

## RELAXIN PATENT VALIDITY EXERCISE

### ANNEX: DOCUMENT 9

#### EPO DECISION ON THE RELAXIN PATENT

##### EXTRACT FROM THE OFFICIAL JOURNAL OF THE EPO 6/1995 388

*Note: It is suggested that this is studied after the validity exercise, for private study or to facilitate group discussion in the review of the exercise. This extract excludes material on procedural issues - where text has been omitted, this is indicated thus: [...]*

#### Howard Florey/Relaxin

**(Oppositions by Fraktion der Grünen im Europäischen Parlament; Lannoye)**

#### HEADNOTE

Human H2-relaxin had no previously recognised existence. The patentee had developed a process for obtaining H2-relaxin and the DNA encoding it, had characterised these products by their chemical structure and had found a use of the protein. Typical claims (set out in full in the Annex to the Decision) of the granted patent were:

1. A DNA fragment encoding human H2-preprorelaxin, said H2- preprorelaxin having the amino acid sequence set out in Figure 2.
2. A DNA fragment encoding human H2-prorelaxin, said H2-prorelaxin having the amino acid sequence set out in Figure 2 with the exception that the signal sequence is excluded.
3. A DNA fragment encoding a polypeptide having human H2-relaxin activity, said polypeptide having an A-chain and a B-chain comprising the following amino acid sequences:

*[see earlier copy of full patent document- Document 7 in this Annex]*

[...]

19. Synthetic human H2-preprorelaxin having the amino acid sequence as set out in Figure 2.
20. Synthetic human H2-prorelaxin having the amino sequence as set out in Figure 2 with the exception that the signal sequence is excluded.
21. A polypeptide having human H2-relaxin activity, said polypeptide having a disulphide bonded A-chain and B-chain comprising the following amino acid sequences:

[see earlier copy of full patent document]

Opposition had been entered by the Fraktion der Grünen, and separately by their Fraktionspräsident (Paul Lannoye), under Articles 100(a) and (b). However, no prior art was cited in respect of the lack of inventive step, the closest state of the art for the subject-matter of Claim 1 being, according to the opponents, the woman from whom the mRNA used to prepare the H2-relaxin cDNA was isolated.

Three days before the oral proceedings the patentee submitted a declaration by Professor E.A. Bauer. The patentee also questioned the admissibility of the opposition by opponent 01, but without specifically requesting that it be declared inadmissible. The issue of admissibility of an opposition filed in the name of a political fraction had also been canvassed in earlier telephone discussions between the formalities officer and the opponents.

**Held**, by the Opposition Division, rejecting the oppositions:

[.....]

4. Since it was common ground among the parties that, until a cDNA encoding H2-relaxin and its precursors had been isolated by the patentee, the existence of this form of relaxin was unknown, the novelty of the granted claims was assured.
5. The opponents' argument as to lack of inventive step failed for the reason that the gene was novel. In isolating the DNA encoding human H2-relaxin the patentee was therefore not preparing a known substance by conventional means but instead providing to the public for the first time a product whose existence was previously unknown.
6. The opponents' argument that the subject-matter of the patent represented a mere discovery was wrong. The consequences asserted by the opponents as to the patentability of such discoveries as the moon (after the Americans landed on it in 1969), *Otzi* (a mummified, around 5,000-year-old man found in the Italian-Austrian Alps) or a new animal found in some remote area, did not follow.
7. In relation to the objection under Article 53(a) (morality), the opponents' arguments as to slavery and the dismemberment of women betrayed a fundamental misunderstanding of the effects of a patent.
8. The argument that human life was being patented was also unfounded, DNA not being 'life' but instead a chemical substance which carries genetic information and which can be used as an intermediate in the production of proteins which may be medically useful.
9. Pending the final formulation of the EU Directive on the legal protection of biotechnological inventions, it was inappropriate for the EPO to impose a moratorium on the patenting of human genes. Nor was there any legal mechanism in the EPC for doing so.
10. The opponents' request that the EPO carry out a referendum as to the public's view in Contracting States on what should be patented was misconceived. The burden of proof lay with the opponents. It was for them to carry out such survey, if they considered that it would assist their case.
11. The Article 53(a) exclusion on the grounds that an invention is contrary to morality was limited to the limited class of case where there was an overwhelming consensus that the exploitation or publication of an invention would be immoral.

