

Internal distribution code:

- (A) Publication in OJ
(B) To Chairmen and Members
(C) To Chairmen
(D) No distribution

**Datasheet for the decision
of 24 February 2009**

Case Number: T 0762/07 - 3.3.08

Application Number: 97200903.9

Publication Number: 0798378

IPC: C12N 15/12

Language of the proceedings: EN

Title of invention:

Estrogen receptor

Patentee:

N.V. Organon

Opponents:

STRAWMAN LIMITED

Karo Bio AB

Headword:

Estrogen receptor/ORGANON

Relevant legal provisions:

EPC Art. 123(2), 54, 56, 89

Relevant legal provisions (EPC 1973):

-

Keyword:

"Main request - admissibility - (no)"

"First auxiliary request - admissibility of disclaimer (no)"

"Second auxiliary request - admissibility of disclaimer (yes)

- novelty (yes) - inventive step - (no)"

Decisions cited:

G 0001/03, T 0190/99, T 1120/00, T 0446/00, T 1449/03,

T 0386/04, J 0015/85

Catchword:

-



Case Number: T 0762/07 - 3.3.08

D E C I S I O N
of the Technical Board of Appeal 3.3.08
of 24 February 2009

Appellant I:
(Patent Proprietor)

N.V. Organon
Kloosterstraat 6
NL-5349 AB Oss (NL)

Representative:

Van Someren, Petronella F.H.M.
Arnold & Siedsma
Sweelinckplein 1
NL-2517 GK The Hague (NL)

Appellant II:
(Opponent 01)

STRAWMAN LIMITED
34 Lovedon Lane
Winchester
Hampshire SO23 7NU (GB)

Representative:

Harding, Charles Thomas
D Young & Co
120 Holborn
London EC1N 2DY (GB)

Appellant III:
(Opponent 02)

Karo Bio AB
Novum
SE-S141 57 Huddinge (SE)

Representative:

Dean, John Paul
Withers & Rogers LLP
Goldings House
2 Hays Lane
London SE1 2HW (GB)

Decision under appeal:

**Interlocutory decision of the Opposition
Division of the European Patent Office posted
13 March 2007 concerning maintenance of
European patent No. 0798378 in amended form.**

Composition of the Board:

Chairman: L. Galligani
Members: F. Davison-Brunel
C. Rennie-Smith

Summary of Facts and Submissions

- I. European patent No. 0 798 378 with the title "Estrogen receptor" was granted with 11 claims for all designated Contracting States, based on European patent application No. 97 200 903.9.

Granted claims 1, 4 to 6 read as follows:

"1. Isolated estrogen receptor having an N-terminal domain, a DNA-binding domain, and a ligand-binding domain, wherein the amino acid sequence of said DNA-binding domain exhibits at least 80% homology with the amino acid sequence shown in SEQ ID NO:3 and the amino acid sequence of said ligand-binding domain of said estrogen receptor exhibits at least 70% homology with the amino acid sequence shown in SEQ ID NO:4, provided that the estrogen receptor does not have the amino acid sequence:

[here follows the amino acid sequence of the rat estrogen receptor as disclosed in document (4), infra, Figure 1].

4. Isolated estrogen receptor according to anyone of claims 1-3, **characterised in that** said estrogen receptor comprises the amino acid sequence of SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:21 or SEQ ID NO:25.

5. Isolated DNA encoding an estrogen receptor according to claims 1-4.

6. Isolated DNA according to claim 5, **characterised in that** said DNA comprises the nucleic acid sequence of

SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:20 or SEQ ID NO:24."

Claims 2 and 3 related to further features of the estrogen receptor of claim 1. Claim 7 related to a recombinant expression vector comprising the DNA according to claim 5 or 6. Claims 8 and 9 were directed to recombinant cells. Claim 10 related to the use of the previously claimed DNAs, vector, cells or receptor in a screening assay for identification of new drugs. Claim 11 related to a method of identifying functional ligands for a receptor according to any one of claims 1 to 4.

- II. Two oppositions were filed against the grant of the patent. In response to the notices of opposition, the patentee replaced its main request (granted claims) by a new main request filed on 22 July 2003 and, then, at the beginning of the opposition oral proceedings on 28 March 2006 asked that it be re-instated. Both opponents argued that this was a procedural abuse. The opposition division admitted the granted claims as the main request and subsequently rejected it as failing to fulfil the requirement of inventive step (claims 4 and 5 when relating to SEQ ID NO:25 and SEQ ID NO:24). The patent was maintained in amended form on the basis of a request where all claims remained identical to the granted claims except that the reference to SEQ ID NO:25 and SEQ ID NO:24 was deleted from claims 4 and 6.
- III. Appellant I (patentee) filed a notice of appeal and submitted a statement of grounds of appeal, requesting that the patent be maintained on the basis of the granted claims. Appellants II and III (opponents 01

and 02 respectively) filed notices of appeal and submitted statements of grounds of appeal. Both of them maintained their arguments that the opposition division should not have allowed the patentee to go back to the granted claims as main request and Appellant III claimed that it was a substantial procedural violation which justified a refund of the appeal fee.

