



The patenting of
biotechnological
inventions involving the
use of biological material
of human origin

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CONTENTS

| | |
|--|----|
| Preliminary note | 7 |
| 1. Initial legal position | 8 |
| 2. Content and objectives of the EU directive and of the draft German transposing law | 10 |
| 3. Objections and criticisms | 13 |
| 3.1. Contested patents and patent applications | 13 |
| 3.1.1. Method for isolating the human genes BRCA-1 and BRCA-2, the mutation of which leads to hereditary breast cancer (EP 0699754, EP 0705902, EP 0705903 and others) | 14 |
| 3.1.2. Gene sequence CCR5, which codes for a receptor on the cell surface (US 6025154) | 15 |
| 3.1.3. Processes in which human cells are used to produce embryos (DE 69422034; EP 0695351 – the “Edinburgh patent”) | 15 |
| 3.1.4. Process for freezing embryos and germ cells, extending to the utilization of the frozen entities (EP 1121015 B 1) | 15 |
| 3.1.5. Process for cloning living organisms (US 6211429) | 15 |
| 3.1.6. Process for the production of neural precursor cells from embryonic stem cells (DE 19756864; EP 1040185) | 16 |
| 3.1.7. Process for the genetic manipulation of pig and human embryonic cells for the production of transgenic tissue (provisional designation WO 99/21415) | 16 |
| 3.2. General objections and criticisms | 16 |
| 4. Opinion of the National Ethics Council | 17 |
| 4.1. Opinion on the general objections | 18 |
| 4.1.1. Issues of ethical and scientific principle | 18 |
| 4.1.2. Restrictions of patent protection | 23 |
| 4.2. Other ethical and constitutional issues | 28 |
| 4.2.1. Prohibitions of patenting under Section 2 (2) of the draft law | 28 |
| 4.2.2. Evidence of origin | 31 |
| 4.2.3. Donor consent | 33 |
| 4.2.4. Freedom of research | 34 |
| Position statement | 35 |
| Position statement in favour of stricter requirements | 36 |
| The members of the German National Ethics Council | 40 |

Preliminary note

The following considerations are concerned solely with biotechnological inventions involving the use of biological material of human origin. Ethically and legally significant issues are also raised by the patenting of biotechnological inventions that use material of animal or plant origin, as well as bacteria and viruses. In particular, the patenting of genes of plant origin and the globalization of the patent law system present appreciable problems for the non-industrial countries from which these plants originate. The patentability of methods for modifying the genetic identity of plants and animals also gives rise to questions of ecological and animal ethics. These call for thorough examination in their own right; however, the National Ethics Council considers this to be beyond the scope of this Opinion.

1. Initial legal position

A large number of heterogeneous biotechnological patents have been granted since the 1970s, not only in the Federal Republic of Germany and the other Member States of the European Union, but also in non-European countries – in particular, the United States. The prerequisites laid down for the granting of these patents, as well as their scope, differ considerably. To maximize the degree of EU harmonization in this field, the European Parliament and the Council of the European Union, after nearly ten years of difficult preliminary work and deliberations and several attempts, adopted Directive 98/44/EC on the legal protection of biotechnological inventions, which took effect in July 1998. The Netherlands, supported by Italy, brought an action against the directive before the European Court of Justice. The action, which, *inter alia*, alleged violations of human dignity (by virtue of the patenting of parts of the human body) and of international obligations (such as the Convention on Biological Diversity of 5 June 1992), was dismissed by the European Court of Justice in its judgement of 9 October 2001. The directive has so far been transposed into national law in Denmark, Finland, Greece, Ireland, Sweden, Spain, Portugal and the United Kingdom, the ten new accession countries and recently also France. Furthermore, by a decision of the Administrative Council of the European Patent Organisation dating from as long ago as June 1999, its main provisions were incorporated, with effect from 1 September 1999, in the Implementing Regulations to the European Patent Convention. Since then, the European Patent Office has consequently granted patents in this field for the entire area covered by the Convention, for several Member States or for just one Member State – for instance, the Federal Republic of Germany. These patents are thought to account for 80-90% of the biotechnological patents in force in Germany. A legally binding answer has not yet been forthcoming to the question of how the European Patent Office should proceed if, for

example, the grant of a patent appears permissible under Article 6 (2) (a) of the directive but is prohibited in Germany by Section 2 (2) No. 1 of the Federal Government's draft law transposing the directive because the term "human life" is interpreted differently by the various European legal authorities (see Section 4.2.1 below). If, in such a case, the Office were to base its decision solely on the provisions of the directive as incorporated in the Implementing Regulations and to disregard concrete formulations laid down in national law – for instance, with regard to *ordre public* (Section 2 (1) of the draft law refers to *ordre public and morality*) – this would give rise to appreciable problems not only for the Federal Republic.

To transpose the directive, the Federal Government in October 2000 introduced a draft law (Bundestagsdrucksache 14/5642), which, however, was lost because it proved impossible to reach agreement, in particular on the question of substance protection, before the end of the relevant electoral term of the Bundestag [Lower House of the Federal Parliament]. In Electoral Term 15, the Federal Government reintroduced the draft law with minor amendments (Bundestagsdrucksache 15/1709), including an appendix containing the opinion of the Bundesrat [Upper House of the Federal Parliament] and the Federal Government's responses to the points raised in it. In addition, on 25 June 2003 the Federal Government confirmed its decision of October 2000 to act at European level, immediately after the entry into force of the transposing law, with a view to the initiation of a process of amendment and to securing certain necessary corrections and clarifications to the directive. Since the directive was not transposed into national law within the period stipulated in the directive itself (by 30 July 2000), the European Commission referred the Federal Republic of Germany to the European Court of Justice in January 2004 for violation of the Treaty. The Court has already found against France in similar proceedings, but that country has now transposed the directive.