[.....]

# TEXT OF DECISION

## Facts and Submissions

I. European patent No. 112 149 is based on European patent application No. 83307553.4 filed on 12 December 1983 and claiming priority from AU 7247/82 filed on 13 December 1982. Mention of the grant of the patent was published in the European Patent Bulletin on 10 April 1991. The proprietor of the patent is the Howard Florey Institute of Experimental Physiology and Medicine.

II. Notice of Opposition was filed on 9 January 1992 by the Fraktion der Grünen im Europäischen Parlament (I) and separately, with an identical text, by their Fraktionspräsident, Mr Paul Lannoye (II).

II.1 The grounds for both oppositions were that the subject-matter of the patent is not patentable (Article 100(a) EPC) for lack of novelty and inventive step (Articles 54 and 56 EPC respectively), that it represents a discovery and as such is not patentable under Article 52(2)(a) EPC, and that it offends against 'ordre public' or morality (Article 53(a) EPC). The opponents requested the revocation of the patent in its entirety. The only document cited was EP -A-169 672.

[.....]

IV. Since all parties had requested oral proceedings, these were appointed with a communication dated 28 March 1994. In the annex to the summons, the preliminary opinion was further expressed that the subject-matter of the claims was novel and inventive and did not constitute a discovery. No comments on the objection under Article 53(a) EPC were made.

V. With letters dated 30 November 1994 and 2 December 1994, three third parties filed observations under Article 115(1) EPC expressing their opposition to the patenting of the present invention.

[.....]

VIII. Oral proceedings took place on 8 December 1994. At oral proceedings the opponents submitted a request to have the Opposition Division declared partial, contending that partiality was demonstrated by an alleged gross mistake made in the annex to the summons to oral proceedings. This request was rejected after deliberation by the Opposition Division.

IX. At the end of the proceedings the chairman announced that the oppositions were rejected under Article 102(2) EPC.

## Reasons for the Decision

[.....]

### 3. *Partiality*

3.1 The opponents asserted that the preliminary opinion set out in the annex to the summons to oral proceedings contained a gross mistake and that this proved the Opposition Division to be biased in favour of the proprietor. This alleged mistake was the statement, made under point 3, lines 10 to 11, that the claimed [H2-relaxin] gene was in the form of a cDNA. According to the opponents, this was untrue since Claim 1 referred to a 'DNA', not a 'cDNA' fragment. The opponents also made much of the fact that the word 'gene', used in the claims of the application as filed, was changed to 'DNA fragment' on grant.

3.1.1 The committal of a gross error during opposition proceedings may indicate partiality but does not necessarily do so. However, no gross error has occurred. Claim 1 relates to a DNA fragment encoding human H2-preprorelaxin, said preprorelaxin having the amino acid sequence set out in Figure 2. This sequence is encoded by a cDNA derived from the H2-relaxin mRNA. The genomic DNA encoding H2-relaxin contains an intron interrupting the coding region (see page 11, lines 49 to 51, of the description). It is in consequence a fact that a DNA fragment encoding the amino acid sequence of Figure 2 (without the amino acids encoded by the intron) is not present in the human genome.

3.1.2 In the light of the above, the Opposition Division takes the view that Claim 1 is directed to a cDNA sequence encoding preprorelaxin despite the fact that the word 'cDNA' is not mentioned in the claim. The Division moreover wishes to emphasise that its decision in the present case would not be affected in anyway even if genomic DNA sequences encoding human relaxin were included in the scope of the claims. This issue is therefore irrelevant, as is the matter of the term 'DNA fragment' (introduced at the grant stage by the Examining Division for uniformity with the parallel human relaxin

patent EP-B-101 309) as opposed to 'gene'. These two terms will be used interchangeably throughout this decision.

3.2 The opponents further alleged that the preliminary conclusions set out in the above-mentioned annex acknowledging the novelty of the claims of the disputed patent and denying that the inventions constituted a discovery revealed partiality on the part of the Opposition Division since these issues had been decided without sufficiently hearing the parties. However, the Division cannot follow this argument either.