- IV. Appellant I filed further submissions in answer to appellants II and III' s statements of grounds of appeal.

- V. The board sent a communication pursuant to Article 15(1) of the Rules of Procedure of the Boards of Appeal (RPBA) indicated its preliminary, non-binding opinion on procedural and substantive matters.

- VI. All appellants filed further submissions in answer to this communication. Appellant I's submissions were accompanied by a main request (granted claims, section I, *supra*), a first auxiliary request (claims accepted by the opposition division) and two further auxiliary requests (auxiliary requests IIa and IIb). Appellant III's submissions included *inter alia* withdrawal of the request for reimbursement of the appeal fee.

- VII. At oral proceedings which took place on 24 February 2009, Appellant I replaced auxiliary requests IIa and IIb by a new auxiliary request identified as auxiliary request IIb.

Claim 1 of **auxiliary request IIb** read as follows:

"1. Isolated estrogen receptor having an N-terminal domain, a DNA-binding domain, and a ligand-binding domain, wherein the amino acid sequence of said DNA-binding domain exhibits at least 80% homology with the amino acid sequence shown in SEQ ID NO:3 and the amino acid sequence of said ligand-binding domain of said estrogen receptor exhibits at least 70% homology with the amino acid sequence shown in SEQ ID NO:4, provided that the estrogen receptor does not have the amino acid sequence:

[here follows the amino acid sequence of the rat estrogen receptor as disclosed in document (4), infra, Figure 1].

or a sequence which is more than 89% identical with that sequence. (emphasis added)

Claims 2 to 11 remained identical to claims 2 to 11 of the request accepted by the opposition division (see II, supra).

VIII. The following documents are mentioned in the present decision:

(2): Green, G.L. et al., Science, Vol. 231, pages 1150 to 1154, 1986;

(4): WO 97/09348 with the publication date of 13 March 1997, the filing date of 9 September 1996, claiming priority from GB 9518272.1 of 8 September 1995, GB 9605550.4 of 15 March 1996, GB 9607532.0 of 11 April 1996 and GB 9609576.5 of 8 May 1996 ;

(6): Enmark, E. et al., Biochemical and Biophysical Research Communications, Vol.204, No.1, pages 49 to 56, 14 October 1994;

(9): Handwritten notes taken by Dr. U. Fuhrmann at Prof. J-A. Gustafsson's presentation at the Keystone Symposium Nuclear Receptor Superfamily, Lake Tahoe, California, USA, 17-23 March 1996;

(18): Environmental Health Perspectives, Vol.104, No.12, pages 1273 to 1274, December 1996;

(21): Ogawa, S. et al., Biochemical and Biophysical Research Communications, Vol.243, No.1, pages 122 to 126, 1998.

IX. Appellant's I submissions in writing and during oral proceedings insofar as relevant to the present decision may be summarized as follows:

Admissibility of the main request

J 15/85 (OJ EPO 1986, 395) relied on by Appellant II concerned an entirely different situation. Unless a patentee explicitly states so, there is no reason to believe any originally granted subject-matter has been abandoned. Returning to the subject-matter as granted in opposition proceedings can never be a surprise and never "late filed". The patentee could not know the outcome of G 01/03 (OJ EPO 2004, 413) so filing claims without a disclaimer was just a bona fide attempt to expedite proceedings. The patentee cannot be blamed if, in the three years between filing those new claims and

the opposition oral proceedings, G 01/03 (supra) decided disclaimers were again allowable. After seeing the opposition division's preliminary opinion (which indicated that the claims filed on 27 July 2003 would not be allowable under Article 123(2) EPC), the opponents could have anticipated that the patentee would at some stage have to come up with a solution. The patentee cannot be blamed for the opponents' failure to see that returning to the original main request was the most elegant way to solve the Article 123(2) EPC issue. Even if not so stated in its decision, the opposition division allowed the re-introduction of the granted claims because it obviated that issue.

At the oral proceedings before the board, Appellant I's representative explained the reason for not reverting to the granted claims earlier than 28 March 2006 as follows. When she took over the case shortly before the opposition oral proceedings, she noted immediately the opposition division's preliminary opinion that the claims filed on 27 July 2003 were not allowable under Article 123(2) EPC and saw that, disclaimers being allowable under certain circumstances pursuant to G 1/03 (supra), the granted claims offered a means to overcome that adverse opinion.

