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D E C I S I O N
of 6 February 2003

Case Number: T 0280/00 - 3.3.8

Application Number: 86307586.7

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Language of the proceedings: EN

Title of invention:
Nucleic acid encoding the alpha or beta chains of inhibin and method for synthesizing polypeptides using such nucleic acid

Patentee:
GENENTECH, INC.

Opponent:
Ajinomoto Co., Inc.

Headword:
Inhibin/GENENTECH

Relevant legal provisions:
EPC Art. 83, 87, 54, 56

Keyword:
"Main request - sufficiency of disclosure - yes"
"Priority rights - yes"
"Novelty - yes"
"Inventive step - yes"

Decisions cited:
T 0465/92, T 0411/98

Catchword:
-

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Case Number: T 0280/00 - 3.3.8

D E C I S I O N
of the Technical Board of Appeal 3.3.8
of 6 February 2003

Appellant I: (Proprietor of the patent)
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Decision under appeal: Interlocutory decision of the Opposition Division of the European Patent Office posted 19 January 2000 concerning maintenance of European patent No. 0 222 491 in amended form.

Composition of the Board:

Chairman: L. Galligani
Members: F. L. Davison-Brunel
S. C. Perryman

Summary of facts and submissions

I. The appeal lies from the interlocutory decision of the Opposition Division to maintain in amended form the patent No. 0 222 491 with the title "Nucleic acid encoding the alpha or beta chains of inhibin and method for synthesizing polypeptides using such nucleic acid" which was granted with 51 claims for Designated Contracting States BE, CH, DE, FR, GB, IT, LI, NL, SE, 51 claims for LU, 43 claims for GR and 43 claims for AT, ES and with priority dates of 3 October 1985, 7 February 1986 and 12 September 1986.

Granted claims 1, 16, 21 and 23 for the Designated Contracting States BE, CH, DE, FR, GB, IT, LI, NL and SE read as follows:

"1. A method comprising culturing a host cell transformed with a vector which includes nucleic acid encoding a human or porcine inhibin α chain and/or a human or porcine inhibin β chain, the amino acid sequences of which are as depicted in Fig 1B (porcine α chain), Fig 2B (porcine β chains), Fig 6A (human α chain) and Figs 8 and 9 (human β chains), or an amino acid sequence variant by way of insertion, deletion or substitution of a said depicted sequence, the variant being substantially homologous with a polypeptide of a depicted sequence but excluding bovine inhibin α chain and the partial bovine inhibin β chain of the sequence

(here follows the partial sequence of the bovine inhibin β chain)

and

1) being cross reactive with antibodies raised against a polypeptide of a depicted sequence; or 2) being cross reactive with cell surface receptors for a polypeptide of a depicted sequence; or 3) having like hormonal activity to a polypeptide of a depicted sequence."

"16. A composition comprising human or porcine inhibin made up of an α and a β chain, the amino acid sequences of said α and β chains being selected from those depicted in Fig 1B (porcine α chain), Fig 2B (porcine β chains), Fig 6A (human α chain) and Figs 8 and 9 (human β chains), and amino acid sequence variants by way of insertion, deletion or substitution of a polypeptide of a said depicted sequence, which variants are substantially homologous with a polypeptide of a depicted sequence, but excluding bovine inhibin α chain and 1) are cross reactive with antibodies raised against a polypeptide of a depicted sequence; 2) are cross reactive with cell surface receptors for a polypeptide of a depicted sequence; or 3) have like hormonal activity to a polypeptide of a depicted sequence; which composition is completely free of unidentified human or porcine proteins."

"21. A composition comprising a homodimer of mature human or porcine inhibin β_A or β_B chains, said chains being as depicted in Fig 2B (porcine β chains) and Figs 8 and 9 (human β chains) or of an amino acid sequence variant by way of insertion, deletion or substitution of a polypeptide of a said depicted sequence the variant being substantially homologous with a polypeptide of a depicted sequence and 1) being cross reactive with antibodies raised against a

polypeptide of a depicted sequence; 2) being cross reactive with cell surface receptors for a polypeptide of a depicted sequence; or 3) having like hormonal activity to a polypeptide of a depicted sequence; which composition is free of the inhibin α chain."