2. Content and objectives of the EU directive and of the draft German transposing law

The directive is consistent with the general principles of patent law, which has the aim of promoting technical innovations and the dissemination of their results by granting inventors, for a specific period – as a rule, 20 years – the exclusive right to the commercial exploitation of their inventions, thereby offering them an opportunity to recoup the expense entailed and in addition holding out the prospect of a fair profit subject to the condition of making the new knowledge generally available by means of a detailed description of their inventions. In this way, inventions can be made available for the benefit of all at the earliest possible stage without inventors running the risk of loss due to commercial exploitation of their inventions by rivals. Patents thus as a rule serve to strike a balance between the interests of society and those of inventors, as well as to promote innovations of use to the community at large by means of an equitable incentive system.

However, the actual exploitation of a patent may be wholly or partially precluded by state-imposed prohibitions, as a patent does not in itself grant a right of use. The directive is also linked to existing international obligations, arising out of instruments such as the Patent Cooperation Treaty of 19 June 1970, the Convention on Biological Diversity of 5 June 1992 and the Agreement on Trade-Related Aspects of Intellectual Property Rights (the TRIPS Agreement) of 15 April 1994. Article 3 of the Charter of Fundamental Rights included in the – albeit not yet ratified – European Constitution, whose provisions include a ban on the reproductive cloning of human beings and on making the human body and its parts as such a source of financial gain, will also be relevant to interpretation of the directive.

In this context, the directive is intended to afford legal certainty in the field concerned for the entire European Union,

with a view to facilitating the promotion of inventions for biotechnology enterprises, thus enabling them to invest more and thereby to enhance their worldwide competitiveness. The European Commission also hopes that the directive will stimulate research, with the prospect of improved medical therapies. At the same time, the directive seeks to address the relevant biological particularities and specific ethical considerations. Yet it is doubtful whether the directive in its present form embodies definitive, non-contradictory responses to the new challenges that have arisen in the sphere of biotechnology. If only because of the rapid pace of progress in the sciences concerned, the directive is inevitably provisional in character. For this reason, the Commission itself emphasizes the need for careful monitoring of future developments. In addition, the Federal Government “has not only decided to transpose the directive into national law, but will also initiate a process of correction at European Community level, where it will seek certain necessary amendments and clarifications” (see the draft law, Bundestagsdrucksache 15/1709, p. 20). This process could also address the criticism occasionally voiced that both the directive and the TRIPS Agreement circumvent international agreements on human rights and the international Convention on Biological Diversity.

At present, the directive at any rate reflects the TRIPS Agreement in providing that inventions may be patented even if they have biological material as their subject-matter (Article 3). Article 5 of the directive stipulates that the “human body at the various stages of its formation and development, including the sequence or partial sequence of a gene, cannot constitute patentable inventions”. The situation differs in the case of 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, “even if the structure of that element is identical to that of a natural element”. Article 6 (1) of the directive prohibits the patenting of inventions whose commercial exploitation would be contrary to *ordre public* or morality, with

the proviso that exploitation shall not be deemed to be so contrary merely because it is prohibited by law or regulation. Examples of non-patentable inventions enumerated in Article 6 (2) are 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 scope of patent protection is dealt with in Articles 8 and 9.

The directive makes no changes to the general prerequisites for the granting of a patent (novelty, inventive step, industrial applicability and adequate disclosure). In Article 5 (3), however, it spells out the prerequisites for patent protection of biological inventions by the sentence: “The industrial application of a sequence or a partial sequence of a gene must be disclosed in the patent application.” Even so, authorities differ on whether and to what extent this clarification restricts substance protection with respect to genes. The directive also has no effect on national provisions precluding the patenting of methods for the therapeutic and surgical treatment of the human body, as well as diagnostic methods (Section 5 (2) of the German Patent Law [PatG]). The same applies to the “privileged status of research” provided for in Section 11 No. 2 PatG.

The draft law consistently transposes the directive’s provisions by the adoption of its wording. However, at some points additions can be found. For instance, Section 1a(3) reads: “The industrial application of a sequence or a partial sequence of a gene must be disclosed in the application concretely together with a specification of the function performed by the sequence or partial sequence”, while the second sentence of Section 2 (2) provides: “The relevant provisions of the Embryo Protection Law shall govern the application of Nos. 1 to 3” (the underlined passages indicate the added words). These additions fall within the scope for such national provisions allowed by the directive. Furthermore, the addition in Section 1a (3) corresponds to Recital 24 of the directive.

The patent legislation of the United States and other biotechnologically important countries, such as Australia, India,

Israel or Singapore, differs in many respects from that of the EU Member States. One significant difference emerging from a comparison of the directive with the relevant American instruments is that these do not provide for a privileged status for research or for statutory exclusion from patentability on ethical grounds. They also apply a wider definition of what constitutes an invention.

3. Objections and criticisms

The process so far has been accompanied by a vigorous debate both in specialist circles and among the public, in the course of which a large number of objections and criticisms have been voiced. A critical opinion on the transposition of the directive into national law has also been expressed by the Bundestag's Commission of Inquiry into the Law and Ethics of Modern Medicine, appointed in Electoral Term 14, in its part-report of January 2001, entitled "The protection of intellectual property in biotechnology".

3.1. Contested patents and patent applications

The granting of specific patents, as well as the filing of certain patent applications, has thus repeatedly aroused criticism on the part of individuals and associations. Some of these cases are described in detail below. They concern in particular issues of scope, subject-matter and the ethical limits of substance protection, and in some cases also the limits applicable to the exploitation of validly granted claims. In a few cases, the question of the patentability of embryos and of cloning arises at the same time. In one instance, the issue is the patenting of stem cells to be derived from cloned embryos, and in another, the possible formation of chimeras – that is, hybrids of animal and human material.

Five of these cases fall within the competence of the European Patent Office (EP), and one within that of the German Patent Office (DE). Two of the enumerated patents were granted by the United States Patent and Trademark Office (US). Although these do not fall within the sphere of application of the directive, they are included to illustrate the international aspects. In one case, there is only the designation “WO” of the World Intellectual Property Organization (WIPO), because the application was withdrawn before any concrete processing by a patent office.