In any event, the claims as granted was the main request on appeal from the filing of the notice of appeal. By definition, that main request was timely filed in the appeal proceedings.

First auxiliary request, claim 1

Article 123(2) EPC, admissibility of the disclaimer

- The disclaimer of the specific rat ER β amino acid sequence introduced in claim 1 was sufficient to delimit the claimed subject-matter from the teachings of document (4) - a document to be taken into account under Article 54(3) EPC. Indeed the rat ER β sequence was the only **specific** sequence disclosed in this document. On page 4 of document (4), ER β sequences with more than about 89% identity to the rat ER β sequence and, also, sequences functionally similar to it were mentioned. These, however, were **generically** defined sequences. One could not be sure that the feature "more than about 89% identity" necessarily implied the now claimed degrees of homology to the specific DBD- and ligand- binding domains SEQ ID NO:3 and SEQ ID NO:4. As for the molecules identified as functionally-similar, there was, of course, no way to assimilate them to ER β molecules with the claimed percentages of homology. The Enlarged Board of Appeal's decision G 01/03 (*supra*, point 3) made it clear that for a disclaimer to be allowable, no more than necessary should be disclaimed. Disclaiming sequences which did not obviously fall within the scope of the claim would certainly be disclaiming more than was necessary.

- Appellants II and III' s argument that, in order to be allowable, the disclaimer should have been present in the application as filed because document (4) - publication date, 13 March 1997 - had been published 12 days before the filing date of the patent in suit (25 March 1997) had no legal basis. Document (4) was not, in fact, published before the **effective** filing

date of the application. Indeed, Article 89 EPC made it totally clear that the right of priority had the effect that the date of priority counted as the date of filing of the European patent application for the purpose of Article 54(3) EPC. Here, the patent in suit enjoyed priority rights from 22 November 1996 and 26 March 1996 and either one of these dates was the effective filing date. As already above mentioned, the publication date of document (4) was 13 March 1997, a much later date although preceding the filing date of 25 March 1997. To argue that this publication date was such an exceptional circumstance that it was legitimate to ignore Article 89 EPC would amount to treating all provisions relating to priority as pointless.

For these reasons, the disclaimer in claim 1 was allowable and sufficient to establish novelty over the teachings of document (4).

Auxiliary request IIb; claim 1

Article 123(2) EPC, allowability of the disclaimer

Appellant II had argued that the disclaimer in claim 1 removed more than was necessary when removing a sequence with more than 89% identity to that of rat ER β . The reason then given was that the "more than 89% identity feature" had no counterpart in the relevant priority document pertaining to document (4) and, therefore, it was not a disclosure under Article 54(3) EPC which must be disclaimed. This argument had been presented for the first time at oral proceedings and the priority documents pertaining to document (4) were not on file. If this issue was to be considered at all,

then the case should be remitted to the first instance for further prosecution.

Article 84 EPC

- The drafting of claim 1 was the one classically adopted when introducing a disclaimer into a claim and the person skilled in the art willing to understand would have no doubt that every subject-matter found after the term "provided that..." belonged to the disclaimer i.e. that the term "that sequence" in the expression "...or a sequence which is more than 89% identical with that sequence" referred to the specific amino acid sequence disclaimed immediately above.

- The alleged mismatch (identity versus homology) between the two parameters used to define the invention and the disclaimed subject-matter would not have been regarded by the skilled person as generating confusion because the "identity" parameter was totally unambiguous and how to evaluate homology was a matter of common general knowledge.

Article 56 EPC; inventive step

Document (9), identified as the closest prior art, amounted to notes being taken during a presentation which took place at a meeting on 17 to 23 March 1996. Even if one was to agree that it disclosed the cloning of rat ER β DNA and, possibly that of a human counterpart, this disclosure remained so fragmented and incomplete that a skilled person aware of it and wanting to clone human ER β DNA would have had no reasonable expectation of success in doing so.

The primers to be used were not identified and, although it was taught that the rat ER β molecule had 95% identity to the prototype ER α molecule in the DNA binding domain, this was at the protein level and not at the DNA level, which meant that no guidance was provided as to how to choose sequences likely to function as primers.

Choosing testis tissue as starting material for isolating human ER β DNA as was done in the patent in suit had been a key choice in being successful. Indeed, a later successful attempt - by a different group - at cloning this DNA had also made use of testis tissue (document (21)). Conversely, ER β was not obtained when cloning from rat cerebellum tissue using the same primers as those which enabled the isolation of rat ER β as described in document (4) (document (6)). The teaching in document (9) that rat DNA cloning was achieved from prostate tissue was misleading to the skilled person and, thus, affected the chances of success when attempting to clone human ER β .

