alpha-interferon/BIOGEN, OJ EPO 1990, 335; T 412/93 Erythropoietin/AMGEN; T 60/89 Fusion proteins/HARVARD; OJ EPO 1992, 268; T 886/91 Hepatitis B virus/BIOGEN; T 906/91 Monoclonal antibody to theophylline/DUPONT.

A recently published decision of the OD of the EPO, however, should be discussed here. The decision's headword was "Novel V28 seven transmembrane receptor" (OJ EPO 2002, 293). The decision is remarkable for many reasons, one of them is that this decision reflects the official or unofficial position of the EPO with respect to "genomics based inventions" (this position is also reflected in an Article of S. Yeats (Director, biotechnology examination and opposition, EPO) in "Global Patent Management" (October 2001), pages 30-32).

According to this opinion, a patent application containing the DNA or polypeptide sequence and an assigned function (on the basis of bioinformatic data) unaccompanied by any supporting experimental (i.e. wet biochemistry) data gives rise to an objection of lack of inventive step. The current view at the EPO is that it is a priori obvious to try to isolate DNAs by standard methods and that there is a reasonable chance of success of obtaining a huge number of random DNA sequences. In order to be patentable, a selection of chemical compounds must not be arbitrary but rather justified by a previously unknown technical effect resulting from the particular structural features distinguishing the numerous other non-selected ones (hereby, the EPO officials cite T 939/92 Triazoles/AGREVO, OJ EPO 1996, 309, which is drawn to triazole sulphonamides of a given formula).

Although bioinformatic data and tools are regarded as highly effective and successful in scientific applications, it is the EPO's position that such computer assisted putative function assignments are generally to be regarded as speculative and not suitable to support an inventive step. Whereas this may be plausible for applications which contain a lengthy list of suggested uses, this seems to be unfair in cases where a specific function was correctly predicted by in silico methods and afterwards (i.e. during examination proceedings) confirmed by wet biochemistry experimental data. However, whether the latter may be sufficient, has to be clarified by the BoA (indeed, the "Novel V28 seven transmembrane receptor" is currently under appeal).

In this "Novel V28 seven transmembrane receptor", a patent was granted with a claim 1 relating to a purified and isolated polynucleotide encoding the amino acid sequence of V28 seven transmembrane receptor set out in SEQ ID NO:28 or a fragment thereof possessing at least one ligand/antiligand binding activity or immunological property specific to said V28 seven transmembrane receptor.

Seven transmembrane receptors (7TMRs) form a superfamily of proteins which are also known as G-protein coupled receptors (GPRs). A document of the prior art for the patent for the novel V28 TMR disclosed (as a review article) 74 proteins which belong to this superfamily. This document discloses structural features of these proteins including regions of high homology shared among all members of the family, ligand binding domains and signal transduction coupling.

The specification of the patent in question disclosed a genomic and a cDNA clone encoding the novel V28 7TMR. The deduced amino acid sequence predicts a structure comprising seven (transmembrane) hydrophilic domains separated by hydrophilic domains and amino acid residues which are conserved within a group of proteins – the 7TMR superfamily. Several methods to identify extracellular and intracellular ligands for V28 7TMR are described, no results of such methods are described.

Following the "problem-solution-approach" the OD formulated the problem to be solved as the provision of the nucleotide sequence encoding an additional 7TMR protein which is predicted to function as a receptor. The subject matter of claim 1 was regarded as solving this invention,

however, this solution was not considered to be inventive:

“This solution cannot be considered to be inventive because document D1 provides a sequence alignment of 74 known 7TM receptors, including IL8 receptor and AT2 receptor, and indicates that sequence similarity is useful in designing cloning strategies for other GPRs (page 1). Similarly, document D5 discloses cloning strategies that led to the identification of 17 different receptors of the 7TM family and refers to the use of degenerate primers in a PCR-based cloning procedure (page 4). Document D2 discloses a procedure whereby degenerate PCR primers are designed so as to identify and amplify receptors of the 7TM family (Figure 1). Therefore, the existence of additional 7TM receptors was predicted in the prior art and the procedure for the identification of said additional members of 7TM receptor family has been well established. Consequently, the disclosure of the primary structure of an additional 7TM protein which is arrived at by following the well established methods disclosed in the prior art is not considered inventive and fails the requirements of Article 56 EPC.”