3.1.1. Method for isolating the human genes BRCA-1 and BRCA-2, the mutation of which leads to hereditary breast cancer (EP 0699754, EP 0705902, EP 0705903 and others)

The original patents covered not only the isolation of the genes but also the isolated genes themselves. Objections were raised to the extension of substance protection to all applications of the genes – in particular, for example, diagnostic procedures, as well as therapies and the production of pharmaceuticals. Another criticism was that the patent proprietor permitted diagnostic tests only on payment of high fees and only in its own laboratories. One of the patents for the gene BRCA-1 (EP 0699754) has now been revoked following opposition proceedings, on the grounds that the application lacked novelty. The revocation is not yet legally effective.

Although the following case concerns an invention that does not relate to biological material of human origin, but whose subject-matter is a virus, it is mentioned here because similar objections have been levelled at it. The relevant patent is for gene sequences of the hepatitis C virus (EP 0318216). These sequences are used in diagnostic procedures and, in particular, for screening donated blood. The patent proprietor also claims the exclusive right to conduct such tests. In this case too, the high licence fees demanded for these tests attracted criticism. In 2003, the European Commission criticized the relevant contracts not on patent-law grounds, but as constituting the abuse of a dominant market position.

3.1.2. Gene sequence CCR5, which codes for a receptor on the cell surface (US 6025154)

The function specified in the patent application was that the gene sequence includes the receptor as a possible site of action of drugs used to treat inflammatory diseases. It became known only later that the receptor also performs an important function in regard to penetration of the AIDS virus into the cell. Whether the patent protection extends to this additional function and applications based on it is disputed.

3.1.3. Processes in which human cells are used to produce embryos (DE 69422034; EP 0695351 – the “Edinburgh patent”)

The patent initially comprised a method for isolating *animal stem cells* with a view to genetic manipulation of these cells and to producing genetically modified organisms. Since the English word *animal* includes human beings, a dispute developed over the permissibility of this extension, because human embryos too might then become the subject of commercial exploitation. The applicant has since restricted the patent to non-human cells.

3.1.4. Process for freezing embryos and germ cells, extending to the utilization of the frozen entities (EP 1121015 B 1)

The subject-matter of this patent is a particularly non-stressful form of preservation of biological material. The dispute in this case centres on the claiming of substance protection for the frozen entities and, specifically, its extension to embryos.

3.1.5. Process for cloning living organisms (US 6211429)

The patent does not distinguish between reproductive and research cloning and extends also to the entities produced by the application of the process. The point at issue, in this case too, is the claiming of substance protection and, in particular, the fact that, in the event of successful reproductive cloning, the patent might also cover a fetus and ultimately even a human being born as a clone.

3.1.6. Process for the production of neural precursor cells from embryonic stem cells (DE 19756864; EP 1040185)

The critique in this case is directed towards the fact that the patented method also develops the precursor cells – i.e. multi-potent cells – from human stem cells, which in turn can also be derived from cloned human embryos. It is pointed out, too, that the embryos from which the stem cells are obtained are always consumed.

3.1.7. Process for the genetic manipulation of pig and human embryonic cells for the production of transgenic tissue (provisional designation WO 99/21415)

The criticism in this case was that the process might yield “chimeras”. The application has since been withdrawn.

It is not for the National Ethics Council to offer a detailed legal assessment of the patent applications and granted patents mentioned above. They and the objections to them are enumerated here only to illustrate the nature of the problems arising. These problems are considered in more detail in Section 4.

3.2. General objections and criticisms

On the basis partly of the individual cases mentioned above and partly of wider considerations, the main objections levelled by critics at the relevant provisions of the directive and of the draft law are as follows: patents on “life” are inherently impermissible; the human genome is a common asset of humanity; genes are not substances, but the material form assumed by information; living organisms and their constituents – which include cells and genes – can only be discovered, not invented.

Other points raised include the following. Since genes have a much higher information content than other substances and hence also possess an indeterminably large number of functions, the scope of patent protection – i.e. the inventor’s right

to exclusive commercial exploitation of his invention – should at any rate be confined to the concrete function of a gene segment as described by the inventor in the application, and should not extend to all other functions not yet even identified or described at the time of the application. All-embracing patent protection of this kind would, owing to the resulting blocking effects, give rise to the formation of monopolies and would drive up the prices, of, say, medicines and tests, to unreasonable levels for patients. It would also have the consequence of excessive remuneration of the patent proprietor. This would be unacceptable in terms of medical and social ethics, from the point of view of solidarity with patients, while the excessive remuneration of the inventor would also be unethical. These considerations, according to this view, make it all the more inappropriate to permit “absolute substance protection” covering all applications of a substance obtained for the first time by technical means.

4. Opinion of the National Ethics Council

Since legislative decisions must now be taken forthwith, the National Ethics Council considers itself called upon to issue an Opinion in accordance with its remit. It therefore presents its views on the issues mentioned in Section 3 (Section 4.1) and on further aspects of the patenting of human biological material that it regards as both ethically and constitutionally relevant (Section 4.2). The assessment criteria used are the same as those applied by the National Ethics Council in its previous Opinions. These are, in particular, human dignity, protection of life, improvement of therapies and considerations of social ethics, on the one hand, and the freedom of economic activity and of research, on the other.

4.1. Opinion on the general objections

4.1.1. Issues of ethical and scientific principle

4.1.1.1. Are patents on “life” permissible

Those who categorically reject biotechnological patents argue from the conviction that “life” is inherently unpatentable. Life is distinguished biologically from inanimate nature by specific characteristics, which include cellular organization, metabolism, variability, the capacity to react to stimuli and the capacity to reproduce. For this reason, genes, nucleic acids and proteins, considered in themselves – that is, independently of and in isolation from living organisms – are not alive. The ethics of their patentability are nevertheless hotly debated. Microorganisms and bacteria, for their part, certainly do constitute living organisms. The current international legal consensus (Article 27 of the TRIPs Agreement) is that they are patentable. This fact has aroused hardly any ethical criticism. It follows that the boundary of patentability does not coincide with the boundary between animate and inanimate nature.