For these reasons, inventive step could be acknowledged.

- X. Appellants II and III's submissions in writing and during oral proceedings insofar as relevant to the present decision may be summarized as follows:

Admissibility of the main request

The opposition division should not have allowed Appellant I to re-introduce the claims as granted as

its main request. It had introduced a new set of claims as main request under cover of a letter of 27 July 2003 which admitted the granted claims were invalid in several respects. The right to revert to the granted claims had not been reserved so they were thereby abandoned. Just as in J 15/85 (supra) where claims were amended so as to allow an application to proceed to grant, so here the granted claims were abandoned to avoid the case being suspended pending the Enlarged Board of Appeal decision in G 01/03 (supra) which was referred on 20 December 2002. The decision in G 01/03 (supra) (which might have favoured the disclaimer in the granted claims) was issued on 8 April 2004 but the patentee waited until 28 March 2006 to return to the granted claims. Failing to inform the opponents of this until the last moment was a clear attempt to disadvantage them. The patentee did not explain why the change was made and the opposition division's decision did not explain why it allowed the change. In T 446/00 of 3 July 2003 it was said to be an abuse of procedure to adopt an unequivocal position on an issue and subsequently to depart from that position without explanation.

First auxiliary request, claim 1

Article 123(2) EPC, admissibility of the disclaimer

- The disclaimer had been introduced into claim 1 to restore novelty over the teachings of document (4) to be taken into account under Article 54(3) EPC. This document disclosed the rat ER β molecule, a novel estrogen receptor-related nuclear receptor. Its specific sequence was given in Figure 1. On page 4, it was also mentioned that molecules with an amino acid

sequence more than 89% identical to the sequence of Fig.1 were part of the invention and that an amino acid sequence functionally similar to the sequence shown in Fig.1 may be from a different mammalian species. In contrast, the disclaimer in claim 1 only comprised the specific rat ER β sequence. This was not sufficient to impart novelty as established in the case law, e.g. T 1120/00 of 22 October 2004, where it was concluded that a disclaimer was not adequately drafted if it failed to comprise an intermediate generalisation (sequences defined by percentages of homology to a specific sequence) contained in the intervening document.

- Document (4) had been published on 13 March 1997, i.e. 12 days before the filing date of the patent in suit and, thus, its content was prior art at the filing date. The disclaimer reflecting the relevant parts of document (4) ought to have already been inserted in the application as filed, as was also the case when disclaiming a non-accidental teaching relevant under Article 54(2) EPC. The principle established by Article 89 EPC that the date of priority shall count as the date of filing of the European patent application for the purpose of Article 54(3) EPC did not apply in the present case which was a truly exceptional one by virtue of intervening document (4) being published before the filing date of the patent in suit whereas in most other cases, intervening documents were published after the filing date of the patent in suit. For these reasons, the disclaimer was not allowable under Article 123(2) EPC and, consequently, claim 1 lacked novelty over the teachings of document (4).

Auxiliary request I Ib, claim 1

Article 123(2) EPC; allowability of the disclaimer

- The teaching in document (4) as regards molecules with "more than about 89% identity" to the rat ER β sequence did not enjoy priority from the first priority document pertaining to document (4) since this priority document disclosed molecules with a 90% identity to rat ER β . Thus, the "more than 89% identity feature" was not a disclosure under Article 54(3)EPC. It needed not be disclaimed. As the disclaimer removed more than was necessary and in accordance with the principle established in G 01/03 (supra, point 3 of the Reasons), it was not allowable.

Article 84 EPC

- The drafting of claim 1 left doubts as to which sequence was referred to as "that sequence" in the expression "a sequence which is more than 89% identical with that sequence". It could equally be the specific sequence which was disclaimed immediately above or the sequences mentioned earlier in the non-disclaimer part of the claim.

- Whereas the claim referred to sequences having homology to specific sequences, the way to identify homology was not defined which amounted to a lack of clarity.

- The claim was confusing as there was a discrepancy between the ways the first sequences mentioned in the claim and the disclaimed sequences were characterised (homology versus identity). The person skilled in the

art would have difficulties in understanding whether or not a molecule of interest fell within the scope of the claim.

Article 56 EPC; inventive step

- The closest prior art to the subject-matter of claim 1 was document (9) which presented the notes taken at a presentation given at a meeting which took place on 17 to 23 March 1996. There, the isolation of the novel rat estrogen receptor-related nuclear receptor ER β had been disclosed. The rat ER β protein was found to have 95% identity with the prototype ER α estrogen receptor in the DNA binding domain and its activity as a receptor had been illustrated by transactivation in CHO cells. The cloning of the equivalent receptor from human tissue with the help of a rat probe had also been referred to. Human tissues containing ER β had been identified. On the basis of this teaching and of the common general knowledge as regards cloning techniques, the skilled person would have had a reasonable expectation of success when cloning the human ER β gene.