"23. A composition comprising a heterodimer of mature human or porcine inhibin β_A with mature human or porcine inhibin β_B, said chains being as depicted in Fig 2B (porcine β chains) and Figs 8 and 9 (human β chains) or of an amino acid sequence variant by way of insertion, deletion or substitution of a said depicted sequence the variant being substantially homologous with a polypeptide of a depicted sequence and 1) being cross reactive with antibodies raised against a polypeptide of a depicted sequence; 2) being cross reactive with cell surface receptors for a polypeptide of a depicted sequence; or 3) having like hormonal activity to a polypeptide of a depicted sequence; which composition is free of the inhibin α chain."

Claims 2 to 15, 17 to 19 and 22 related to further features of the method of claim 1 and of the compositions of claims 16 and 21, respectively. Claim 20 related to compositions comprising a prodomain of the human or porcine inhibin. Independent claim 24 related to non-chromosomal DNA encoding porcine or human inhibin chains defined in the same manner as in claim 1. Dependent claims 25 to 29 related to further features of the DNA of claim 24. Claims 30 to 33 related to a vector comprising the DNA of claims 21 to 27. Independent claim 34 related to a host cell transformed with a replicable vector defined in the same manner as in claim 1. Claims 35 to 38 related to further features of the host cell of claim 34.

Claims 39 to 51 were related to various cell-free compositions containing the prodomains sequences of the human or porcine α or β inhibins or containing polypeptides comprising said prodomains or variants thereof.

The claims for the Designated Contracting State LU were the same as the claims mentioned above except that the exclusion of the partial bovine inhibin β chain was omitted.

Neither the bovine inhibin α chain nor the partial bovine inhibin β chain were excluded from the claims filed for GR or for AT and ES which corresponded *mutatis mutandis* to the claims filed for the Designated Contracting States BE, CH, DE, FR, GB, IT, LI, NL and SE.

II. The Opposition Division accepted sufficiency of disclosure in relation to all claimed embodiments. They refused the granted claim request because claim 21 relating to $\beta_A\beta_A$ dimers of human origin lacked novelty over the teachings of document (5) (see below), under Article 54(3)(4) EPC . The patent was maintained on the basis of an auxiliary request which only related to inhibins of porcine origin.

III. Appellants I (Patentees) filed an appeal as well as Appellants II (Opponents). They paid the appeal fee and submitted statements of grounds of appeal.

IV. The Board sent a communication under Article 11(2) of the Rules of procedure of the Boards of Appeal together with the summons for oral proceedings.

V. Appellants I submitted eight auxiliary claim requests in preparation for the oral proceedings.

VI. At oral proceedings, Appellants I submitted as main request, an amended version of the granted claims for all Designated Contracting States which differed therefrom only by the deletion of the inhibin variants characterised by feature (2) from all claims which contained them, and by the consequent re-numbering of feature (3).

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

(2): Mason, A. J. et al., Nature, Vol. 318, pages 659 to 663, 19/26 December 1985,

(3): Ling, N. et al., Nature, Vol.321, pages 779 to 782, 19 June 1986,

(5): EP-B-0 210 461,

(8): WO 86/ 00 078

(P1): US 783 910 of 3 October 1985

(P2): US 827 710 of 7 February 1986

VIII. Appellants' II arguments in writing and during oral proceedings insofar as they relate to the present decision may be summarized as follows:

Article 83 EPC; sufficiency of disclosure in relation to the subject-matter of claims 1, 16, 21 and 23

The description did not contain enough information for the skilled person to be able to reproduce the claimed inventions comprising inhibin variant chains having like hormonal activity to a polypeptide of a depicted sequence. On the basis of the teachings of the patent in suit, it was impossible to identify such variants

once they were produced because one would not know which hormonal activity had to be tested: the αβ inhibin dimers had many such activities, the ββ dimers had a different hormonal activity from the αβ dimers. And, besides, individual α or β chains which were comprised within the claims were not expected to have any activity at all.

Article 87 EPC: priority rights
Claims 21 and 23

These claims comprised porcine and human inhibin β homo- or heterodimers, **having hormonal activity.**

The priority document (P1) (priority date: 3 October 1985) disclosed porcine inhibin β homo- or heterodimers whereas the priority document (P2) (priority date: 10 February 1986) disclosed, in addition, human inhibin β homo- or heterodimers. Irrespective of their origins, the chains which composed the dimers were said in both priority documents to be separated in vitro by unfolding: this implied that they were not linked by S-S bridges ie. that the corresponding dimers could not have hormonal activity.

In the same manner, the β_B β_B homodimers obtained by expression of the DNA disclosed in Fig.2B (porcine β_B chain) and Figure 9 (human β_B chain) would remain in the cytoplasm of the host recombinant cells and, therefore, the β_B chains could not be associated by means of S-S bridges ie. could not be hormonally active.