„The opposition division agrees with the view of opponent 1 that V28 clone represents an arbitrary choice from seven clones identified (V31, V28, V112, R20, RM3, R2, R12, examples 1–11 of the specification), thus, indicating that the conditions were not optimised in any way to identifying V28 clone specifically. More significantly, the difficulty involved in the choice of conditions would support an inventive step argument directed to a method for the identification of 7TM proteins which is not the subject-matter of the present claim.”

It will be interesting to see how the BoA will examine this case, especially in view of the fact that for inventions in other fields of technology it is always necessary to show that it was obvious to try any combined teaching of the prior art with a reasonable expectation of success, i.e. that the opponent (or in examination proceedings: the EPO) has to show that it was obvious to try to provide such alternative molecules and that it was possible to identify them with a reasonable expectation of success. If this general route is followed also in the case of genomic inventions as for the present case it is therefore necessary to show that the skilled artisan had an incentive to look for new family members of the 7TMR family. In this connection it is important to note that the „hope to succeed“ may not be confused with the „reasonable expectation of success“.

INDUSTRIAL APPLICATION

Industrial applicability is not a real issue for other fields of inventions than biotechnology (apart from the exclusion of therapeutical, surgical and diagnostical methods performed on the human or animal body according to Art. 52(4) EPC). This patentability criterion does not impose any problems for non-biotech inventions. For biotechnological inventions, however, the Directive has stipulated additional prerequisites for acknowledging industrial applicability (see above): first, the industrial application of a sequence or a partial sequence of a gene must be (explicitly) disclosed in the patent application and second, the necessity of specifying the “function” of the protein (or its part) in the application.

The practice at the EPO does even go at least one step further, as also outlined in the above mentioned article of Yeats: Although it is accepted that Art. 57 EPC simply asserts that an invention has industrial application if it can be made or used in any kind of industry and that this is certainly always possible for DNA, this is – according to EPO’s opinion – inappropriate, because DNAs and proteins are, as natural products, almost always prepared by routine methods. A more “meaningful” approach for the EPO is “to assume that a concrete use of a gene sequence is necessary”, i.e. that “the patent application should propose a particular means of putting the sequence to commercial use”. According to the EPO, the “assignment of a biological function can

serve as an industrial application only if it points to a practical use of the sequence, since it could otherwise not be used in any kind of industry”. This means that for example the tentative characterisation of a DNA as encoding an orphan receptor (i.e. a receptor for which a ligand is not yet known) does not suffice, because it is not apparent how this function can be put to use if the receptor ligand is unknown. The EPO requires the patent application to “contain enough data to provide a sound prediction of the intended use”. In this connection it is remarkable that the EPO position is that “additional data submitted at a later date will be accepted only in support of the original disclosure, not as a substitute for it”.

This opinion is exemplified in the “Novel V28 seven transmembrane receptor” decision of the OD: In relying on the aforementioned opinion of EPO on industrial applicability the opponents argued that the claimed novel V28 7TMR lacks this patentability requirement, because the patent does not contain any experimental data supporting the disclosed uses in the patent which were proposed based on computer predictions. These potential uses have been regarded as “speculative, i.e. are not specific, substantial and credible” by the OD. The headnote contains the following conclusion:

“A list, in the description, of speculative functions of a protein is not in itself a reliable basis for acknowledging industrial application of this protein. A DNA sequence encoding a protein without a credible function is not a patentable invention.”

It is therefore necessary for fulfilling this requirement to provide “credible” function in the description showing “real world” industrial applicability (“utility” ??), i.e. an individual credible function (activity) of the polypeptide encoded by the DNA. Of course the best way to provide such credible individual data is to present experimental (wet biochemistry) data in the application as filed. This, however, is not a trivial task, if the polypeptide has been only predicted on the basis of isolated DNA.