- Appellant I may have chosen to start the cloning experiment from testis tissue rather than prostate tissue as was disclosed in document (9). Yet, this was only a choice on its part rather than a feature susceptible of imparting inventive step because human ER β was also present in human prostate tissue as taught not only in document (9) but also in document (4) which provided the relevant evidence in Figure 8. Rat ER β may not have been isolated from rat brain tissue by using the same primers as were used in document (4) to

isolate rat ER β from prostate tissue, but this was hardly surprising as ER β was present in much lower quantity in brain tissue (document (4), Fig.8).

The subject-matter of claim 1 failed to fulfil the requirements of Article 56 EPC.

XI. Appellant I requested that the decision under appeal be set aside and the patent be maintained as granted or, in the alternative, that the appeals of the opponents be dismissed, or that the patent be maintained on the basis of the auxiliary request IIb filed during the oral proceedings.

Appellants II and III requested that the decision under appeal be set aside and that the patent be revoked.

Reasons for the decision

Admissibility of the main request

1. Appellant I's submission that a patentee may always revert to the granted claims is, with one exception, correct. In decision T 386/04 of 9 January 2007, which made a thorough review of the relevant case law, it was said (see Reasons, point 1):

"There is therefore nothing in principle to prevent a patentee from later seeking to amend his request so as to ask for the patent to be maintained in the form as granted (or in more limited terms), either in the course of proceedings before the opposition division or on appeal. Indeed, he is entitled to as of right....

- The exception to this principle is where it would amount to an abuse of procedure to allow the proprietor to revert to the granted claims."
2. Thus, the argument of Appellants II and III that the patentee in this case abandoned the granted claims is exaggerated. The patentee was perfectly entitled to file other claims in response to the notices of opposition and, at a later date, to revert to the granted claims in an attempt to avoid the opposition division's opinion and to take advantage of the decision in G 01/03 (supra) which had been issued meanwhile. However, Appellant I's arguments are also exaggerated. Its submissions that the opponents could have anticipated a further change of claims and that it was not to blame if the opponents could not see that re-introduction of the granted claims was the most elegant way to avoid the opposition division's opinion are disingenuous. Any party is entitled to rely on the position another party expressly adopts as being its true position and to have proper notice of any change in such position. Patent proceedings are not guessing-games.
 3. The board must decide, ignoring the parties' exaggeration, whether or not the patentee's behaviour was an abuse of procedure such as to deny it the right to revert to the granted claims. In this respect the board has not read or heard any submissions from the parties which change the provisional view it expressed in its communication of 10 July 2008, namely that while it was understandable that the patentee might have had second thoughts after decision G 01/03 (supra) was issued, it was equally understandable that the

- opponents could infer from the lapse of two years thereafter that the patentee would not revert to a disclaimer in reliance on G 01/03 (supra), and that the most important factor was that the patentee gave no indication of second thoughts until the opening of the oral proceedings on 28 March 2006.
4. That the change of main request was not announced earlier because the need to change was only noticed by the new representative is not an acceptable reason for either surprise or lateness - the opponents had nothing to do with either the change of request or the change of representative. Any notice, however short, would have been better than none but the patentee elected to keep the change to itself until the last possible moment. That is not how litigation should be conducted: cards should be put on the table, not kept up the sleeve. Contrary to Appellant I's argument, depending on the circumstances any change - even reverting to granted claims - can be a surprise and can be late-filed.
5. Appellant III referred to T 446/00 of 3 July 2003 in which a patentee specifically stated, in answer to a challenge from the opponent, that it would not rely on a certain claim and then later re-introduced that claim without explanation. That was held to be an abuse of procedure (see Headnote 2 and Reasons, points 4.1.1, 4.1.2 and 4.5.3). In the present case there was no such specific retraction, but the effect of three years silence broken only at the very last possible opportunity must be viewed as having much the same effect. In T 1449/03 of 26 September 2006, a patentee's departure for the first time at oral proceedings from a

position previously and persistently held was not allowed *inter alia* because the opponent might have been lulled into a feeling of false security (see Reasons, points 2.8 and 2.9).

6. In all the circumstances, the board finds that the manner in which Appellant I reverted to the claims as granted was an abuse of procedure which the opposition division should not have allowed. It follows that the same request should not be admissible on appeal since otherwise Appellant I would be allowed to avoid the consequences of its abuse of procedure. Article 12(4) RPBA specifically refers to the power of the board to hold inadmissible requests which were not admitted in first instance proceedings; that power must inevitably extend to requests which were admitted by a decision of the first instance which is over-ruled on appeal.