Consequently, claims 21 and 23 did not enjoy priority from either of the first two priority dates and, thus, like document (5) (relevant priority date: 2 February 1985), documents (2) and (3) published in December 1985 and June 1986, respectively, were to be taken into account for the assessment of novelty and/or inventive step.

Article 54 EPC; novelty
Claim 21

Document (5) disclosed a polypeptide: BUF-3 with the same partial amino acid sequence and the same properties as the β_A chain. Like β_A, BUF-3 was said to exist as a dimer and the slight difference in molecular weight between them could be attributed to variations in the glycosylation patterns. BUF-3 could thus be regarded as falling within the category of β_A variants, if not as β_A itself. Claim 21 lacked novelty over the teachings of document (5) insofar as it related to β_A homodimers or to variants thereof.

Claim 23

Document (3) was prior art under Article 54(2) EPC in relation to claim 23 which did not enjoy priority rights from either P1 or P2. As it disclosed the human β_A β_B heterodimer, it was detrimental to the novelty of said claim.

Article 56 EPC; inventive step of human inhibin chains

The closest prior art for all claimed human inhibins was document (2), as this document disclosed the α and β chains of porcine inhibin. The difference between these teachings and the claimed invention was that in the latter case, the inhibins were of human origin. The problem to be solved could thus be regarded as

providing active human inhibin. Alternatively, it could be defined as using porcine inhibin encoding DNA as a tool for the isolation of the corresponding human sequences.

The formulation of this problem was obvious because at the priority date there existed a need for producing human inhibin as it could be understood from reading the "background part" of the patent in suit or from the mentioning of human inhibin in document (8).

At the priority date, the skilled person was capable of constructing a cDNA bank as well as synthesizing oligonucleotide probes. He/she was also aware of the high degree of homology existing between proteins from animals and humans, for example TGF mentioned in document (2). Thus, once the problem had been formulated, it would only require routine work to produce the solution. The claimed subject-matter was not inventive.

IX. Appellants' I arguments in writing and during oral proceedings insofar as they relate to the present decision may be summarized as follows:

Article 83 EPC; sufficiency of disclosure in relation to the subject-matter of claims 1, 16 21 and 23

The argument of lack of reproducibility of the variants "having like hormonal activity to a polypeptide of a depicted sequence" was brought up for the first time during oral proceedings and, thus, could not be taken into account.

And, besides, the variants being identified in the claims as variants of **inhibin** chains, it was clear that the hormonal activity to be tested was that of inhibin, which the skilled person knew how to measure at the priority date as indicated in the introductory part of the patent in suit.

Article 87 EPC; priority rights
Claims 21 and 23

Document (P1) disclosed in a generic manner homo- and heterodimers of natural porcine inhibin β chains. Document (P2) disclosed the same molecules but of human origin. In both documents, the variants were further defined as being either immunologically cross-reactive with antibodies against the corresponding natural β chains or as having like hormonal activity to the corresponding natural inhibin β chains, it being that of inhibin where the α and β chains are associated. Accordingly, all claimed porcine inhibins enjoyed the first priority date whereas all claimed human inhibins enjoyed the second one.

Appellants' II allegation that claims 21 and 23 comprising hormonally active ββ dimers did not enjoy any of the first two priority dates because ββ dimers as disclosed in the priority documents (P1) and (P2) could not have been hormonally active failed in the absence of any evidence to support it.

Article 54 EPC; novelty
Claim 21

Document (5) disclosed a polypeptide, BUF-3, the monomeric form of which had a different molecular weight from that of β_A. Even if one was to attribute this difference to different glycosylation patterns,

this would not mean that the molecules would necessarily be the same: in fact, their amino acid sequences could not be compared in full since the amino acid sequence of BUF-3 was only partially characterized. As for the BUF-3 homodimer, it had a very different molecular weight from that of the β_A homodimer (25000 instead of 32000). Document (5) could not be considered as a clear and unambiguous disclosure of the human inhibin β_A chain, let alone of a homodimer thereof.

It had also been argued that BUF-3 belonged to the category of homodimers of β_A chain variants. Yet, the BUF-3 monomer had not been shown to fulfill the same immunological or functional criteria as the β_A chain variants composing the claimed variant homodimers. Thus, this argument, too, must fail.

