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Disclosure Problems for Living Material - Illustrated on the Basis of the Practice of the European Patent Organisation [1]

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Abstract. A patent application must describe, *i.e.* disclose, the invention in a manner sufficiently clear for it to be carried out by a person skilled in the art. The disclosure is an essential requirement for a patent to be granted. However, for biological inventions, this can lead to problems. To resolve these problems, ways have been found to enable the disclosure requirement to be met even in the field of modern biology. This was achieved by the possibility to deposit biological material and by following the decisions of the European Patent Organisation (EPO).

Keywords: Biological inventions · Biotechnology · Deposit · Disclosure · Patents · Reproducibility

1. Introduction

Patents grant the inventor a time-limited and territorially-limited exclusivity right that enables him to exclusively market his invention for a restricted period of time. Thereby the inventor is compensated for the time and investment incurred in producing the invention. This exclusivity right is justified by the fact that, in making his invention generally available through publication, an inventor enables the public at large to benefit from it in the sense that knowledge is increased and specialists in the field are stimulated to make further technical advances [2]. In order to make this interaction function it must be guaranteed that the patentee discloses his invention to the public in a sufficiently clear way such that the technical doctrine may be reproduced and may be used free of charge and without any restrictions after expiry of the patent. To become entitled to patent protection, apart from fulfilling the requirements of patentability as laid down in the European Patent Convention (EPC) in Articles 52 to 57, sufficiency of disclosure of the claimed invention (Art. 83) is an essential requirement for granting and maintaining a patent. The fulfilment of this requirement in the field of 'biological inventions', whose subject matter is often either living material, or living material is needed to carry out the invention, is beset with difficulties that do not occur with inventions in conventional fields, such as mechanics or electrotechnology. Living material cannot be described in words, *i.e.* at least not always to the extent necessary to sufficiently disclose the invention as a technical teaching. The extent to which this problem has been solved is illustrated by the decisions of the EPO, as well as by the special regulation for depositing living material.

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2. Disclosure of Inventions According to EPC Art. 83

In the EPC (European Patent Convention), the rule on the 'disclosure of the invention' in Art. 83 is worded as follows: *'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'.* Insufficiency of disclosure gives grounds for opposition and for revocation (Art. 100 and Art. 138). The concept of disclosure in the EPC is uniform, *i.e.* it applies both to the invention disclosed in a patent application and to documents to be recognised as prior art. Disclosure of the invention is effected on the basis of the whole patent specification, except for the associated abstract, *i.e.* on the basis of the content of the patent claims, the description and the drawings [3][4]. For inventions in the field of biology, a special rule was created to supplement the disclosure with the possibility of depositing biological material at recognised depository institutions. The person having ordinary skill in the art serves as the criterion for judging whether a disclosure in the patent application is sufficient. Through the disclosure, he must be in a position to reproduce the invention. He is a fictitious person, to whom reference is made at various points where an evaluation of technical facts must be made. The person having ordinary skill in the art is not a specialist, but is proficient in his specialist subject and a 'man of practice' who has average knowledge and ability. He is able to think logically but does not act intuitively or inventively. He is thus distinct from the inventor [5].

3. Problems in Reproducing Biological Inventions

3.1. *Identical Reproduction*

Many inventions from the field of biology refer to living biological material which is either required as starting material for a process or is itself the subject matter of the invention, *e.g.* human tissue, from which a gene is isolated, a cell line which is used for expression of a protein, or a microorganism which segregates *e.g.* a new antibiotic. In all these cases, the reproducibility of the invention peremptorily depends on the biological material employed. However, living material changes during the course of time, making it difficult to reproduce the invention. Microorganisms, for example, undergo a genetic drift. This drift causes a slow change in the genome of the microorganism from generation to generation. Thus, 'identical' genes have a certain variability, called allele variants. Alleles, which encode proteins 'having the same function', appear in particular when genes are isolated from tissue of different sources. This makes it practically impossible to reproduce them in a way to form an identical invention. The extent to which this is a problem for a sufficient disclosure is illustrated by a series of decisions from the Technical Boards of Appeal of the EPO. The EPO has sought an appropriate stance to enable patent protection of such inventions and at the same time to meet the requirements of sufficiency of disclosure according to Art. 83.