First auxiliary request; claim 1

Articles 123(2) and 54 EPC; admissibility of the disclaimer, novelty

7. Claim 1 relates to estrogen receptors identified by their percentages of homology to the human ER β estrogen receptor over two specific domains of the molecule, the DNA binding domain and the ligand binding domain. It contains a disclaimer of the specific rat ER β protein sequence disclosed in document (4) (Fig.1).
8. Document (4) is a patent application to be taken into account for the purpose of assessing novelty under Article 54(3) EPC, inasmuch as it enjoys priority from the two priority documents GB 9518272.1 and GB 9605550.4 respectively filed on 8 September 1995 and

15 March 1996, that is, earlier than the filing date of the earliest priority document of the patent in suit, EP 96200820 filed on 26 March 1996. It was published on 13 March 1997, i.e. shortly before the filing date of the patent in suit (25 March 1997).

9. Document (4) discloses not only the now disclaimed specific rat ER β protein sequence but it mentions also on page 4 that:

"An amino acid sequence which is more than about 89% identical with the sequence shown in Fig.1 ... is substantially the same amino acid sequence for the purposes of the present application", and

"An amino acid sequence functionally similar to the sequence shown in Fig.1 ... may be from a different mammalian species."

10. The Enlarged Board of Appeal's decision G 01/03 (*supra*; point 2.1 of the Order) establishes the purpose of a disclaimer:

"A disclaimer may be allowable in order to:
- restore novelty by delimiting a claim against state of the art under Article 54(3) and (4) EPC."

11. The point to be decided when assessing whether the disclaimer in claim 1 is allowable is, thus, whether or not it delimits the claimed subject-matter from the above mentioned teachings on page 4 of document (4). Otherwise stated, should a sequence being 89% **identical** to the rat ER β sequence be regarded as a sequence with at least 80% homology to the human ER β sequence in its

DNA binding domain (SEQ ID NO:3) and with at least 70% homology to the human ER β sequence in its ligand-binding domain (SEQ ID NO:4) ?

12. A comparison of the rat ER β and the human ER β DNA binding domains (Fig.1, document (4) and SEQ ID NO:3) shows them to be 98.5% identical (one difference over 66 amino acids). A comparison between the rat ER β and the human ER β ligand-binding domains (Fig.1, document (4) and SEQ ID NO.4) shows them to be 92.7% identical (17 differences over 233 amino acids). It follows therefrom that molecules with 89% identity to rat ER β have 87.6% (98.5 x 89) identity and 82.5% (92.7 x 89) identity with, respectively, the DNA- and ligand-binding domains of human ER β . Such molecules are, of course, molecules with at least 80% homology to the DNA binding domain, SEQ ID NO:3 and at least 70% homology to the ligand binding domain, SEQ ID NO:4. They, thus, fall within the scope of the claim.

13. Appellant I argued that the disclosure in document (4) of molecules with 89% identity to the rat ER β molecule was a **generic** disclosure which, as such, could not take away the novelty of the claimed molecules identified by their percentages of homology to the human ER β molecule over specific domains which, as such, had to be considered a more **specific** disclosure than the disclosure in document (4). The board does not find this argument convincing. Disclosing an 89% identity to rat ER β would be understood by the skilled person as meaning that this percentage of identity is achieved over the length of the molecule. Indeed, there is no reason to believe that the 89% identity would be unevenly distributed with a percentage of identity

higher than 89% being found in the domains other than the DNA- and ligand- binding domains and with a percentage of identity lower than 89% being found in these last two domains. In fact, it is even the contrary which could be expected to happen, since the N-terminal region (domains A/B) is highly variable in size and sequence whereas the DNA binding domain (domain C) is highly conserved and the ligand binding domain (domain D) is moderately conserved (patent in suit, page 3, [003] to [006]). Thus, as shown above, document (4) discloses molecules with 87.6% and 82.5% identity to the human ER β sequence in the DNA- and ligand- binding domains; this disclosure is no more generic than the definition of the claimed molecules. In fact, it could even be seen as more specific since "identity" is a narrower feature than "homology".

14. For the reasons given in point 12, supra, the disclaimer is considered to be insufficient to delimit the claimed subject-matter from the teachings of document (4).

15. A further argument was presented by Appellant II as to why the disclaimer may not be allowable, namely that it should have been inserted in the text of the application as filed which is the basis for the patent in suit because document (4) was published on 13 March 1997 i.e. before the filing date of said application. Although dealing with this point is not strictly necessary in view of the findings in point 14, supra, the following observations are made. Article 54(2)(3) EPC reads as follows:

"(2) The state of the art shall be held to comprise everything made available to the public by means of a written or oral description, by use, or in any other way, before the date of filing of the European patent application.