A fundamental critique concerns the patenting of the human body at the various stages of its formation and development, as well as of isolated elements of the human body. Their patenting would run counter to the respect for life and its non-disposability, and hence also to the protection of human dignity. In this respect, the draft law, like the directive, takes account of the special status of human life by expressly prohibiting the patenting of the human body “at the various stages of its formation and development”. The issue of the patentability of human embryos and human embryonic stem cells will be discussed in more detail in Section 4.2.1. It will then become clear that exclusions from patentability are appropriate in these cases too.

4.1.1.2. The genome – a common asset of humanity?

It is asserted that genomes, and, in particular, the human genome, have not been created by human beings, but are a

common asset of humanity. The genomes ought, for this reason, to be freely available to anyone for research and application. The first point arising here is whether this assumption does not apply equally to inanimate nature. If not, however, the further question would arise as to the existence of relevant differences between animate and inanimate nature or between individual elements of these that would justify a distinction as regards patentability. Account would have to be taken, for example, of possible differences, as discussed below, between other chemical substances and DNA molecules or genes (see Section 4.1.1.4).

As already stated in Section 2, the freedom of research is guaranteed in German law by the privileged status accorded to research. It is therefore not threatened by the patenting of genes and their functions and applications. Those in favour of patenting also point out that, with regard to application – except in the rare case of absolute substance protection (see Section 4.1.2.1) – it is not the genome as such that is claimed, so that fundamental genetic research is unaffected by patent protection.

4.1.1.3. Economic aspects

It is further argued that pharmaceutical research and development to market may call for the investment of very large sums – estimated at up to several hundred million euro in certain recent cases. Such a level of expenditure can be justified only by patent protection for a certain period, to allow a reasonable estimate of the payback required on the investment. Rather than facilitating the development of new pharmaceuticals, the complete exclusion of inventions based on exploitation of the human genome or human genes would therefore make it substantially more difficult or even impossible. This, it is argued, would not constitute reasonable use of an avowed “resource for mankind”.

However, a possible counter-argument is that the isolation of genes alone does not yet involve a high level of expenditure

and costs for pharmaceutical companies, but that these arise only in the course of research and development of a drug to market. Furthermore, the desired effect – covering the inventor’s outlay – can still be achieved if patent protection is confined to functions.

The issue here is ultimately the scope of patent protection, and not its total elimination. Another problem arising independently of the extent of patent protection is that the monopolization of parts of the genome or of specific genes might also impede the development of medicinal products and cause problems with the treatment of patients.

4.1.1.4. Are genes substances or information, or both?

A fundamental problem in identifying inventive step in the field of biotechnology is the difficulty of determining what has been invented and is consequently intended to constitute the protected subject-matter. The question here is what should be covered by the exclusive right of exploitation protected by a patent: a natural substance – a piece of deoxyribonucleic acid having a specific composition – or an item of information and a function mediated by this substance?

The problem arises because genes in effect have a twofold character: they are, on the one hand, material (the chemical compound deoxyribonucleic acid, or DNA) and, on the other, the media of genetic information used by cells for the biosynthesis of specific proteins. As natural substances, genes would, according to the decisions of the Federal Court of Justice, in principle be patentable if they were made available for commercial exploitation by whoever describes them for the first time. The precedent for absolute substance protection for natural substances was the Federal Patent Court’s Antamanid judgement of 1977 (GRUR 1987, 238f.). However, not only have methods of isolating DNA, as well as its substance-related composition, been known for a long time, but it has also for many years been possible to sequence this compound. Although the importance of the substance-related properties or

genes is not disputed, it is clear in this situation that, as a rule, the making available of a hitherto unknown DNA sequence does not in itself constitute an invention.

A stricter criterion of the novelty of an invention in this field is the description of the information contained in a DNA sequence, or of a specific function performed by it, which is thereby made available for application. Now a specific DNA sequence may include the information not only for one protein but for several. These may differ and be partly independent of each other, as, for example, in the case of DNA sequences that code for a number of proteins or of alternatively spliced reading frames. The total information content of DNA sequences is therefore unpredictable both for the applicant who files a patent and for its examiner. The granting of a patent for the entire information content of an isolated DNA sequence would therefore excessively reward the person who isolates the sequence and describes one of its applications.

An objection raised to this view is that information is contained not only in DNA but also in quite different substances discovered earlier. For example, the possible applications of certain medicinal substances of non-biological origin are stated to vary so greatly that the first invention for a given application could be followed by subsequent inventions for other applications. The correct view, it is argued, is that many substances possess different functions, and hence different potential applications, according to the circumstances in which they deploy their activity. This would apply equally to substances of inorganic and organic origin. However, this does not yet answer the question whether such substances can be regarded as information carriers in the same way as DNA, and whether the functions of DNA can be compared with those of other molecules.

Ordinary molecules contain only information about their own structure. The sequence of DNA, by contrast, also includes information for the biosynthesis of other molecules (e.g. RNA or proteins), which may in turn have different functions. The

function of DNA in this case is that of instruction: it provides cells with information necessary for the biosynthesis of proteins. Additional information from the cell itself is admittedly required for the correct processing of this information, so that neither the structure nor the function of a protein is completely described by a DNA sequence; nevertheless, this capacity for instruction distinguishes DNA from all other known natural substances (except RNA, which, however, belongs to the same class of molecules as DNA).

Again, unlike other molecules, DNA has the capacity for replication – that is, for identical duplication in the process of cell division and the transmission of hereditary characteristics. Some consider these peculiarities of DNA as an information carrier, as compared with other substances, to be only quantitative, while others regard them as qualitative in nature. At any rate, this situation must be taken into account in the debate on the patentability of DNA sequences.

4.1.1.5. Can living organisms and their elements be invented at all?

Living organisms as such, and consequently also human organisms and their elements, including their genes, can not be invented, but only discovered. For this reason, genes are not patentable unless other circumstances relevant in patent law also apply. This is clear from general considerations of patent law, and is moreover also expressly stated in the directive (Recital 16).