The decision *T 347/87* 'Method of producing human growth hormone/ GENENTECH' [6] was based on an application which had been rejected due to insufficient disclosure. The application described *inter alia* a method of producing a plasmid which contains the gene for a human growth hormone and can be expressed in bacteria. In its rejection, the Examining Division argued that the starting material, human tumour tissue, from which the growth hormone had originally been isolated, might not be isolatable in identical form again because of the allelic phenomenon. Therefore the described plasmid could not be exactly reproduced. The Board of Appeal decided, however, that the lack of ability to identically reproduce the plasmid did not necessarily mean that the claimed invention could not be reproduced and referred to *T 292/ 85* 'Polypeptide expression/GENENTECH' [8]. In this decision, in connection with the 'production' of human hormones, the view was clearly taken that the production of human hormones would be sufficiently disclosed, although each person, as a source, could only provide an individual variant of the DNA precursors of the hormone (point 3.3.2 of the reasons). In the decision *T 301/87* 'Alpha-Interferons/BIOGEN' [9] the Board took this point of view as well. The patent claimed *inter alia* recombinant plasmids for the cloning of alpha-interferon sequences. The alpha-interferon sequences were clearly defined by DNA insertions of deposited plasmids which encode alpha-interferons, as well as by sequences hybridising thereon. The claimed sequences, yield end products having the same biological activity. The identical reproduction of each representative of this class is not guaranteed owing to the techniques employed. This is not necessary for a sufficient disclosure, and is stated by the Board in the decision as follows: '*...variations in the construction within a class of genetic precursors, such as recombinant DNA molecules claimed by a combination of structural limitations and functional tests, are immaterial to the sufficiency of the disclosure provided the skilled person could reliably obtain some members of the class without necessarily knowing in advance which member would thereby be made available.*' (point 4.5 of the reasons). Another field of biological inventions, in which identical reproduction is also discussed, are patent applications in which monoclonal antibodies are claimed. For this it is referred to the decision *T 299/86* 'Monoclonal Antibody/ZECHER ET AL.' [10] in Section 4 concerning depositing requirements.

3.2. *An Undue Burden to Repeat an Invention*

In several decisions from Technical Boards of Appeal, the criteria under which reproducibility of biological inventions would be classified as an undue burden for the person having ordinary skill in the art were stated. The decision *T 223/92* 'Human immune interferon/ GENENTECH' [11] is based on a patent from 1981. The claimed invention describes *inter alia* the isolation, cloning and expression of human γ-interferon which was previously unknown in isolated form. Both the nucleotide sequence and the corresponding amino acid sequence of the γ-interferon gene were given in the description. An opposition was lodged against the patent for lack of sufficient disclosure. The Board had to give serious thought to the question of whether the provision of a DNA sequence in 1981 enabled those skilled in the art to reproduce the invention. It was of the opinion that this was possibly a time-consuming and cumbersome way, but, in the given circumstances, without undue burden of experimentation and without needing inventive skill. This was based on the fact that the provision of the DNA sequence opens up other routes to reproduce the invention, such as the synthesis of the described DNA sequence (point 3.1 of the reasons). In this connection, the decision *T 412/93* 'Erythropoietin/ KIRIN-AMGEN' [12] is mentioned, in which the objection of an undue burden in reproducing the invention is raised again. In the patent, erythropoietin was claimed, and the method of cloning associated therewith was described. The decision argues that a laborious and time-consuming process that is required to reproduce an invention does not amount to an undue burden if the procedure is unequivocal and certain. An undue burden is deemed to apply to those inventions, whose execution depends on random components and therefore do not lead to the result with certainty, *e.g.* the production of monoclonal antibodies by hybridoma technology (Section 4). An example of this is in decision *T 418/89* 'Monoclonal antibodies/ORTHO' [13]. In the patent on which this decision is based, a claimed monoclonal antibody was defined purely functionally on the basis of its affinity for human T-cells. A general method of producing a hybridoma with the assistance of these cells as antigen was described. The written description was considered too vague, since reproduction using human T-cells as antigen would create a multitude of diverse antibodies. Due to its purely functional description, the claimed antibody can only be selected with a huge amount of effort, if at all, from the multitude of possible antibodies (point 3.4 and 3.7 of the reasons).