3.2.1 It is usual in opposition proceedings to send out together with the summons to oral proceedings a note in which the topics considered essential to discuss are identified and, if appropriate, provisional comments on the positions adopted by the parties are made (see Guidelines, C-VI, 3.2). In the present proceedings, the established practice of the European Patent Office with respect to the patentability of newly-isolated natural substances was considered to be so clear that it was felt to be justified to give an opinion on the issues of novelty and discovery in the annex to the summons to oral proceedings on the basis of the written submissions of the opponents. This did not mean that a final decision had been reached on these points, nor did it in any way preclude the opponents from presenting further arguments at oral proceedings. It should moreover be noted that no comment was made in the annex concerning the objection under Article 53(a)EPC.

3.3 In view of the above, the opponents' allegation of bias on the part of the Opposition Division is regarded as unfounded.

#### **4. Novelty and inventive step (Articles 54 and 56 EPC)**

4.1 The opponents contend that the subject-matter of the opposed patent lacks novelty since the gene encoding relaxin was always present in the female human body; the proprietor has merely isolated it in a conventional way. The Opposition Division does not agree.

4.2 First, as already explained above (see point 2.1 and onward), the claimed DNA fragments encoding relaxin and its precursors (prepro- and pro-forms) are cDNAs, that is, DNA copies of human mRNA encoding relaxin. cDNAs do not occur in the human body. The sequences of Claims 1 to 7 are hence novel for this reason alone.

4.3 Moreover, even if Claims 1 to 7 are interpreted as including in their scope genomic DNA fragments encoding H2-relaxin, there is no question of lack of novelty of these claims. According to Article 54(1)EPC, an invention shall be considered to be new if it does not form part of the state of the art. In Article 54(2) EPC, the state of the art is defined as comprising everything *made available to the public* before the filing date of the European patent application (emphasis added).

4.3.1 It is common ground among the parties that until a cDNA encoding human H2-relaxin and its precursors was isolated by the proprietor, the existence of this form of relaxin was unknown. It is established patent practice to recognise novelty for a natural substance which has been isolated for the first time and which had no previously recognised existence (see Guidelines, C-IV, 2.3). Indeed, the opponents recognised that this principle may provide, in their words, a formal basis for novelty of the relaxin DNA (see Notices of Opposition, page 5, second sentence). In view of this practice, the novelty of the present claims is assured.

4.4 The opponents' assertion that Claims 1 to 4 are not patentable because the chemical structure of the DNA fragments of those claims is completely undefined cannot be accepted. The DNA is defined in terms of the amino acid sequence it encodes, a generally acceptable terminology and one which is widely used and perfectly understandable to the skilled person. It is true that a very large number of DNA sequences may fall under the scope of the claim, including sequences which possibly occur in nature and differ from those exemplified in the patent. However, this has no bearing on the patentability of the claims. It should be noted that alleged lack of clarity of claims or lack of support for their full scope are not grounds for opposition under Article 100 EPC.

4.5 In the light of the above, the claims are regarded as novel.

4.6 Lack of inventive step was also cited by the opponents as grounds for their opposition, on the basis of alleged lack of novelty of the claimed DNA fragments encoding H2-relaxin and the fact that the means used to isolate the DNA were conventional; according to the opponents, who cited no prior art, the closest state of the art for the subject-matter of Claim 1 is the woman from whom the mRNA used to prepare the H2-relaxin cDNA was isolated.

4.6.1 The opponents' argument must fail for the sole reason that the gene was not known, but is rather regarded as novel (see above). In isolating the DNA encoding human H2-relaxin, the proprietor was not preparing a known substance by conventional means, but providing to the public for the first time a product whose existence was previously unknown. This is regarded as inventive whatever the methods used to prepare the product. The claims are considered to involve an inventive step because there is no pertinent real prior art (as opposed to the 'woman') available rendering the claimed subject-matter obvious.