The situation is different if the isolation of a gene and hence the making available of that gene for subsequent applications in itself constitutes an inventive step of the degree required by patent law. This may be the case, for example, where novel techniques for isolating a specific gene are invented. The result is something that cannot simply be discovered, so that this at any rate constitutes an essential prerequisite for the granting of a patent that also, in accordance with the current provisions of patent law, includes substance protection. In the present state

of the art of gene isolation and sequencing, however, such cases surely represent the absolute exception, as will be explained in more detail in the next section.

4.1.2. Restrictions of patent protection

4.1.2.1. Is “absolute substance protection” inappropriate?

The first question to be considered in this connection is whether and to what extent cases of “absolute substance protection” can and should exist at all for biological substances of human origin, or whether a restriction of patent protection is appropriate or indeed essential on ethical grounds. Current patent law permits substance protection of this kind for human genes, in accordance with the considerations adduced in Section 4.1.1.5, if the making available of a gene satisfies all the prerequisites of patent law – in particular, those of inventive step and novelty. Opinions differ – even within the National Ethics Council – on the above question.

Some hold that a decision is necessary in each individual case as to whether the concrete provision of a gene meets these conditions of patent law, because, in particular, the boundaries of the criteria of inventive step and novelty are fluid, so that the requirements as to inventive step become more stringent with time. According to this view, the sequencing of a gene, a nucleic acid or a protein has, with scientific progress, substantially become the state of the art and the technologies for isolating and sequencing these substances have now become standard methods. As a rule, it can therefore be assumed that the determination of such sequences and hence, for instance, the making available of a given DNA, by themselves, can no longer be deemed to constitute an invention today. Moreover, it is argued, the sequences of the human genome are already substantially known. In the case of human beings, it is therefore now virtually impossible to imagine a case in which the isolation or determination of a DNA sequence can still be regarded as comprising an inventive step.

Advocates of this position consider exclusion of comprehensive substance patents extending beyond the current legal position to be inappropriate. Indeed, in their view, it is doubtful whether this would at all be permissible under Article 27 of the TRIPs Agreement. Difficult questions would also arise in respect of patents already granted. In particular, any attempt to define a boundary between an invention and a discovery in this field, differing from that enshrined in the general patent legislation, would appear to have little prospect of success. For this reason, determination of the relevant boundaries in the small number of cases still to be expected should continue to be left to patent practice, which, after all, has hitherto applied increasingly stringent criteria for inventive step in the field of biotechnology.

Others argue that, regardless of the provisions of patent law, the first-time isolation of genes by novel technical means and the resulting provision of these genes for subsequent relevant applications does not constitute an invention. This is because it is not the genes but the technical process for their isolation that has been invented. In this case too, genes are therefore considered not to be patentable. Moreover, the mere technical isolation of a gene cannot justify absolute substance protection – that is, the granting of a patent covering all functions of an isolated gene, including unknown functions.

The protagonists of this position therefore consider it appropriate for a clear regulatory answer, extending beyond the current legal position and the provisions of the draft law, to be given to the question of when a patentable invention exists in the relevant field. They are thus unwilling to leave the answer to this question, and hence also determination of the boundary between an invention and a discovery, to patent practice or the courts. In their view, although the criteria for inventive step applied by patent practice have become more stringent, not a single relevant case is at a stage that promises an early or definitive answer to this question.

With regard to the natural gene sequences discussed above, it is essential to distinguish cases in which the inventive step

consists in a substantial modification of the natural sequence of a DNA and in the production of a protein derived from it, which thus does not occur in nature. Depending on the prior art, patent protection in this case should extend to the modified sequence and the newly produced protein as a whole, and not to specific functions of the sequence and of the protein. The decisive step lies in the modification of the natural state or of a specific sequence and in the associated invention of novel proteins and functions.

4.1.2.2. Restriction of substance protection by the specification of functional applications

The following consideration is concerned not with the question of “absolute substance patents”, as discussed above, but with the patenting of an invention that already presupposes the isolation of the gene and relates to functional applications that are described in detail. Differing degrees of restriction of protection are called for in these cases.

It is true that the human genome contains only a limited number of genes, currently estimated at 30 000. It is also the case that genomes possess a very much greater information content than other substances and perform an indeterminably large number of functions. The same applies to the functions of the proteins for which the genes code. For this reason, depending on the extent of protection, patents in this field may also, by virtue of overlapping gene sequences with different functions, result in more extensive blocking effects than those occurring in other spheres. For the same reason, a return substantially in excess of the necessary and appropriate level (“excessive remuneration”) cannot be ruled out.

Where absolute substance patents or patents with broad claims have been granted in the past, retroactive restrictions are as a rule inappropriate. Such situations can at most be to some extent remedied by the imposition of a compulsory licensing requirement (Section 24 of the German Patent Law [PatG]). The draft law (Article 1 No. 9) proposes to facilitate

the granting of these licences by amending the provision contained in Section 24 (2) PatG so as to abolish the current additional requirement of “public interest” for the granting of compulsory licences in all the cases of dependence mentioned therein. Careful monitoring will be necessary to determine whether this facilitation is sufficient. At any rate, use should be made of the instrument of compulsory licensing in all suitable cases.

In the future, however, a further limitation will accrue from the new provision of Section 1a(3) of the draft law, which reads as follows: “The industrial application of a sequence or a partial sequence of a gene must be disclosed in the application concretely together with a specification of the function performed by the sequence or partial sequence.” This requirement to specify the function of the sequence or partial sequence is, according to the explanatory memorandum of the draft law (p. 10), not merely a formal requirement of the application procedure. The description of the function, according to the explanatory memorandum, is in fact the fundamental criterion of determination of the gene segment to be patented, to which the patent must be restricted. This addition to current patent law, reflecting Recital 25 of the directive, is intended to avoid the overlapping of gene sequences with different functions and hence also inappropriate blocking effects and excessive rewards.