3.3. *Reproducibility Over the Whole Breadth of the Claim*

A further prerequisite of sufficient disclosure is the requirement of being able to reproduce the invention over the whole breadth of the claim. For inventions in the field of biology, under certain circumstances broad claims that are only supported by one practical example are also permitted. From *T 292/85* 'Polypeptide-expression/GENENTECH I' [14], it can be seen that biological inventions are sufficiently disclosed if the person skilled in the art has been clearly shown at least one way to carry out the invention. In the patent, a transformation method and a re-

combinant plasmid appropriate for this purpose were claimed in a very fundamental way. The claimed plasmid was defined by purely functional features. All plasmids with a heterologous DNA sequence, which are translated in transformed bacteria into the corresponding polypeptides, fall under the claim. However, the claim was supported in the description by one practical example, in which the production of only one appropriate plasmid was described. The Board had no objections to the broad claim and considered it to be sufficiently supported by the example and disclosed over the whole breadth. It elaborated:

'An invention (here: biological) is sufficiently disclosed if at least one way is clearly indicated enabling the person skilled in the art to carry out the invention. Then the non-availability of some particular variants or unsuitability of some unspecified 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 (cf. point 3.1.5 of the Reasons)' (Headnote 1).

In decision *T 19/90* 'Onco mouse/ HARVARD' [15], the criteria for satisfactory support of broad claims was specified. The indication of only one way in which the skilled person could carry out the invention is only sufficient if no verifiable doubt exists that the invention can be carried out over the whole area claimed. In the patent on which the decision was based, there was claimed *inter alia* a method of producing a transgenic non-human mammal with an increased tendency to develop neoplasms, as well as the corresponding transgenic animals as such. In the description, the process and 'just' a transgenic mouse was disclosed. The patent was refused by the Examining Division for lack of sufficient disclosure since there was doubt that the invention could also be carried out on mammals which are not classified as rodents. Therefore, the claims were considered to be unrealistically broad. The Technical Board of Appeal overruled the decision of the Examining Division again for lack of '*serious doubts substantiated by verifiable facts*' (point 3.3 of the reasons).

In decision *T 612/92* 'Monocotyledonous plants/RIJKSUNIVERSITEIT LEIDEN' [16], the disclosure was deemed insufficient to allow reproduction over the whole area claimed. The invention consisted of a process for transfecting foreign DNA into the genome of monocotyledonous plants. The technique being claimed was already known for dicotyledonous plants and thus represented the use of an already known technique in a new field of application. For this reason, special attention was placed on the fact that the invention is reproducible over the whole area claimed. In the description, the use of the process was demonstrated with two species of monocotyledonous plants. The Board considered this to be insufficient to be able to carry out the process over the whole area claimed, *i.e.* with all monocotyledonous plants. (point 10 of the reasons).