Claim 23

This claim enjoyed the second priority date and, therefore, document (3) which was published after that date was not citable against novelty.

Article 56 EPC; inventive step of human inhibin chains

The only inhibins known as substances at the priority date were the porcine and bovine inhibins. Human inhibin, on the contrary, was solely known as an activity, materials hitherto identified as inhibin having widely ranging molecular weights. There was no reason to believe that there would exist in humans the exact counterpart of porcine inhibin. Document (2) did not give the information nor did it suggest that human and porcine inhibins might have a high degree of

homology. Thus, in using the porcine inhibin encoding DNA to help isolate the human inhibin encoding DNA, the skilled person would understandably have had a wish to succeed but no reasonable expectation of success of doing so.

Document (8) (page 2) mentioned inhibin substance or substances which meant that at the priority date, the skilled person still had doubts as to the agent responsible for inhibin activity. It taught that bovine inhibin had quite a different molecular weight from that of porcine inhibin. Furthermore, if the two inhibins showed some degree of homology, it was in different parts of the molecules. Accordingly, even a comparison between porcine and bovine inhibins did not suggest that cross species hybridisation may be of use to isolate the human inhibin DNA.

X. Appellants I requested that the decision under appeal be set aside and the patent be maintained on the basis of the main request filed at oral proceedings on 6 February 2003 (claims 1 to 51 for BE, CH, DE, FR, GB, IT, LI, NL, SE; claims 1 to 51 for LU; claims 1 to 43 for GR; claims 1 to 43 for AT, ES as filed at oral proceedings on 6 February 2003; Description: pages 6 and 7 as filed at oral proceedings on 6 February 2003 and pages 3 to 5, 8 to 23 as granted, and Figures as granted).

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

Reasons for the decision

Main request
Article 83 EPC; sufficiency of disclosure in relation to the subject-matter of claims 16, 21 and 23.

1. Appellants II argued that the homo- or heterodimers comprising variant chains of inhibin α, β_A or β_B functionally defined by their "like hormonal" activity (feature 2) were not sufficiently disclosed. Appellants I objected to this argument being considered since it had been presented for the first time at oral proceedings.

2. The decision of the Opposition Division under sufficiency of disclosure (paragraph 3.2) mentions that:

"The Opposition Division has no reasons to doubt that the variants can be tested **in all aspects**" (emphasis added). Thus, it is clear that the fulfilment of Article 83 EPC in relation to the functional properties of the variants is an issue which was decided upon by the first instance. Accordingly, the Board, whose function it is to review said decision, will consider the issue of the reproducibility of homo- and heterodimers comprising inhibin variant chains as functionally defined by feature 2).

3. The α, β_A or β_B chain variants have to have "like hormonal activity to a polypeptide of a depicted sequence", said polypeptide being the α, β_A or β_B chains of natural human or porcine inhibins characterised by their sequences. In the description of the patent in suit, inhibin is defined on page 3, lines 9 to 14 as a protein which acts specifically at the pituitary level to inhibit the secretion of follicle-stimulating

hormones, which activity may be measured by many biological assays. On page 3, lines 42 to 44 it is taught that the inhibin activity is the property of either one of two dimers A and B comprising the same α chain and a β_A or β_B chain linked by disulfide bridges. On page 4, lines 13 to 15, it is disclosed that individual α or β chains are not hormonally active.

4. In the Board's judgment, the skilled person presented with this information would have no difficulty in identifying the α, β_A or β_B inhibin chain variants with like hormonal activity as those variants which give positive results in the inhibin bioassays when in a dimeric association with the natural complementary chain. Thus, it is concluded that the variant chains can be reproduced as well as the homo- or heterodimers comprising them. Sufficiency of disclosure is acknowledged.

Article 87 EPC; priority rights

5. The priority document (P1) discloses in a generic manner porcine $\alpha\beta$ heterodimers (inhibin) and porcine β_A and β_B or β_A β_B homo- or heterodimers on page 22, lines 7 to 24. The porcine α and β variant chains as claimed, in particular, in claims 16, 21 or 23 are disclosed on page 9, line 26 to 33. The DNA sequences encoding the porcine α, β_A or β_B inhibin chains are shown in Figure 1B and Figure 2B.

The priority document (P2) is concerned with human as well as with porcine inhibin chains. The disclosures in the passage bridging page 24, line 24 and page 25, line 5 as well as on page 11, lines 16 to 22, which apply to human as well as to porcine inhibin chains are the same as the ones in the priority document (P1). The DNA sequences encoding human α, β_A and β_B inhibin chains are shown in Figure 6A, 8 and 9 respectively.