ENABLING DISCLOSURE

Sufficiency of disclosure is one of the major issues for biotechnological inventions due to the complexity and potential unpredictability of biological systems. In order to comply with this patentability requirement the description has to provide enough information to enable the skilled reader to put the claimed invention into practice without undue burden and without needing inventive skill. The scope of a granted patent should correspond to its technical contribution to the state of the art. Claims may therefore not be considered as allowable if they encompass subject matter which can be performed only with undue burden or application of inventive skill. The guiding principle is always that the skilled person, having read the description, should be able to readily perform the invention over the whole area claimed (leading cases: T 409/91 Fuel oils/EXXON, OJ EPO 1994, 653 and T 435/91 Detergents/UNILEVER, OJ EPO 1995, 188).

It follows that although in certain cases one example may be sufficient to support broad claims with functionally defined features, this may be rather the exception for meeting the enabling disclosure requirement. Therefore it is necessary to provide enough examples in the application for demonstrating that the claimed invention is enabled over the whole scope of the claims.

For defining the subject matter of a biotechnological invention it is often necessary to rely on functional terminology for receiving appropriate protection. This means that besides structural (physical) features, such as DNA or amino acid sequences, qualitative features, such as a certain activity or affinity, are present in the claims, if such features cannot otherwise be defined more precisely without restricting the scope of the invention and if their reduction to practice is not an undue burden. The leading case in this respect is T 292/85 Polypeptide expression/GENENTECH, OJ EPO 1989, 275:

“The suggested features in the claims are essentially functional terms in this particular context, in spite of structural connotations, and may cover an unlimited number of possibilities. It follows that the features may generically embrace the use of unknown or not yet envisaged possibilities, including specific variants which might be provided or invented in the future. This Board concurs with the decision of another Board (T 68/85 -3.3.1., "Synergistic herbicides", OJ EPO 1987, 228) in which the possibility of using functional terminology in claims was approved if "such features cannot otherwise be defined more precisely without restricting the scope of the invention" and their reduction to practice was not an undue burden. The Board sees no valid reason why this should not be equally true for the field of biotechnology as in other fields of technology. In appropriate cases, such as the present, it is only possible to define the invention (the matter for which protection is sought – Article 84 EPC) in a way which gives a fair protection having regard to the nature of the invention which has been described, by using functional terminology in the claims.

What is also important in the present case is the irrelevancy of the particular choice of a variant within the functional terms "bacteria", "regulon" or "plasmid". It is not just that some result within the range of polypeptides is obtained in each case but it is the same polypeptide which is expressed, independent of the choice of these means. A term of this kind must, of course, be clear and enable the skilled person to find suitable specimens without undue difficulty. In the present application enough choice is available, although some vehicles and hosts are preferred for practical reasons.

The objection raised against the terms "plasmid" and "bacteria" that they are too broad since some of them rely on yet unavailable entities is untenable.

The Board is of the opinion that this is quite normal practice in many technical fields where terms as "carriers", "resilient means", or "amplifying means" are commonplace and embrace new components, be they inventive or not. This is not to mention that very often the generic indication of a kind of an article in the claim is followed by the non-exclusive term "comprising" and the characteristics of modifying features, leaving completely open the actual features of the rest of the article, apart from the necessity that its functioning should be as expected.

The above examples show that the need for a fair protection governs both the considerations of the scope of claims and of the requirements for sufficient disclosure. Unless variants of components are also embraced in the claims, which are, now or later on, equally suitable to achieve the same effect in a manner which could not have been envisaged without the invention, the protection provided by the patent would be ineffectual.

Thus it is the view of the Board that an invention is sufficiently disclosed if at least one way is clearly indicated enabling the skilled person to carry out the invention. Consequently, any non-availability of some particular variants of a functionally defined component feature of the invention is immaterial to sufficiency as long as there are suitable variants known to the skilled person through the disclosure or common general knowledge, which provide the same effect for the invention. The disclosure need not include specific instructions as to how all possible component variants within the functional definition should be obtained.”