The contribution which the invention makes to the prior art also belongs to the criteria of sufficient disclosure over the whole area claimed. In *T 694/92* 'Modification of plant cells/ MYCOGEN' [17], the Board summarised the connection between sufficient disclosure and the breadth of the claim in dependence on the contribution to the prior art: '*...In certain cases a description of one way of performing the claimed invention may be sufficient to support broad claims with functionally defined features, for example where the disclosure of a new technique constitutes the essence of the invention and the description of one way of carrying it out enables the skilled person to obtain without undue burden the same effect of the invention in a broad area by use of suitable variants of the component features [...]. In other cases, more technical details and more than one example may be necessary in order to support claims of a broad scope, for example where the achievement of a given technical effect by known techniques in different areas of application constitutes the essence of the invention and serious doubts exist as to whether the said effect can readily be obtained for the whole range of applications claimed (see T 612/92 of 28th February 1996). However, in all these cases, the guiding principle is always that the skilled person should, after reading of the description, be able to readily perform the invention over the whole area claimed without undue burden and without needing inventive skill [...]. On the other hand, the objection of lack of sufficient disclosure presupposes that there are serious doubts, substantiated by verifiable facts, in this respect, see T 19/90 (OJ EPO 1990, 476, see point 3.3 of the Reasons.*' (point 5 of the reasons).

4. Deposit of Biological Material as a Possible Means of Disclosure

In many instances, living material cannot be described or illustrated by drawings in the patent application in a way that allows to identify and reproduce it. This concerns *e.g.* microorganisms that have either been newly discovered and isolated or produced by mutagenesis or by fusion. For this reason, a special rule was created for biological inventions. If such an invention involves the use of or concerns biological material, the applicant is allowed to deposit this material at a recognised depository institution in order to comply with the disclosure requirement (Rule 28 EPC). In this way, the deposit, together with conventional disclosure means such as description, drawing and claims, offers a further means of disclosure. Whereas the description is always required, the decision whether to deposit biological material is left to the applicant.

4.1. *Rule 28 EPC: Deposit of Biological Material*

The deposit of biological material is described in Rules 28 and 28a. A sample of deposited material must be issued to anybody on request after publication of the patent application. If a right to inspect the files according to Art. 128, paragraph 2 (Rule 28 (3)) exists, it may even be issued earlier. The sample shall only be issued if the requester undertakes 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. This restriction applies as long as rights from the application or from the patent are in force. For the period up to grant of the patent or for twenty years from the date of filing if the application has been refused or withdrawn, the applicant has the choice to restrict issuing of a sample only to a nominated expert that is officially recognised (Rule 28 (4)).

4.2. *What Type of Biological Material May Be Deposited?*

In the original wording of Rule 28, the term 'microorganisms' was used instead of 'biological material'. Since, however, in a biological sense, the definition of microorganisms is very narrow and refers only to prokaryotes, single-celled eukaryotes (protists) as well as to yeasts and fungi, the term microorganism was extended in EPO practice to include also plasmids, viruses and cell cultures. Since the amendment of Rules 28 and 28a (in

force since October 1, 1996), the new term 'biological material' applies. In the context of Rule 28, this new term includes any material that contains genetic information and is capable of self-reproduction or of being reproduced in a biological system (Rule 28 (6a)).

4.3. *When is the Deposit of Biological Material Necessary for Complete Disclosure?*

Up to the introduction of the so-called expert solution (October 1, 1996), the deposit presented a risk to the applicant. Any competitor could gain easy access to an unprotected invention if under certain circumstances, the patent was not granted or was rejected. Even nowadays, the deposit goes beyond the conventional disclosure, in that the invention is made available to the public in the form of a 'ready-to-use item' and does not have to be reproduced 'by hand'. For this reason, whenever possible, the applicant will not file a deposit. According to Rule 28, a deposit is only necessary if the biological material used to carry out the invention cannot be sufficiently described nor made available to the public. Biological material is recognised as being available to the public if it is commercially available or has already been deposited by a third party at a recognised depository institution, provided that this is known to the examiner [18]. Biological material is also recognised as being available to the public if it is available to everybody without restrictions in the laboratory of the researchers who are working in the field of the invention. On this basis, a cell line that had not been deposited was recognised as being available to the public in the decision *T 923/92* 'Human t-PA/GENENTECH' [19]. There, several processes were claimed, in which mRNA from a Bowes melanoma cell line was used, *inter alia* to produce t-PA cDNA. The cell line had not been deposited. The Board stated: '*a large body of evidence shows that Bowes melanoma cells were generally available and freely exchanged in the scientific community among all those engaged in a research programme on t-PA (...) and that neither secrecy agreements nor contractual obligations among the research workers restricted the use or dissemination of the cells...*' (point 44i of the reasons).