The success of this provision depends on the interpretation in this context of the phrase “specification of the function performed by the sequence or partial sequence”, as required by Section 1a (3) for the concrete description of industrial applicability. Three possible interpretations can be imagined:

- a) According to a broad interpretation, patent protection could be deemed to extend to the protein for which a gene codes. The function of the gene sequence would then consist in the coding for precisely this protein. All functions of this protein would then also be protected.

- b) An intermediate interpretation might be that only the specified function of the protein is protected – for instance, that of being the receptor for a hormone. Other, as yet unknown, functions would then not be covered.
- c) A narrow interpretation of the phrase would have the consequence that protection would extend not to the described function as a whole but only to its concretely specified application – for example, the treatment of a specific disease.

Opinions differ, within the National Ethics Council as elsewhere, on which interpretation is appropriate. According to one view, the overwhelming weight of evidence favours interpretation c), on the grounds that it results in a situation that comes closest to the objective outlined in the explanatory memorandum to the draft law, because it on the one hand reduces the dangers of overlapping and excessive remuneration, while, on the other, permitting the payback estimates essential to the development of new pharmaceuticals (see Section 4.1.1.3 above).

Others hold that interpretation b) would as a rule be more appropriate. If a new function of a protein is disclosed by research, the appropriate remuneration aimed for by patent law can perfectly well consist in the extension of patent protection to all industrial applications that make use of the disclosed function, which thus include ones not explicitly claimed.

Notwithstanding these differences, the protagonists of the first position, in common with most European Union Member States that have so far transposed the directive into national law, consider that the question of the correct interpretation should, in this case too, be left to patent practice and not be decided on a statutory basis. Only patent offices and the courts can, in their view, take account of all the subtleties of an individual case. In individual cases, too, it would be easier for them to decide whether different functions of a gene are in each case determined by one specific gene segment. However, further developments should be carefully monitored.

Others, on the other hand, consider the formulation of Section 1a (3) of the draft law to be insufficiently concrete. On this

point too, they therefore call for an explicit formulation to the effect not only that patent applications should describe the function performed by the sequence or partial sequence of a gene, but also that the scope of the patent claim should extend solely to this described function and application. They point to the existence of corresponding provisions in France, Spain and Portugal.

4.2. Other ethical and constitutional issues

4.2.1. Prohibitions of patenting under Section 2 (2) of the draft law

Other aspects of both ethical and constitutional relevance are the prohibitions of patenting embodied in Section 2 (2) of the draft law. They are based on the correct consideration that certain acts of exploitation would constitute particularly serious violations of *ordre public*, and especially of human dignity. The general principle of patent law that the prohibition of certain acts necessary for an application precludes only the protected application, but not the granting of the patent, is rightly considered to be inadequate in these cases. Significantly, the enumeration in Article 6 (2) of the directive is preceded by the words “among others”, while that of Section 2 (2) of the draft law commences with the word “*insbesondere*” [“especially”], so that these enumerations are not exhaustive. Opinions differ, however, on whether prohibitions of patenting should be based on a general European *ordre public* or on the relevant national *ordre public*. The answer to this question would determine whether the European Court of Justice or national courts had ultimate competence for interpretation and additions. In the present situation, however, a European *ordre public* can presumably be said to exist only where the relevant legal conceptions of all member countries coincide – for instance, on the prohibition of reproductive cloning, of germ line modification or of the production of hybrid entities (see Recital 38 of the di-

rective). In the absence of such a consensus, the right of binding determination of what constitutes *ordre public*, on the basis of their fundamental values, cannot be taken away from the Member States. Neither the fundamental treaties of the European Union nor the draft Constitution provide that the Member States have placed this fundamental competence at the disposal of the European Union. Should the European Patent Office nevertheless grant patents that violate German *ordre public*, they may not be exploited at least in the Federal Republic. The same applies to any such patents granted by other international or foreign offices. Where such patents extend to the Federal Republic, revocation proceedings can be instituted against them.

This has the following implications:

The prohibition of the patenting of processes for cloning human beings contained in Section 2 (2) No. 1 of the draft law admits of differing interpretations. Article 6 (2) (a) of the directive, which is here copied, unquestionably bans the patenting of processes for reproductive cloning throughout the European Union. This prohibition also follows from Article 3 of the Charter of Fundamental Rights. However, the prohibition is not unequivocal in the case of research cloning, because the term “human beings” is defined differently by the individual European Union Member States and also because, for this reason, research cloning is not addressed in Article 3 of the Charter of Fundamental Rights. The fact that, for example, the United Kingdom has transposed the directive into national law including this provision, even though research cloning is permitted in the UK, would otherwise be incomprehensible. In the Federal Republic, by contrast, the relevant instrument is the Embryo Protection Law, whose applicability to the interpretation of the prohibitions enumerated in Section 2 of the draft law is now explicitly laid down in the second sentence of Section 2 (2). However, many take the view that the Embryo Protection Law should be interpreted as prohibiting research cloning. This

situation would change if different legislative provisions were adopted in Germany. National competence for decisions in this particularly sensitive ethical field is thus preserved.

The prohibition of germ line interventions contained in Section 2 (2) No. 2 is unequivocal and leaves no scope for divergent interpretations. An embryo as such cannot – at least in the Federal Republic – constitute a patentable invention because it falls within the purview of the phrase “human body, at the various stages of its formation and development” used in Section 1a (1) of the draft law and is therefore excluded from patentability. However, the significance and scope of the prohibition pursuant to Section 2 (2) No. 3, which excludes the use of human embryos for industrial or commercial purposes from patent protection, is again unclear. The very term “embryo” is defined differently in the individual member countries. Moreover, the formulation could suggest that patenting is permissible for processes and, where applicable, also the substances thereby obtained when embryos are used not for commercial or industrial but for therapeutic or research purposes – that is to say, when they are consumed, for instance, for the production of embryonic stem cells and stem cell lines. Such an interpretation might be regarded as finding support in Recital 42 of the directive, which provides that “in any case such exclusion” from patenting “does not affect inventions for therapeutic or diagnostic purposes which are applied to the human embryo and are useful to it”. In this connection, though, some consider that there is no consensus on whether this means usefulness to the individual embryo concerned or to the category of embryos in general. The embryo would be consumed in the latter case only. The question of drawing an unequivocal distinction between commercial and therapeutic purposes would also be left open. Pharmaceuticals, for example, are produced with both of these objectives in view. Finally, it seems difficult to reconcile the industrial applicability of the invention, as a condition of patentability, with the prohibition on using the invention for commercial purposes.