With respect to potential inoperable variants of a functionally defined feature, the Board, in addressing this question, concludes:

“Whilst the Board is satisfied that there are sufficient choices of bacteria available, and that there might be more suggested in the future, the question of non-operability of some bacterial variants may arise. Whilst there is so far no reason to doubt that homologous regulons would also reliably work in the microbial environment

of their origin, the term "bacteria" might include inherently inoperable species or variants. However, the main claim refers to a "suitable bacterium", and Claim 10 to a bacterium transformed with the claimed plasmids, which in any case imply to the skilled reader that this should be a bacterium in which the homologous regulon is "at home" and can be operative. In addition, the bacteria to be used may be modified to enhance their suitability. Whilst such express or implied functional limitations are acceptable in the present application, since the applicability of the method to any kinds or most species of bacteria has not been effectively challenged, this may not be the case if the skilled person cannot easily find his way to put the invention into effect, for instance with the specially recommended bacteria or plasmids. It is, therefore, also the view of the Board that the unsuitability of some unspecified particular variants of a functionally defined component feature of the invention is immaterial as long as there are suitable variants known to the skilled person through the disclosure or common general knowledge which provide the same effect for the invention.

The burden of finding workable candidates is related to the relevance of such functional feature to the inventive step, i.e. its essentiality to the quality or quantity of the effect obtained and thereby to its distinguishing power against the relevant prior art. Some features may contribute to the core of the invention and others only assist their use, and the skilled person might, therefore, be in a more difficult or an easier position to find suitable choices. For instance, bacteria themselves only enter a further, dependent aspect of the invention (Claim 10). In view of the supplementary role of bacteria as housings for expression and of the general character of the term representing a further restriction of the claim in question, it would also be unreasonable to impose an additional limitation to its scope for the reason alone that some of the specimen may not be suitable at all."

In T 301/87 Alpha-interferon/BIOGEN OJ EPO 1990, 335, the BoA mentioned that the "requirement for sufficiency is not a matter of satisfying the perfectionist but to enable the skilled person to handle the invention in normal practice".

In T19/90 Oncomouse/HARVARD OJ EPO 1990, 476, the Board further held that "the mere fact that a claim is broad is not itself a ground for considering the application as not complying with the requirements for sufficient disclosure under Art. 83 EPC. Only if there are serious doubts, substantiated by verifiable facts, may an application be objected to for lack of sufficient disclosure.

Sufficiency of disclosure is always connected to reproducibility of the invention. This does not necessarily have to be an exact reproducibility of the given example. In T 281/86 Preprothaumatin/UNILEVER OJ EPO 1989, 202, the Board reasoned:

"It is always the case in chemistry that the outcome of experiments show some fluctuations in yield, quality etc. This is irrelevant for sufficiency unless the invention requires certain characteristics in this respect. It should therefore be even less relevant if only the conditions and the means used to carry out a process show inevitable variations as long as the ultimate result is the same.

It is therefore the view of the Board that there is no requirement under Article 83 EPC to the effect that a specifically described example of a process must be exactly repeatable. Variations in the constitution of an agent used in a process are immaterial to the sufficiency of the disclosure provided the claimed process reliably leads to the desired product. As long as the description of the process is sufficiently clear and complete, i.e. the claimed process reliably leads to the desired product."

It is important to note that for assessing inventive step and sufficient disclosure for the same invention, the same level of skill has to be considered. Factors which may contribute to an undue burden are e.g. experimental uncertainties (T 187/93 Vaccines/GENENTECH), incomplete

guidance, including wrong references, in the specification (T 639/95 Biopolymers/MIT) or if scientific research is necessary in order to carry out the invention in some areas claimed (T 694/92 Modifying plant cells/MYCOGEN; OJ EPO 1997, 408).