However, public access to non-deposited biological material was deemed unproven in the decision *T 815/90* 'Hepatitis-A virus/USA' [20]. There, certain conditions were attached to the issue of material. According to the Institute practice at that time, biological material generally would not be made available prior to publication of the associated research findings (points 3.2.2, 3.2.3, 3.2.4 of the reasons). What are the criteria for depositing biological material that is not available to the public? This question was examined in several decisions. In decision *T 223/92* 'Human immune interferon/GENENTECH' [11], the Board decided that there is no legal requirement in the EPC which would force a deposit if the disclosure requirement could also be met in written form (point 3.2 of the reasons). The question of the necessity for a deposit was also discussed in *T 412/93* 'Erythropoietin/KIRIN-AMGEN' [12]. Here, the appellant argued that the invention could be reproduced only with an undue burden without a deposit. The Board confirmed its stand as in *T 223/92* 'Human immune interferon/GENENTECH' [11], and again stressed that the deposit does not serve to facilitate carrying out the invention if it can also be carried out by following the written description. To come to the opposite conclusion would correspond to a 'best mode' requirement, which is not part of the European Patent system (points 75 and 76 of the reasons).

In *T 923/92* 'Human t-PA/GENENTECH' [19], it was decided that a deposit is not necessary if the biological material required to carry out the invention is freely available on the priority date and thus belongs to the prior art. Regarding this point, the Board stated: '*...Further, no evidence was produced that the cells would be available only to some selected laboratories for a limited time period. Thus, in the Board's judgement, the Bowes melanoma cells were part of the state of the art already at the priority date. Under these circumstances the Board cannot agree to the appellants' position that it would have been the respondents' obligation to ensure their availability for the life-time of the patent in suit by means of a deposition under Rule 28 EPC*' (point 44i of the reasons). However, deposited biological material must be available during the entire duration of a patent in a reproducible (living) state. Thus, this decision is not without its problems.

4.4. *Deposit Requirement in the Case of a Claim for Certain Monoclonal Antibodies or in the Case of a Generic Claim*

A special situation arises in the case of monoclonal antibodies which are produced by the hybridoma technique. In this key technology, which was developed by Köhler and Milstein and published in 1975 [21], a test animal is immunised with an antigen. In the immune response, the spleen cells of the animal are isolated, and activated antibody-forming B-lymphocytes are separated from these cells. These B-lymphocytes are fused with myeloma cells to form the so-called hybridoma. The hybridoma can indefinitely produce a mono-specific, *i.e.* monoclonal antibody which recognises the antigen originally used. Normally, several different hybridoma are obtained in this way, each of them producing a different set of antibodies that all recognise the original antigen.