It is stated in document (P1) (page 22, lines 19 to 23) and (P2) (page 25, lines 2 to 5) that "...in preparing mature inhibin, the recombinant host is transformed with DNA encoding both the α and either of the β chains. The **intact hormonally active** molecule is then assembled by the host cell **in vivo**..." (emphasis added).

6. Appellants II argue that the generic disclosure of ββ dimers on the one side and the provision of the specific β DNA sequences in the Figures, on the other, does not amount to teaching ββ dimers **with hormonal activity** (ie. where the two subunits are linked together by disulfide bridges), which ββ dimers are comprised in claims 21 and 23 and, thus, may not serve as a basis for the acknowledgment of priority. They point out, in particular, to the statement on page 22 of the priority document (P1) that the ββ dimers may be separated by unfolding, which, in their view, implies that they could not be linked by such bridges. They also argue that the mature β_B inhibin chain encoded by the specific DNA isolated in the patent in suit could only be found in the cytoplasm of recombinant cells ie. would never form disulfide bridged dimers in such a reducing environment.

7. No evidence, however, is provided that the passage in priority document (P1) relating to the unfolding of the ββ dimers necessarily leads to the conclusion that no S-S bridged ββ dimers could be formed in a recombinant host cell. This evidence would be all the more necessary given that, as mentioned above, the priority document teaches that hormonally active, ie. S-S bridged αβ dimers are formed under the very same conditions (see point 5, supra). In the same manner, it has not been shown that if mature β chains are obtained

by recombinant expression of the DNA depicted in Figures 2B (porcine β_B) and Figure 9 (human β_B), then they would be found in the cytoplasm.

8. In the Board's judgment, the contents of the priority documents (P1) and (P2) as summarized in point 5 above respectively constitute an adequate description of the same subject-matter in the part of the claims referring to Figures 1B and 2B and in that referring to Figures 6A, 8 and 9. Thus, all claimed embodiments comprising porcine inhibins enjoy the first priority date and all claimed embodiments comprising human inhibins enjoy the second priority date.

Article 54 EPC; novelty
Claim 21

9. Document (5) (publication date: 3 November 1993, relevant priority date: 2 August 1985) is state of the art under Article 54(3) EPC. It discloses a human differentiation inducing factor: BUF-3 which is isolated in dimeric form from human malignant leukemia cells. This factor is argued by Appellants II to be identical to the human β_A β_A dimer of claim 21. As a monomer, BUF-3 has a molecular weight of 16+/- 1 Kd compared to 14 Kd for β_A; as a dimer, it has a molecular weight of 25 +/- 1 Kd compared to 32 Kd for β_A β_A. The amino acid sequences of BUF-3 and human β_A have 32 and 16 amino acids in common in stretches of 35 and 16 amino acids, respectively.

10. In accordance with the case law of the Boards of Appeal, an invention lacks novelty over the prior art if its subject-matter is clearly and directly derivable from said prior art and if all of its features are known from that prior art (see, for example, T 465/92, OJ EPO 1996, 32 and T 411/98 of 11 January 2000).

11. This is not the case here. Even if one is to accept that the difference in molecular weights between the BUF-3 and β_A monomers is due to different degrees of glycosylation, the difference observed between their dimeric forms is too big to be explained in the same manner. The amino acid sequences of the two polypeptides cannot be compared over their whole length as the BUF-3 amino acid sequence is not available in its entirety. As for considering BUF-3 as a variant of the human β_A monomer, there is no evidence in document (5) that BUF-3 possesses any of the functional features characterising said variants. For these reasons, it is concluded that document (5) does not provide a clear and unambiguous teaching of β_A and its dimer and, therefore, that it does not destroy the novelty of the subject-matter of claim 21.

Claim 23

12. The novelty of the β_A β_B dimer was challenged on the basis of the teachings of document (3). This document was published on 19 June 1986 ie. after the second priority date of the patent in suit, which priority date is valid for all claimed embodiments (see points 5 to 8 above). Accordingly, document (3) is not a prior art document and the argument of lack of novelty fails.

13. There are no other documents on file which are of relevance to novelty. The requirements of Article 54 EPC are fulfilled.

Article 56 EPC; inventive step

14. It was argued that the claims comprising/relating to human inhibins such as claims 16, 21 or 23 lacked inventive step. Human inhibin chains are disclosed for the first time in the second priority document and, thus, enjoy the second priority date (7 February 1986).