The last point is specifically important for “reach-through” claims to antagonists and ligands obtained e.g. by performing claimed screening processes. These ligands are then characterised in the claims by defining them via the screening process. Since these “reach-through” claims are generally not accompanied by a structural definition of the resulting products (if these products were known, they could be directly claimed instead of defining them by the screening process), they generally fail the enabling disclosure requirement. This question has also been addressed in the “Novel V28 seven transmembrane receptor” decision of the OD insofar that although the claimed molecule was identified as a receptor, the specification did not contain a specific example for such a V28 7TMR ligand. Although the specification contained several methods how such a ligand may be identified, the OD concluded that “this undertaking constitutes an undue burden for the skilled person seeking to perform the claimed invention”. In this case, the first document wherein a receptor function was reported for the V28 7TMR was published three years after the publication of the application.

Another leading case with respect to sufficient disclosure is T 188/97 NANBV/CHIRON CORPORATION. In this decision, the BoA examined the enablement requirement for claims drawn to inventions concerning the Hepatitis C Virus (HCV; old name: Hepatitis non-A, non-B Virus (NANBV)). The genome of the virus (about 10kb) codes for a large polypeptide, which is expressed as a whole and then processed to several structural and non-structural viral polypeptides. The patent in question disclosed the exact nucleic acid sequence of 77 % of the genome of one HCV strain; the 5' part of the genome was not sequenced but was also contained in deposited clones. One of the claims to be examined read:

“31. A polynucleotide in substantially isolated form comprising a contiguous sequence of nucleotides which is capable of selectively hybridising to the genome of hepatitis C virus (HCV) or the complement thereof, wherein HCV is characterized by:
a positive stranded RNA genome;
said genome comprising an open reading frame (ORF) encoding a polyprotein; and the entirety of the said polyprotein having at least 40% homology to the entire polyprotein of a viral isolate from the genome of which was prepared cDNAs deposited in a lambda gt-11 cDNA library with the American Type Culture Collection (ATCC) under accession n. 40394.”

This claim therefore encompassed all polynucleotides of any HCV virus subtype. It had therefore to be decided whether the disclosure enables the isolation and characterisation of the rest (the 5' 23 %) of the genome of this specific HCV strain and the whole genome of other HCV variants.

Since the method of genome walking is explained and exemplified in the specification and the cDNA was deposited, the Board concluded “that the skilled person had at her/his disposal the tools necessary to carry out genome walking over the whole length of the genome and that enough technical information was made available to carry out said method.” The Board further concluded “that the skilled person could have isolated the whole of the HCV genome without undue burden or exercise of inventive skills.”

In relying on T 412/93 Erythropoietin/AMGEN the Board accepted that much time and effort may be requested to obtain the complete sequence of the HCV and to isolate further HCV genomes. However, since the sequences of probes and primers for these tasks are disclosed in the patent in suit, this time and effort will be spent in the framework of routine experimentation. The board

therefore concluded that no undue burden or exercise of inventive skill is involved and accepted claim 31 with respect to Art. 83 EPC.

The main claim with respect to the polypeptides derived from these polynucleotides read as follows:

*"1. A polypeptide in substantially isolated form comprising a contiguous sequence of at least 10 amino acids encoded by the genome of hepatitis C virus (HCV) and comprising an HCV antigenic determinant wherein HCV is characterized by:
a positive stranded RNA genome;
said genome comprising an open reading frame (ORF) encoding a polyprotein; and the entirety of the said polyprotein having at least 40% homology to the entire polyprotein of a viral isolate from the genome of which was prepared cDNAs deposited in a lambda gt-11 cDNA library with the American Type Culture Collection (ATCC) under accession n. 40394."*

This claim comprises any antigenic polypeptide, be it natural or obtained by chemical synthesis or by expression in a recombinant organism, from polypeptides of all HCV viruses, with conformational as well as linear epitopes. The Board denied acceptability under Art. 83 EPC:

"In the Board's judgment, the sheer amount of time and effort necessary to carry out the claimed subjectmatter over its whole scope is well beyond what the average skilled person would consider as undue burden although potentially useful techniques existed. And the patent in suit fails to give adequate information on how to isolate conformational epitopes and how to produce qualifying panels. Thus, the description is not sufficient for the subject-matter of claim 1 to be reproduced without undue burden or exercise of inventive skills.