The deposit according to Rule 28 for inventions whose subject matter is a specific monoclonal antibody is even today an important prerequisite for fulfilling the disclosure requirement according to Art. 83. This is in contrast to many other inventions from the field of biotechnology. Antibodies are deposited in the form of their corresponding hybridoma cells. Two basic cases may be distinguished for patents claiming monoclonal antibodies. In case 1, the antibody is claimed generically and is defined by its affinity for a specified antigen. The claim includes all the different monoclonal antibodies, which can be defined as one class based on their binding properties to the antigen. If the antigen is new, *e.g.* a new protein, and if no antibodies directed against this protein are known, then generic claims are normally permissible. Under these circumstances, the deposit of a hybridoma is not necessary, since to reproduce the invention, it is sufficient if the person having ordinary skill in the art obtains a monoclonal antibody from the group of possible antibodies falling under the claim by means of the description. Case 2 relates to patents in which a certain monoclonal antibody is claimed, which is distinguished from those already known *e.g.* by its binding properties. Under these circumstances, it is usually necessary to deposit the corresponding hybridoma, since the effort in reproducing exactly the same antibody means a huge amount of effort, and its success is questionable. The protection, which the patent offers in this case, is restricted to the deposited antibody. The standpoint in respect of the necessity for a deposit may be illustrated by the following decisions. In decision *T 299/86* 'Monoclonal antibody/ZECHERT ET AL.' [10], a monoclonal antibody was defined on the basis of its affinity for alpha-interferon. In the description, a hybridoma, which had not been deposited, was given as an example. The method of reproducing this hybrido-

ma was described. However, the hybridoma as such was not claimed. The application was rejected by the Examining Division for the reason that the hybridoma mentioned in the example could not be reproduced identically by the person skilled in the art. The Board shared this view, but argued that the hybridoma had not been claimed as such and that the description enables the person skilled in the art to produce antibodies to alpha-interferon which correspond to the claimed monoclonal antibody (point 9 of the reasons).

In *T 418/89* 'Monoclonal antibody/ORTHO' [13], the Board decided that the invention cannot be carried out without undue burden and thus the requirements of Art. 83 are not met. In the patent an antibody was deposited in form of its hybridoma, but it was established that this did not correspond to the one that was specified in the written disclosure. Thus, the deposited hybridoma could not contribute towards the disclosure. The attempt by the patentee to claim the allegedly new hybridoma as such was not possible, as a mere deposit of a hybridoma without any corresponding written description does not provide a sufficient disclosure (point 5.3 of the reasons). In the decision *T 349/91* 'Monoclonal hybridoma antibody/THE WISTAR INSTITUTE' [22], protection was claimed for a monoclonal antibody to a more fully defined epitope of a known antigen. The appropriate hybridoma had been correctly deposited. However, apart from the deposited antibody, protection was also claimed for 'corresponding' antibodies, which were similarly aimed at the epitope which was more fully defined, *inter alia* by its molecular weight. Protection was not granted for this broad scope however. It was decided that there was insufficient disclosure to enable the person skilled in the art to reproduce the 'corresponding' antibodies as well as the deposited antibody. Even if screening for 'corresponding' antibodies is facilitated by having the deposited antibody, as submitted by the patentee, the renewed isolation of an antibody to a more fully defined epitope is not deemed to be reproducible without undue burden (point 5 of the reasons). In the patent, only the antibody corresponding to the hybridoma was deemed to be sufficiently disclosed.

5. Discussion

The patenting of living material used to have and still has (Art. 53b EPC) many hurdles to overcome in the history of patent law. For a long time, inventions in biology were denied to have technical character, a requirement that has to be fulfilled for a patentable invention. This only changed with the elucidation of the genetic material and the understanding that biological processes are also causal and thus predictable and governable. In the BGH (Federal Court of Justice; Germany) decision 'Rote Taube' [23], biological inventions were declared to have technical character and thus are patentable in this respect. However, as in this decision, lack of reproducibility was often a stumbling block to patenting. This lack of reproducibility was based on the inability to describe inventions which depend on living material in such a way that it is possible to reproduce them, *e.g.* a microorganism cannot be created *de novo* according to a written description.

From the outset, the EPO granted patents for inventions whose subject matter is living material or which relate to living material. It is possible to comply with the sufficiency of disclosure requirement by means of a deposit, if it is not possible to do so 'in written form'. In this way, even patent protection for microorganisms *per se* will be granted, since they can be reproduced by propagating the deposited microorganisms.