## **5. Discovery (Article 52(2) EPC)**

5.1 The opponents further assert that the subject-matter of the patent represents a discovery and is hence not patentable under Article 52(2)(a) EPC. This argument ignores the long-standing practice of the European Patent Office concerning the patentability of natural substances. As explained in the *Guidelines*, C-IV, 2.3, to find a substance freely occurring in nature is mere discovery and therefore unpatentable. However, if a substance found in nature has first to be isolated from its surroundings and a process for obtaining it is developed, that process is patentable. Moreover, if this substance can be properly characterised by its structure and it is new in the absolute sense of having no previously recognised existence, then the substance *per se* may be patentable.

5.2 The above guideline is highly appropriate in the present case. Human H2-relaxin had no previously recognised existence. The proprietor has developed a process for obtaining H2-relaxin and the DNA encoding it, has characterised these products by their chemical structure and has found a use for the protein. The products are therefore patentable under Article 52(2) EPC.

5.3 The opponents complained that equating discoveries with inventions led to unduly broad patents which prevented anyone else from making, in the case at issue, a selection invention on H2-relaxin. However, the Opposition Division finds it perfectly justified to grant broad protection in view of the fact that H2-relaxin has been made available to the public for the first time. This does not exclude the possibility of further inventions, for example improved derivatives of the protein, better processes for its preparation, and so on. The situation is comparable to that existing for inventions relating to air pumps, to use the example repeatedly mentioned by the opponents, where the original inventor of an air pump would certainly have been entitled to a broad patent.

5.4 The opponents also contended that the above reasoning would mean that discoveries such as the moon (after the Americans landed on it in 1969), *Otzi* (a mummified, around 5,000-year-old man found in ice in the Italian-Austrian Alps) or a new animal found in some remote area would also be patentable. However, this is not the case. As already pointed out, the mere finding of something freely occurring in nature is not an invention. An invention must have a technical character, that is, should constitute an industrially applicable technical solution to a technical problem, and must be reproducibly obtainable without undue burden. A product must furthermore be novel in the sense of having had no previously recognised existence and must in addition be inventive. None of the discoveries cited by the opponents fulfil these criteria.

5.5 In conclusion, the subject-matter of the disputed patent does not represent a discovery and is hence not excluded from patentability under Article 52(2) EPC.

## **6. Morality (Article 53(a) EPC)**

6.1 The opponents contended that the subject-matter of the disputed patent, insofar as it relates to a DNA fragment encoding human H2-relaxin and its precursors, offends against the provisions of Article 53(a). They argued essentially as follows:

- (a) The patent teaches that in order to repeat the invention, tissue is to be taken from a pregnant woman. The isolation of the DNA relaxin gene from tissue taken from a pregnant woman is immoral, in that it constitutes an offence against human dignity to make use of a particular female condition (pregnancy) for a technical process oriented towards profit.
- (b) The patenting of human genes such as that encoding H2-relaxin amounts to a form of modern slavery since it involves the dismemberment of women and their piecemeal sale to commercial enterprises throughout the world. This infringes the human right to self-determination.

(c) The patenting of human genes means that human life is being patented. This is intrinsically immoral.

6.2 Before discussing the opponents' arguments, it seems opportune to take a look at Article 53(a) EPC and at the EPO Guidelines dealing with this Article. Article 53(a) states that European patents shall not be granted in respect of inventions the publication or exploitation of which would be contrary to 'ordre public' or morality, provided that the exploitation shall not be deemed to be so contrary merely because it is prohibited by law or regulation in some or all of the Contracting States.

6.2.1 The provisions of Article 53(a) have only very seldom been invoked. While patent applications must be examined for compliance with all Articles of the EPC, including Article 53(a), the function of this Article has to be seen as a measure to ensure that patents would not be granted for inventions which would universally be regarded as outrageous. This interpretation is reflected in the relevant passages of the Guidelines (C-IV, 3.1). There it is stated that Article 53(a) EPC is likely to be invoked only in rare and extreme cases, for example that of a letter bomb. In addition, some general guidance is given as to when such a case might arise:

A fair test to apply is to consider whether it is probable that the public in general would regard the invention as so abhorrent that the grant of patent rights would be inconceivable. If it is clear that this is the case, objection should be raised under Article 53(a); otherwise not.