However, these points need not be considered further, because they too are governed, according to the second sentence of Section 2 (2) of the draft law, by the Embryo Protection Law, which provides for an absolute ban on embryo-consuming techniques and consequently also on the production of embryonic stem cells and stem cell lines. For this reason, the grant of a patent for such techniques in, or having effect in, Germany is precluded. The situation is presumably different in the case of the patenting of embryonic stem cells produced outside the Federal Republic, of stem cell lines derived from them and of modifications to both of these, if the relevant stem cells or stem cell lines have been imported legally in compliance with the Stem Cell Law of 28 June 2002, because the deciding ground for the prohibition of patenting does not then apply. National competence for decisions in this field, which also involves sensitive ethical issues, is at any rate preserved.

It follows from the foregoing that further prohibitions do not apply to the patenting of other cells (see Section 4.1.1.1 above) – for example, somatic cells – and of microorganisms. Such prohibitions cannot be derived, in particular, from the notion of *ordre public* on the grounds that “life” is at issue. This is because, as stated earlier, the *ordre public* of the Federal Republic comes into play only with respect to entities having the capacity to give rise to born human beings.

4.2.2. Evidence of origin

If an invention has as its subject-matter biological material of plant or animal origin or if it involves the use of such material, Section 34a of the draft law, like Recital 27 of the directive, requires its geographical origin, if known, to be specified in the application. There is no mention of sanctions for failure to comply with this directory provision. The Federal Government – reflecting the coalition parliamentary groups’ motion of 10 March 2004 – intends, following its decision of 25 June 2003, to seek at EU and international level to have the directory provision replaced by a mandatory requirement or to aim for a

system with sufficient flexibility to allow mandatory provisions to be included in national legislations. Even if the nature of any concrete sanctions for infringing such a provision is as yet undetermined, the intention is noteworthy, because it is only by means of such evidence that the fair and equitable sharing of the benefits arising out of the use of genetic resources can be assured. Such sharing, in the field of plants and animals, is one of the objects outlined in Decision III/17 of the Conference of the Parties to the Convention on Biological Diversity.

Some have drawn attention to an internal instruction by the President of the German Patent Office (Communication 11/94 of 8 August 1995) that already included a directory provision on the filing of sequence protocols requiring the statement of origin of the relevant material to include the name of the individual concerned in the case of material of human origin. Those who make this point consider it in any case hard to understand why the requirement of such evidence should be dispensed with in the case of material of human origin. The origin of this material, in their view, may perfectly well be relevant, for instance to facilitate the sharing of poor countries in medical progress and its results. For example, with biological material of human origin as well as with other material, patenting for a minimum term of 20 years could have the consequence that people in poor countries are deprived of access to the therapeutic innovations thereby protected, even if substantive research and inventions accrued precisely from material originating from such countries. An objection to this argument is that human genes as a rule differ hardly at all from continent to continent. Again, it is usually no more difficult to obtain such material from industrialized states than from poor countries. It is surely impossible to give a final answer to these questions at present. For this reason, further discussion at international, European and also national level is recommended, eventually leading to the appropriate conclusions. The issues surrounding evidence of origin could also be dealt with in the context of the provision of evidence of informed donor consent (see Section 4.2.3).

4.2.3. Donor consent

Recital 26 of the directive provides that, in the case of an invention based on biological material of human origin, the donor, where a patent application is filed, must have had an opportunity of expressing free and informed consent, in accordance with national law, to the taking of the material. In the Federal Republic, this is supposed, according to the explanatory memorandum to the draft law, to be already assured, “for instance, by provisions of public-health, criminal and data-protection law”. Any shortcomings in enforcement “must be dealt with under that legislation” (see p. 8 of the draft law). This notion is not universally accepted. German law at any rate contains no concrete provisions as to the nature of the information to be furnished in each case, on which the validity of the consent will depend in the specific instance. According to the National Ethics Council’s Opinion on biobanks, it should include, for example, details of “any commercial prospects of the proposed research (including the possibility of filing patent applications on the results)” (p. 15). However, such a consideration is at present irrelevant to the granting of patents, because the current applicable law does not even require evidence of general consent.

Since an important sphere of individual autonomy is at issue here, this seems unacceptable. Instead, a provision should be added to the draft law making it mandatory to furnish evidence, subject to observance of the provisions governing personal rights and of the data protection legislation, that the donor has consented and that appropriate information, including in particular information on the possibility of a patent application, has preceded the consent. In the unlikely event of there being no national competence in this respect notwithstanding Recital 26, a provision to this effect should be included in the general legislation that is in any case proposed (e.g. in the Genetic Diagnosis Law already announced). A particular argument in favour of such a provision, which was also demanded by the Bundestag’s Commission of Inquiry into the

Law and Ethics of Modern Medicine in 2001, and of appropriate sanctions for non-compliance, is that this issue arises in this form only in connection with biological material of human origin. In certain circumstances, an affirmation in lieu of oath included in the application, confirming that the relevant statements of consent have been deposited or that the material was donated at a time when such consent was not yet required, could constitute sufficient evidence. If the material was donated outside the Federal Republic, evidence of compliance with the provisions applicable to informed consent in the country concerned will presumably have to suffice. This may also include a reference to relevant individual statements of consent.

However, any tendency towards the adoption of provisions allowing donors to share in benefits accruing from the exploitation of a patent should be avoided, as this would encourage the commercialization of tissue donations (see p. 76f. of the National Ethics Council's Opinion on biobanks).