Many other factors that are necessary for sufficient disclosure had to be developed first for biological inventions. This was not an easy undertaking, since at the start of the existence of the EPO, life sciences were a young and very rapidly progressing branch of research. When evaluating the disclosure, one was frequently confronted with pioneering inventions of Nobel Prize winners, which then quickly developed into routine methods. Thus, it proved *e.g.* difficult to define the competent person skilled in the art for biological inventions. However, a solution was found by defining it as a research team. The disclosure must ensure that the invention can be carried out. Problems in respect of reproducibility exist that cannot be solved by the deposit of biological material. For example, when using the same starting material and the same process steps, many biological inventions cannot be identically reproduced. This is due to the peculiarities of living matter. For example, the large variability in living organisms, such as freely occurring random genetic combination, unforeseeable outcomes in the case of induced mutations, prevent this in general. Therefore, a guideline to judicial practice was developed, in which reproduction did not have to be identical *e.g.* to a described process, provided that the desired result was obtained, *i.e.* the claimed invention, *T 281/86* 'Preprothaumatin/UNILEVER' [24]. However, the more special a claim, the more problematic the reproduction requirement. For example, if a monoclonal antibody or a DNA sequence is claimed *per se*, the disclosure must enable reproduction that leads exactly to the claimed monoclonal antibody or the claimed DNA sequence, since the person skilled in the art has no room for play for 'possible variants'.

Many biological inventions are fundamental processes, the usage of which extends to a broad range, *e.g.* the production of a transgenic animal. In practice, it is impossible to demonstrate how this process can be carried out on all conceivable animals. However, it would be inappropriate for the applicant to be granted protection only for a scope precisely defined by examples. The EPO grants the inventor protection appropriate to the invention. Thus, it is possible to obtain broad protection, even though reproducibility of the invention was demonstrated only by one example, as *e.g.* for pioneering inventions. This is on condition that the invention has been disclosed over the whole range by this example and can be reproduced over the whole range. If there are no serious doubts, the invention is deemed to have been sufficiently disclosed.

Finally, it is to be said that by depositing biological material, especially at the start of biotechnology, the possibility was created of meeting the disclosure requirement according to Art. 83, so as to comply with this essential condition for patent protection. This 'early' patent protection certainly contributed to the rapid development of modern biology, in that high investment costs of research for economic application could be safeguarded. Nowadays, better methods are available and new ones are continuously developed that allow to modify genes in a clearly defined way. With these methods, defined influence on the metabolism of a microorganism or on the properties of a protein may be exerted, whereby a deposit is unnecessary. In the beginning of genetic engineering, it was a very complex task to indicate the whole sequence of isolated genes or of the corresponding proteins in the patent specification. These genes were often deposited in the form of plasmids or transformed microorganism. Nowadays, sequencing is routine work and can be carried out without great financial outlay and in a short time, so that

it is no longer necessary to make a deposit. Areas in which the deposit can still play a role are either monoclonal antibodies, which are precisely claimed, or microorganisms, which have been isolated because of special characteristics. In the field of monoclonal antibodies, however, new techniques for their preparation such as the so-called antibody libraries, could make a deposit superfluous, since assuming that the antibody library is open to the public, they can be described in such a way that it is possible to reproduce antibodies without corresponding hybridoma cells. This begs the question whether the deposit will still play a role in the future. Situations might be conceivable, similarly to monoclonal antibodies, in which a transgenic animal is claimed *per se* (provided that Art. 53b and new Rules 23b to 23e permit this in the future). Reproduction would only be possible with undue burden, if at all, since the exact site of integration of 'trans-genes' is not yet predictable. Thus, the animal would have to be deposited, *e.g.* in the form of germ cells or since 'Dolly' [25] even in the form of somatic cells, since these cells now conform to the requirements of depositable material. However, highly sophisticated methods that will be developed in future and that can be described exactly might make a deposit superfluous in this field as well.

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