(3) Additionally, the content of European patent applications as filed, the dates of filing of which are prior to the date referred to in paragraph 2 and which were published on or after that date, shall be considered as comprised in the state of the Article"

As for Article 89 EPC, it establishes that:

"The right of priority shall have the effect that the date of priority shall count as the date of filing of the European patent application for the purposes of Article 54, paragraphs 2 and 3, and Article 60 paragraph 2."

Reading these articles of the law in combination leaves absolutely no doubt that the provisions of Article 89 EPC are to be applied before those of Article 54 EPC.

16. In the present case, the effective filing date of the patent in suit is, thus, either one of its priority dates i.e. 22 November 1996 or 26 March 1996 and document (4) is certainly not a pre-published document, the teaching of which would have had to be disclaimed in the application as filed. Appellant II's argument is, thus, irrelevant.
17. As the disclaimer is not allowable under Article 123(2) EPC (see point 14 supra), the subject-matter of claim 1

lacks novelty under Article 54(3) EPC over the teachings of document (4).

Auxiliary request IIb; claim 1

Article 123(2) EPC; admissibility of the disclaimer

18. The disclaimer in claim 1 now comprises sequences which are more than 89% identical with the rat ER β protein sequence. At oral proceedings, Appellant II presented for the first time the argument that while document (4) disclosed molecules which were more than 89% identical with the rat ER β protein, this disclosure did not enjoy priority because in the relevant first and second priority documents pertaining to document (4), it was molecules with 90% identity with rat ER β which were disclosed. Therefore, in its view, the "more than 89% identity" was not a disclosure under Article 54(3) EPC and the disclaimer in fact removed more than was necessary to establish novelty. For this reason and following the principle established in point 3 of the decision G 01/03 (supra) that a disclaimer should not remove more than was necessary to establish novelty, the disclaimer in claim 1 should not be allowed.

19. This argument is a fully new argument and what would be the relevant evidence, namely the first and second priority documents pertaining to document (4), is not on file. As it stands, this appraisal of document (4) was even "left aside" by appellant II itself during the oral proceedings when the first auxiliary request was discussed. Then, appellant II took the view that the disclaimer of "only the specific rat ER β " was not allowable under Article 123(2) EPC since such case law as T 1120/00 (supra) established that a disclaimer was

not properly drafted when it failed to comprise the intermediate generalisations (i.e. sequences defined by way of homology to a given specific sequence) which an intermediate document may contain. In document (4), the intermediate generalisation is precisely molecules with 89% identity to the rat ER β specific sequence. Under the circumstances, the board decides to disregard the argument as being both late filed and not properly substantiated.

20. Appellants II and III further argued that the disclaimer was not sufficient because it failed to mention molecules functionally related to rat ER β , a teaching to be found on page 4 of document (4) (see point 9, supra). However, this teaching is so vague that it is totally unclear whether or not it covers any molecules falling within the scope of claim 1. For this reason, there is no need to disclaim it.

21. It is concluded that the disclaimer in claim 1 fulfils the requirements of Article 123(2) EPC.

Article 84 EPC, clarity

22. In accordance with the case law (see e.g. T 190/99 of 6 March 2001), a patent must be construed by a mind willing to understand, not a mind desirous of misunderstanding. In the board's judgment, the person skilled in the art would find it perfectly clear that the expression "a sequence which is more than 89% identical with that sequence" found at the end of the disclaimer was part of the disclaimer and that the term "that sequence" within it referred to the specific rat

ER β sequence directly above, which is also part of the disclaimer.

23. Whereas it is true that two "measuring systems" (percentage of identity vs. percentage of homology) are used in claim 1, this does not introduce a lack of clarity because firstly, there is no doubt as to with which molecules the identity or homology criteria should be used and, secondly, standard methods were known in the art to establish percentages of homology.
24. It is concluded that the requirements of Article 84 EPC are fulfilled and furthermore that since the disclaimer is allowable under Article 123(2) EPC, the claimed subject-matter is novel under Article 54(3) EPC over the teachings of document (4).