Therefore, documents (2) and (8) may be taken into account for the assessment of inventive step as they were published on 19 December 1985 and 3 January 1986, respectively.

15. Document (2) is the closest prior art. It describes the isolation of porcine α, β_A and β_B inhibin encoding DNAs from ovarian follicular fluid. On page 659, right hand column, it is disclosed that the clones containing these DNAs are screened by using a long DNA probe, the sequence of which is derived from the known amino acid sequences of the α, β_A and β_B chains. The similarity between porcine and bovine ovarian inhibins at the structural level is mentioned. On page 662 (passage bridging the left-and right hand column), it is stated that on account of the cysteine distribution and of sequence homology, both inhibin subunits and the human growth factor TGF-β probably belong to one gene family.

16. Starting from the closest prior art, the problem to be solved may be defined as providing a further inhibin molecule.

17. The solution given to this problem is to clone and express the DNA sequences encoding the **human** inhibin chains.

18. Ever since the existence of inhibin was postulated, the protein *per se* has always been an elusive protein (see background part of the patent in suit). Yet its activity is of great interest as it inhibits the secretion of the follicle-stimulating hormone. Thus, in

the Board's judgment, the skilled person wanting to solve the above mentioned problem would have thought that **human** inhibin was a particularly desirable protein to produce if only because of its potential interest in medicine.

19. The question which remains to be answered is whether or not there existed a reasonable expectation of success on the basis of the available prior art that the desired aim might be achieved by choosing the recombinant route leading to the isolation of the inhibin encoding DNA and to the subsequent production of human inhibin.

20. Document (2) does not mention human inhibin chains at all. This is also true of document (8) which only mentions humans in the context that bovine inhibin can be used in males or females of the human (page 20, lines 25 and 26), which suggestion, if anything, would lead the skilled person away from producing human inhibin.

21. In document (8), bovine inhibin was isolated from natural sources, in document (2), as mentioned above, porcine inhibin DNA was isolated by using a probe made from the knowledge of the porcine inhibin amino acid sequence. In choosing cross species hybridisation (**porcine** DNA as a screening tool for isolating **human** inhibin DNA), Appellants I significantly departed from the latter teaching, which would, on the contrary, have directed the skilled person to put his/her efforts in isolating and partially characterising human inhibin as a start to the cloning procedure. Neither document (8) nor document (2) give any pointer to the direction taken by Appellants I.

22. Document (2) mentions that bovine and porcine inhibins show some similarity at the amino acid sequence level and underlines the similarity between porcine inhibin, and human and mouse TGF-β, also at the amino acid sequence level, thus drawing attention to the homology which sometimes exists between proteins of various mammals and, possibly, between the corresponding encoding DNAs. The Board accepts that the knowledge of this hypothetical homology would have given the skilled person some hope that he/she might succeed in isolating a mammalian gene by cross-species hybridisation. Yet, in the Board's judgment, this hope does not amount to a reasonable expectation of success, in the absence of any indication/suggestion in the prior art that some degree of homology could be expected to exist between the human inhibin gene to be cloned and its presumed already known counterpart in another species.

23. For these reasons, inventive step is to be acknowledged also for the claimed human inhibin chains.

24. The inventive merit of the embodiments relating to porcine inhibin was not put into question by Appellants II. Nor does the Board, in agreement also with the finding of the Opposition Division, see any reasons to question it. Thus, the claim request as a whole meets the requirements for inventive step.

25. The main request for the Designated Contracting States BE, CH, DE, FR, GB, IT, LI, NL, SE filed at oral proceedings on 6 February 2002 fulfills the requirements of the EPC. The claim requests for the other Designated Contracting States filed at oral proceedings do not differ from this main request in a manner which would alter this conclusion of patentability.

26. No objections have been raised to the amended description, pages 6 and 7 which have been adapted to the claim requests.

Order

For these reasons, it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the first instance with the order to maintain the patent on the basis of the following documents:

Claims 1 to 51 for BE, CH, DE, FR, GB, IT, LI, NL, SE; claims 1 to 51 for LU; claims 1 to 43 for GR; claims 1 to 43 for AT, ES as filed at oral proceedings on 6 February 2003;

Description: pages 6 and 7 as filed at oral proceedings on 6 February 2003 and pages 3 to 5, 8 to 23 as granted; and

Figures as granted.

The Registrar: The Chairman:

A. Wolinski L. Galligani

TDB