4.2.4. Freedom of research

Apart from a mention of plant varieties (Section 11 No. 2a of the draft law), neither the directive nor the draft law contains any specific provisions to safeguard the freedom of research. These appear superfluous in the draft law because an overall "privileged status of research" is already provided for in Section 11 No. 2 of the Patent Law and therefore applies also to biotechnological inventions. These may consequently be exploited for research purposes even without a licence provided that experiments are carried out on, and not with, the protected subject-matter. The constitutionality of the privileged status of research, which also includes clinical trials, was confirmed by the Federal Constitutional Court in its judgement of 10 May 2000 (1 BvR 1864/95).

Position statement

On the basis of these considerations, a majority of members of the National Ethics Council has made the following recommendations:

The efforts of the Federal Government to transpose European Directive 98/44/EC into national law are applauded and should be finalized as soon as possible. In this connection, the National Ethics Council takes it that the provision laid down in Section 1a (3) of the draft law is intended not as a formal requirement of the application procedure, but as a limitation on the content of patent protection (see Section 4.1.2.2). The National Ethics Council further recommends additional provisions (if necessary outside the field of patent law) on the furnishing of evidence of donor consent, which must be preceded by the furnishing of information on the possibility of filing of a patent application (see Section 4.2.3). However, failing imposition of the requirement of donor consent advocated here, a legal obligation to furnish evidence of origin (see Section 4.2.2) would surely be problematical.

There is no need for further additional regulation at present. Again, the abolition of comprehensive substance protection for the few cases in which the making available of a gene might in the future still be regarded as a novel invention would conflict with Article 27 of the TRIPs Agreement. Instead, it seems sufficient for the time being to leave the concrete handling of substance protection, the limitation of patent protection and determination of its concrete form to patent practice in accordance with Section 1a (3) of the draft law.

The National Ethics Council recommends careful monitoring of further developments and, in particular, of the practice of patent offices, including the European Patent Office, and of the courts. This applies specifically to the handling of “substance protection” and of prohibitions on the grant of patents on *ordre public* grounds, as well as to the handling of the award of compulsory licences, as already facilitated by the draft law – a system that should be applied in all suitable cases. The

criteria applied in each and every relevant decision on these aspects should be disclosed and constantly clarified. Should the course of decisions in practice give rise to misgivings in terms of the considerations developed in this Opinion, the National Ethics Council recommends action to seek the necessary changes and clarifications in the context of the correction process at European Union level already proposed by the Federal Government.

Position statement in favour of stricter requirements

Although the members of the National Ethics Council whose names appear below also welcome the Federal Government's efforts to transpose the European directive into national law, they regret that, in view of the lapse of time since the adoption of the directive and of the European Commission's reference of the Federal Republic to the European Court of Justice, it is no longer possible to review a number of fundamental points in the directive. In these circumstances, it is particularly important to take full advantage of the currently existing scope for national regulatory approaches and freedom of action, as has been done, for example, in France, Portugal and Spain and is proposed in Italy. However, any aspects not covered by the directive must, as the Federal Government proposes, be notified as of now to the European Commission and be incorporated in the explanatory memorandum to the draft law, with a view to initiating a revision of the directive as soon as possible.

Yet a system that is both convincing and effective will ultimately be achievable only if, along the lines of the decisions on public-health issues taken by the WTO Ministerial Conference in Doha in 2001, efforts are made to secure amendment of the TRIPs Agreement or at least a common interpretation providing for additional flexibility in its application. Independently of such action, the European Patent Office should attempt to reach

agreement with the US Patent and Trademark Office and the Japanese Patent Office on as far as possible harmonizing their decision criteria. Specific recommendations:

1. The relevant legal instrument should provide that the scope of protection of a claim to a DNA sequence isolated from the human body and not newly synthetically developed should be limited to the technical application of a function specifically set forth in the patent description and claim. Contrary to the provision laid down in Section 1a (3) of the draft law, it is insufficient for the industrial application of a sequence to be described in the patent application with a specification of its function: the function must be included in the claim. The concrete function to be specified and its application must be deemed to constitute the legally binding limits of the protection afforded by the patent. The same applies to non-human gene sequences. In addition, the relevant law should provide that the rights conferred by the granting of such a patent may not be cited against a subsequent claim for the same sequence if that claim is for another, specific application of this sequence.
2. The relevant law must clearly state that reproductive human substances (oocytes, sperm cells or gonadal tissue), human organs and embryos, as well as human embryonic stem cells and stem cell lines, are not patentable. The same applies to processes for the formation of chimeras using human germ cells and to parthenogenetic processes involving the use of human genetic material, as well as to the organisms and/or biological entities obtained by these processes. The wording of Sections 1a (1) and 2 (2) of the draft is inadequate in this respect and must be corrected.
3. The scope of protection for elements of the human body must not extend beyond the concrete technical application of a function, which must be precisely described in the patent application; that is, the claim in the patent ap-

plication and in the granted patent must be confined to this technical application. This is the only way to preclude “strategic patents”. Section 1a (2) of the draft should be amended to take account of this requirement.

4. There should be a statutory obligation to furnish evidence of the origin of the biological substances of human and non-human origin used in each case.
5. The relevant law must provide for mandatory free and informed donor consent, which must be preceded by adequate information that must extend also, and in particular, to the possibility of filing a patent application. Due evidence of the protection of donors’ personal rights and of compliance with data protection requirements must be furnished.
6. In view of the manifest difficulties of specifying clearly and in binding form what constitutes an “invention”, the explanatory memorandum to the law must explicitly state that, pending the adoption at European level of provisions precisely defining the prerequisites for and limits of an “invention”, the term must be interpreted as restrictively as possible.
7. Precisely with regard to the patent procedures here at issue, it is essential to consider not only the prerequisites for the granting of a patent but also, and in particular, the consequences of patenting. Particular importance therefore attaches to compulsory licences, especially in the case of diagnostic or therapeutic methods. Such licences should therefore be granted in a deliberately targeted manner.
8. Both the patent offices of the EU Member States and the European Patent Office must disclose and constantly clarify the criteria used whenever *ordre public* is invoked. This is the only way to ensure clear and prompt recognition of the limits of a patent application and of the underlying reasons for them.

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