Article 56 EPC; inventive step

25. The closest prior art is the oral disclosure by Prof. J-A. Gustafsson on 22 March 1996 at the Keystone Symposium - Nuclear Receptor Superfamily as reflected by document (9), namely the notes taken by Dr U. Fuhrmann who was a member of the public attending the presentation. As would be expected, these notes are written in very much of a short-hand style. However, it has not been disputed that they convey the following information :
- A novel estrogen receptor (ER β) DNA had been cloned from rat prostate tissue. The ER β protein showed 95% identity to the prototype of the hormone receptor family, identified as ER or as α , in the DNA binding domain and 55% identity to this protein in the ligand binding domain. A corresponding ER β receptor existed in

- human tissues such as prostate, ovaries, uterus tissues, even in the central nervous system. The ER β receptor DNA of human origin had been or could be cloned with the help of a rat DNA probe.
26. It should be noted that post-published document (18), only to be taken as an expert opinion, also reported the same information when reviewing what had been disclosed at the symposium.
27. Starting from the closest prior art, the problem to be solved may be defined as reducing to practice the suggestion made by Prof. J-A. Gustafsson during his presentation (cf. document (9)) of isolating human ER β DNA/human ER β receptor protein.
28. The solution provided is to isolate ER β cDNA from a human testis cDNA library using primers, the sequences of which were derived from an ER β cDNA fragment, itself isolated from a cDNA library from human peripheral blood leukocytes. This fragment was obtained by using degenerate primers based on conserved regions of the DNA binding and ligand binding domains of the human hormone receptor family (patent in suit, Example A, [0059] to [0065]).
29. As the presence of ER β in human tissues was known from the presentation of Prof. J-A. Gustafsson (cf. document (9)), the fact of attempting to isolate ER β DNA from human tissues does not in itself contribute to inventive step. The issue to be decided is whether or not the person skilled in the art would have had a reasonable expectation of success when doing so. It is noted in this respect that Prof. J-A. Gustafsson during

his presentation (cf. document (9)) provided the information that the rat ER β protein is 95% identical to the prototype of the hormone receptor family, namely ER α (sequence described in prior art document (2)), in the DNA binding domain and that there also exist 55% identity between the two in the ligand binding domain. For the skilled person, that must have been a most useful item of information because it suggested that human ER β could be expected also to have a high degree of identity to prototype ER α . Of course, the observation made by Prof. J-A. Gustafsson during his presentation (cf. document (9)) related to sequence identity at the protein level. Yet, the percentages of protein sequence identity which he mentioned were high enough to strongly encourage the use of oligonucleotide primers derived from conserved regions in the DNA- and ligand- binding regions of members of the hormone receptor family (ER α). In fact, this was the strategy used in the patent in suit in the first step in the cloning of the human ER β DNA (see point 23). It was never argued that once an initial ER β DNA fragment had been isolated, any difficulties had been encountered in carrying out the cloning to its end.

30. Appellant I would seem to regard the use of a cDNA library from human testis tissue as indicative of inventive step, remarking that a successful post-published attempt at cloning human ER β DNA (document (21)) had also made use of testis tissue as starting material. In this respect, a first observation is that the ER β cloning as described in the patent in suit was initiated with a cDNA library from human peripheral blood leukocytes. This certainly goes against the idea that the use of a testis cDNA library in the last steps

of the experiment was a purposive choice indicative of inventive step. Apparently, nothing would have prevented the appellant from starting with the cDNA library from testis tissue as this was how the cloning was done in post-published document (21). Furthermore, the choice of testis tissue does not necessarily imply that the cloning could not have been achieved with a reasonable expectation of success starting from human prostate tissue which was disclosed by Prof. J-A. Gustafsson during his presentation (cf. document (9)) as containing the ER β molecule.

31. Appellant I pointed to the fact that earlier experiments failed to isolate rat ER β DNA from brain tissue (cf. prior art document (6)). Of course, this is not necessarily indicative that inventive step would be needed to isolate human ER β DNA from testis tissue.

32. To summarize, the person skilled in the art knew from the presentation by Prof. J-A. Gustafsson (cf. document (9)) that a human analog to rat ER β existed and the possibility of cloning human ER β DNA had already been envisaged in the art. He/she also knew that rat ER β protein was very much identical to the ER α prototype of the family of hormone receptor in the DNA binding domain, which suggested that human ER β might have the same property. This knowledge made it obvious to start the cloning of human ER β DNA with primers originating from conserved sequences in the DNA encoding the DNA binding site. No specific difficulties were encountered when cloning, the solving of which might have warranted an acknowledgement of inventive step. None of the post-published information provides any evidence that the

success in cloning was due to the specific choice of a cDNA library from testis tissue.

33. For these reasons, the subject-matter of claim 1 which relates to molecules having homology to human ER β in the DNA- and the ligand-binding domains does not fulfil the requirements of Article 56 EPC.

34. In the course of the written and oral proceedings, further objections were raised by Appellants II and III against the patentability of other claims. These need not be reviewed as a decision could be reached on the basis of claim 1 alone.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.
2. The patent is revoked.

The Registrar

The Chairman

S. Sanchez Chiquero

L. Galligani