6.2.2 Article 53(a) constitutes an exception to the general principle, set out in Article 52(1) EPC, that patents shall be granted for inventions which are industrially applicable, novel and inventive. The Boards of Appeal have repeatedly found that such exceptions are to be narrowly construed (see T320/87, <sup>1</sup> OJEPO 1990, 76, point 6 of the Reasons, and T19/90, <sup>2</sup> OJ EPO 1990, 486).

6.3 Turning now to the opponents' specific allegations relating to the present human H2-relaxin DNA, the patenting of the DNA would indeed be abhorrent to the overwhelming majority of the public if it were true that the invention involved the patenting of human life, an abuse of pregnant women, a return to slavery and the piecemeal sale of women to industry. However, the Opposition Division emphatically rejects these arguments.

6.3.1 With regard to the isolation of mRNA from tissue taken from pregnant women, the proprietor stated that the women who donated tissue consented to do so within the framework of necessary gynaecological operations. There is no reason to perceive this as immoral. Indeed, human tissue or other material, such as blood, bone, and so on, has been widely used for many years as a source for useful products, often proteins but now also RNA or DNA, which are unavailable elsewhere. Many life-saving substances (such as bloodclotting factors) are isolated in this way and many have been patented. Every evidence indicates that this practice is perfectly acceptable to and even welcomed by the vast majority of the public. Moreover, the use for other purposes of parts of the human body removed during the course of an intervention is explicitly approved in Article 13 of the Draft Bioethics Convention of the Council of Europe provided there are appropriate information and consent procedures.

6.3.2 The Opposition Division therefore agrees with the proprietor that there was nothing immoral about the isolation of the relaxin DNA. Contrary to the opponents' remarks concerning the repeatability of the invention, the isolation procedure need not be repeated in order to carry out the invention since a DNA fragment encoding human H2-relaxin can simply be chemically synthesised.

6.3.3 As for the opponents' assertions concerning slavery and the dismemberment of women, these are considered to betray a fundamental misunderstanding of the effects of a patent. A patent confers on its proprietor the right to exclude for a limited period of time third parties from commercially using the patented invention. It cannot be overemphasised that patents covering DNA encoding human H2-relaxin, or any other human gene do not confer on their proprietors any rights whatever to individual human beings, any more than do patents directed to other human products such as proteins, including human H2-relaxin. No woman is affected in any way by the present patent--she is free to live her life as she wishes and has exactly the same right to self-determination as she had before the patent was granted. Furthermore, the exploitation of the invention does not involve dismemberment and piecemeal sale of women. The whole point about gene cloning is that the protein encoded by the cloned gene--in this case human H2-relaxin--is produced in a technical manner from unicellular hosts containing the corresponding DNA; there is therefore no need to use human beings as a source for the protein. The

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<sup>1</sup> Lubrizol/Hybrid Plants [1990] EPOR 337

<sup>2</sup> Harvard/Onco-Mouse [1990] EPOR 501

only stage at which a woman was involved was at the beginning of the making of the invention, as a (voluntary) source for the relaxin mRNA.

6.3.4 Finally, the allegation that human life is being patented is unfounded. It is worth pointing out that DNA is not 'life', but a chemical substance which carries genetic information and can be used as an intermediate in the production of proteins which may be medically useful. The patenting of a single human gene has nothing to do with the patenting of human life. Even if every gene in the human genome were cloned (and possibly patented), it would be impossible to reconstitute a human being from the sum of its genes. The opponents apparently do not object to the patenting and exploitation for medical purposes of other human substances such as proteins (even the H2-relaxin protein). However, no moral distinction can be seen in principle between the patenting of genes on the one hand and other human substances on the other, especially in view of the fact that only through gene cloning have many important human proteins (for example, erythropoietin and the interferons) become available in sufficient amounts to be medically applied.