The present situation is comparable to that dealt with in the case T 412/93 (see supra) where sufficiency of disclosure was denied in relation to the subject-matter of a claim directed to a cDNA encoding erythropoietin. The then competent board came to the conclusion that although there were methods available to attempt the cloning of said cDNA and that, therefore, it could be envisaged that the task would be performed in years to come, the patent in suit did not provide sufficient and complete information for the skilled person to accomplish this task without undue burden or exercise of inventive skills."

In claiming the subject matter of the invention it therefore has to be carefully considered whether the claim is small enough to be enabled by the teachings provided (and by the knowledge in the art at the time of filing) and still large enough to provide sufficient protection.

CLARITY OF CLAIMS

The clarity of the claims as required by Art. 84 EPC is – according to the decision practice of the EPO – always closely related to the question of enablement (although one has always to keep in mind that Art. 84 is not a reason for opposition). Therefore, it is also necessary for complying with Art. 84 that the scope of a granted patent corresponds to its technical contribution to the state of the art. The need for a fair protection has explicitly been recognised, e.g. in T 292/85 Polypeptide expression/GENENTECH, OJ EPO 1989, 275. A claim which includes within its scope subject

matter which, in the light of the disclosure in the description, can be performed only with undue burden or application of inventive skill or cannot be performed at all is also non-allowable in the light of Art. 84 EPC (in addition to Art.83 EPC).

For complying with the requirements of Art. 84 the wording of a claim should not leave the addressee guessing as to whether something falls within its terms (T 923/92 t-PA/GENENTECH). A claim must contain all the essential technical features necessary to obtain the desired technical effect on which the invention is based.

In drafting an allowable claim it is – despite the possibility of including functional wording – also necessary to ascertain that the claim does not only cover desired end results without telling the skilled reader how to achieve this result. Claims such as “Protease having the enzymatic activity of hydrolysing a peptide bond between a Ser and a Met amino acid residue in a polypeptide” or “Method for producing recombinant human insulin comprising cultivation of a recombinant host cell comprising a vector capable of expressing human insulin and recovery of the expressed human insulin” are – apart from potential prior art questions – not allowable because they are exclusively based on the aim of the invention but not indicating the necessary structural features for achieving this aim.

Instead of providing BoA decisions, hereinafter some examples are listed showing possibilities how to claim nucleotides, polypeptides, vectors, monoclonal antibodies, microorganisms and transgenic species:

CLAIM EXAMPLES (ALLOWED CLAIMS):

1. NUCLEIC ACID SEQUENCES:

T 301/87 Alpha-interferons/BIOGEN OJ EPO, 335:

“1. A recombinant DNA molecule for use in cloning a DNA sequence in bacteria, yeasts or animals cells, said recombinant DNA molecule comprising a DNA sequence selected from:

- (a) the DNA inserts of Z-pBR322(Pst)/HcIF-4c, Z-pBR322(Pst)/HcIF-2h, Z-pBR322(Pst)/HcIF-SN35, Z-pBR322(Pst)/HcIF-SN42 and Z-pKT287 (Pst)/HcIF-2h-AH6, said DNA inserts being exemplified, but not limited to, the DNA inserts of the recombinant DNA molecules carried by the microorganisms identified by accession numbers DSM 1699-1703, respectively,*
- (b) DNA sequences which hybridise to any of the foregoing DNA inserts and which code for a polypeptide of the IFN-alpha type, and*
- (c) DNA sequences which are degenerate as a result of the genetic code to the DNA sequences and inserts defined in (a) and (b) and which code for a polypeptide of the IFN-alpha type.”*

T 281/86 Preprothaumatin/UNILEVER OJ EPO 1989, 202:

“1. A DNA sequence selected from the group consisting of DNA sequences encoding

- (a) non-processed preprothaumatin according to the formula of Figure 2 (preprothaumatin gene), or (b) partly processed preprothaumatin according to the formulae of Figure 3 (prothaumatin gene) and Figure 4 (prethaumatin gene), and*
- (ii) the various allelic forms of the preprothaumatin gene given in Figure 5, and*
- (iii) the mutated various allelic genes encoding preprothaumatin with one or more mutations at positions 47, 507 and 513 as given in Figure 6.”*

T 866/95 Factor VIII/GENETICS INSTITUTE

The granted patent upheld in opposition and appeal:

„1. An isolated recombinant vector containing DNA coding for human factor VIII: C, comprising a polydeoxyribonucleotide having the sequence : 5'CGC AGC TTT CAG AAG AAA ACA CGA CAC TAT TTT ATT GCT GCA GTG GAG AGG3' „

The application as filed contained the following main claim:

„1. A DNA sequence coding for human factor VIII : C substantially free of other human genes.“

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“A DNA isolate comprising a continuous sequence encoding human serum albumin of the amino acid sequence depicted in Fig. 3 hereof and genetic variants thereof.”

T 412/93 Erythropoietin/KIRIN-AMGEN

T 636/97 Erythropoietin II/KIRIN-AMGEN (this claim was also held valid in the UK Court of Appeal Decision of Kirin Amgen vs. TKT of 31st July 2002)

“1. A DNA sequence for use in securing expression in a procaryotic or eucaryotic host cell of a polypeptide product having at least part of the primary structural confirmation [sic] of that of erythropoietin to allow possession of the biological property of causing bone marrow cells to increase production of reticulocytes and red blood cells and to increase hemoglobin [sic] synthesis or iron uptake, said DNA sequence selected from the group consisting of:

(a) the DNA sequences set out in Tables V and VI or their complementary strands;

(b) DNA sequences which hybridize under stringent conditions to the protein coding regions of the DNA sequences defined in (a) or fragments thereof; and

(c) DNA sequences which, but for the degeneracy of the genetic code, would hybridize to the DNA sequences defined in (a) and (b).”

2. POLYPEPTIDES (PROTEINS)*T 412/93 Erythropoietin/KIRIN-AMGEN*

T 636/97 Erythropoietin II/KIRIN-AMGEN (this claim was also held valid in the UK Court of Appeal Decision of Kirin Amgen vs. TKT of 31st July 2002)

“19. A recombinant polypeptide having part or all of the primary structural conformation of human or monkey erythropoietin as set forth in Table VI or Table V or any allelic variant or derivative thereof possessing the biological property of causing bone marrow cells to increase production of reticulocytes and red blood cells to increase hemoglobin synthesis or iron uptake and characterized by being the product of eucaryotic expression of an exogenous DNA sequence and which has higher molecular weight by SDS-PAGE from erythropoietin isolated from urinary sources.”

T 223/92 Human gamma-interferon/GENENTECH

“1. Human immune interferon of the amino acid sequence depicted in Figure 5 hereof and alleles thereof, free from other proteins with which it is ordinarily associated.”

EP 0 029 191 B1 (example for a “Fingerprint” claim)

“A protein, PP₁₁, characterized by

(A) a carbohydrate content of 3.9.±.0.9%, consisting of 2.6.±.0.5% of hexoses, 1.0.±.0.3% of hexosamines, 0.05.±.0.03% of fucose and 0.26.±.0.07% of neuraminic acid;

(b) a sedimentation coefficient $S^{0}_{20,w}$ of 3.5.±.0.2 S

- (c) a molecular weight of $44,300 \pm 6,000$, determined in an ultracentrifuge;
 (d) a molecular weight of $62,000 \pm 3,000$, determined in polyacrylamide gel containing sodium dodecyl-sulfate (SDS);
 (e) an extinction coefficient $E_{1\text{ cm}}^{1\%}$ (280 nm) of 13.4 ± 1.0 , and
 (f) an electrophoretic mobility similar to that of the α_1 -globulins.”

3. VECTORS and MICROORGANISMS:

T 292/85 Polypeptide expression/GENENTECH; OJ EPO 1989, 275

“1. A recombinant plasmid suited for transformation of a bacterial host wherein the plasmid comprises a homologous regulon, heterologous DNA, and one or more termination codon(s), the heterologous DNA encoding a desired functional heterologous polypeptide or intermediate therefor which is not degraded by endogenous proteolytic enzymes, said DNA being positioned in proper reading frame with said homologous regulon between said regulon and the termination codon(s), whereby on translation of the transcription product of the heterologous DNA in a suitable bacterium, the resulting expression product is said desired functional polypeptide or intermediate therefor in recoverable form.

T 181/87 DNA transfer vector/THE REGENTS OF THE UNIVERSITY OF CALIFORNIA

“1. A DNA transfer vector comprising at least a portion of the nucleotide sequence encoding the hepatitis B surface antigen and being substantially free of the nucleotide sequence encoding the hepatitis B core antigen.”

T 162/86 Plasmid pSG2/HOECHST OJ EPO 1988, 452

“1. Plasmid pSG2, characterised in that it is obtainable from a culture of *Streptomyces ghanaensis* ATCC 14 672, has a contour length of $4.58 \mu\text{m}$ and a molecular length of about 13.8 kilobases (kb) and in that it is not fragmented by the restriction endonucleases *Eco RI*, *Bam HI*, *Sal I*, *Hpa I* and *Hin dII*, but is cleaved by the restriction endonuclease *Hin dIII* into a fragment with a length of about 14 kb, by *Cla I* into two fragments with lengths of 10.15 and 3.65 kb, by *Pst I* into two fragments with lengths of 10.85 and 3.0 kb, by *Bgl II* into two fragments with lengths of 11.25 and 2.6 kb, and by *Bcl I* into three fragments with lengths of 11.6, 1.25 and 1.0 kb.”

Moreover, the following wordings are possible:

“1. Plasmid pDAUV 2, which has the nucleotide sequence according to SEQ ID NO 52”

“1. Plasmid pDAUV 2, which is contained in *E. coli* ATCC 1234”

“1. The live strain of *Anacystis nidulans* PCC 7120”

However, the claim

“1. Plasmid pDAUV 2”

is not patentable because of lack of clarity due to the arbitrary nomenclature.

4. MONOCLONAL ANTIBODIES:

T 418/89 Monoclonal antibody OKT1/ORTHO; OJ EPO 1993, 20

“8. Monoclonal antibody which is produced from hybridoma ATCC CRL 8000 (OKT1)”

T 906/91 Monoclonal antibody to theophylline/DUPONT

“1. Monoclonal antibody to theophylline having 5% or less cross-reactivity with caffeine.

2. A monoclonal antibody according to Claim 1 having 30% or less cross-reactivity with theobromine and 5% or less cross-reactivity with 3-methylxanthine.”

5. TRANSGENIC PLANTS OR ANIMALS:

T 19/90 Oncomouse/HARVARD; OJ EPO 1990, 476

“19. A transgenic non human mammalian animal whose germ cells and somatic cells contain an activated oncogene sequence as a result of chromosomal incorporation into the animal genome, or into the genome of an ancestor of said animal, said oncogene optionally being further defined according to any one of claims 3 to 10.” (opposition proceedings are pending; interlocutory decision reduced the “mammalian animal” to “rodent”)

T 1054/96 Transgenic plants/NOVARTIS II; OJ EPO 1998, 511; referred to the EBo as G1/98 (OJ EPO 2000, 111)

“19. A transgenic plant and the seed thereof comprising recombinant DNA sequences encoding
a) one or more lytic peptides, which is not lysozyme, in combination with;
b) one or more chitinases; and/or
c) one or more -1,3-glucanases in a synergistically effective amount.”

*Daniel Alge
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