6.4 Besides the specific arguments set out above, the opponents also made broad statements regarding the immorality of patents on human genes in general. They maintained that patent applications relating to inventions in the field of genetic engineering cannot be treated the same way as applications relating to, for example, air pumps, but represent a special case requiring particular consideration under Article 53(a) EPC. They expressed the view that there existed among members of the public and all possibly concerned parties such as doctors, churches, and so on a consensus that human genes should not be patented, adding that only the EPO and the branch of industry concerned was in favour of patenting human genes. In this connection, the opponents also referred to the draft *Directive on the legal protection of biotechnological inventions* in the European Union (EU). The opponents insisted that the EPO should impose a moratorium on the granting of patents directed to human genes until this Directive has been implemented and not bring about a *fait accompli* in the meantime by granting patents such as the one under discussion.

6.4.1. The above argument completely ignores the current dispute within the EU (conciliation procedure) concerning the terms of the proposed EU Directive. While the European Parliament, of which the present opponents are members, has voted to prohibit the patenting of human genes in the Directive, the Council of Ministers is in favour of patenting isolated human genes and the 'Common Position' of the Directive adopted by the Council on 7 February 1994, explicitly allows this. No further evidence is required to refute the opponents' contention that only the EPO and industry are in favour of patenting human genes.

6.4.2 In view of the disagreement concerning the EU Directive, it is not clear at present what its final form will be and whether it will be in favour of or against patenting human genes. The imposition of a moratorium by the EPO on patenting human genes would in consequence be inappropriate and moreover impossible because there is no legal mechanism in the EPC for doing so.

6.4.3 As for the opponents' general assertions concerning the alleged intrinsic immorality of patenting human genes, these are founded on the premise that there is an overwhelming consensus among the Contracting States that the patenting of human genes is abhorrent and hence prohibited under Article 53(a). This assumption is false.

6.4.4 The disagreement between two bodies of the EU regarding the EU Directive (see above) perfectly reflects the current turbulent state of the public debate on biotechnology. Whether or not human genes should be patented is a controversial issue on which many people have strong opinions. Insofar as these opinions are often based rather on personal beliefs than on reasoned arguments, the discussion resembles those on other disputed questions such as abortion or the death penalty. Like the present opponents, many members of the public and other interested bodies appear to be against the patenting of human genes. However, their position is far from clear-cut since, as illustrated by the present proceedings, there is much confusion concerning the practical effects of a patent directed to a human gene. Properly informed on this point, those currently against such patents might well feel differently. Moreover, the view expressed tends to depend on the question being asked. For example, most people will probably say no if asked whether they approve of patents on human life; some may also reject the patenting of DNA encoding human proteins such as H2-relaxin. Nevertheless, the same people, if asked in the context of human health and well-being, will often approve of gene therapy, which, after all, necessarily involves a far more direct manipulation of human individuals than patents such as the present one could ever do. In view of this ambiguity, it may be concluded that the opinion of society on the question of patenting human genes is complex and not yet definitively formed.

6.5 Obviously recognising that the EPO is not the right institution to decide on fundamental ethical questions, the opponents requested that the EPO carry out a referendum to find out what the public in the Contracting States really wants to be patented. This request is refused since in opposition proceedings the burden of proof lies with the opponent--if they felt that such a survey might assist their case, it was up to them to carry it out. In any case, the Opposition Division wishes to point out that even if such a referendum were feasible, there is no provision in the EPC that only those inventions actively approved of by the public should be patented. If such a provision existed, it is arguable that the number of patents granted would be decimated since there are plenty of fields other than biotechnology (which the Opposition Division, unlike the opponents, does not see as a special case) in which patents may well be objectionable to parts of the public. Only in those very limited cases in which there appears to be an overwhelming consensus that the exploitation or publication of an invention would be immoral may an invention be excluded from patentability under Article 53(a).

6.6 In conclusion, neither does the opposed patent offend against widely- accepted moral standards of behaviour by promoting slavery, the sale of women, and so on, nor is there a clear consensus among members of the public in the Contracting States that patenting human genes such as that encoding H2-relaxin is immoral. In view of this, the patent is not considered to offend against Article 53(a) EPC.

### **Order**

For the above reasons it is decided that the grounds for opposition do not prejudice the maintenance of the patent as granted. The opposition is therefore rejected in accordance with Article 102(2) EPC.