BESCHWERDEKAMMERN DES EUROPÄISCHEN PATENTAMTS

BOARDS OF APPEAL OF THE EUROPEAN PATENT OFFICE

CHAMBRES DE RECOURS DE L'OFFICE EUROPEEN DES BREVETS

Internal distribution code:
(A) [ ] Publication in OJ
(B) [ ] To Chairmen and Members
(C) [X] To Chairmen
(D) [ ] No distribution

Datasheet for the decision of 27 March 2006

Case Number: T 0973/03 - 3.3.04

Application Number: 92900527.0

Publication Number: 0563093

IPC: C12N 15/33

Language of the proceedings: EN

Title of invention:
A composition used as a therapeutic agent against chronic viral hepatic diseases

Patentee:
MEDEVA HOLDINGS B.V.

Opponent:
SmithKline Beecham Biologicals SA

Headword:
Therapeutic agent against chronic viral hepatic diseases/MEDEVA

Relevant legal provisions:
EPC Art. 83, 100(b)

Keyword:
"Sufficiency of disclosure - (no)"

Decisions cited:
T 0182/89, T 0548/91, T 0694/92, T 0636/97

Catchword:
-

Europäisches Patentamt | European Patent Office | Office européen des brevets

Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 0973/03 - 3.3.04

D E C I S I O N
of the Technical Board of Appeal 3.3.04
of 27 March 2006

Appellant: (Patent Proprietor)
MEDEVA HOLDINGS B.V.
Churchill-Laan 223
NL-1078 ED Amsterdam (NL)

Representative:
Campbell, Patrick John Henry
J.A. KEMP & CO.
Gray's Inn
14 South Square
London WC1R 5JJ (GB)

Respondent: (Opponent)
SmithKline Beecham Biologicals SA
89 rue de l'Institut
B-1330 Rixensart (BE)

Representative:
Privett, Kathryn Louise
GlaxoSmithKline
Corporate Intellectual Property (CN9.25.1)
980 Great West Road
Brentford, Middlesex TW8 9GS (GB)

Decision under appeal:
Interlocutory decision of the Opposition Division of the European Patent Office posted 4 July 2003 concerning maintenance of the European patent No. 0563093 in amended form.

Composition of the Board:

Chair: G. Alt
Members: R. Gramaglia
D. S. Rogers

Summary of Facts and Submissions

I. European patent no. 0 563 093 with the title "A composition used as a therapeutic agent against chronic viral hepatic diseases" was granted with 20 claims for the Contracting States AT, BE, CH, LI, DE, DK, FR, GB, IT, LU, MC, NL, SE, with 20 claims for the Contracting State ES and with 40 claims for the Contracting State GR.

II. Claim 1 as granted for all Designated Contracting States except ES and GR reads:

"1. Use of a composition for the production of a medicament for the treatment of chronic viral hepatitis, said composition comprising a combination of

a) at least one polypeptide sequence having one or more antigenic T cell-activating epitopes and

b) a carrier capable of presenting the epitope sequence(s) a), wherein the polypeptide sequence(s) a) is bound to carrier b) by covalent or hydrophobic bonding."

III. The patent was opposed under Article 100(a) EPC, lack of novelty (Article 54 EPC) and inventive step (Article 56 EPC); under Article 100(b) EPC, that the European patent did not disclose the invention in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art, and under Article 100(c) EPC, that its subject-matter extended beyond the content of the application as filed.

IV. The patent proprietor filed a main request and an auxiliary request during the opposition proceedings.

Claim 1 of the main request differed from claim 1 as granted by the insertion of the expressions "caused by a hepatitis virus" and "of the hepatitis virus" (in bold below) and read:

"1. Use of a composition for the production of a medicament for the treatment of chronic hepatitis **caused by a hepatitis virus**, said composition comprising a combination of

a) at least one polypeptide sequence having one or more antigenic T cell-activating epitopes **of the hepatitis virus** and

b) a carrier capable of presenting the epitope sequence(s) a), wherein the polypeptide sequence(s) a) is bound to carrier b) by covalent or hydrophobic bonding."

Claim 1 of the auxiliary request differed from claim 1 as granted by the insertion of the expressions "caused by a hepatitis B virus" and "of the hepatitis B virus" (in bold below) and read:

"1. Use of a composition for the production of a medicament for the treatment of chronic hepatitis **caused by a hepatitis B virus**, said composition comprising a combination of

a) at least one polypeptide sequence having one or more antigenic T cell-activating epitopes **of the hepatitis B virus** and

b) a carrier capable of presenting the epitope sequence(s) a), wherein the polypeptide sequence(s) a) is bound to carrier b) by covalent or hydrophobic bonding."

V. The opposition division maintained the patent in amended form on the basis of the auxiliary request. The opposition division decided that the main request did not comply with the requirements of Article 83 EPC. It was held that the molecular structures of hepatitis B virus (HBV) and hepatitis C virus (HCV) were different. Information about origin and sequence of suitable hepatitis C virus T-cell activating epitopes was however missing in the patent in suit and successful treatment of hepatitis C was neither disclosed in the patent nor in any of the available documents. Therefore, the opposition division had serious doubts whether the results disclosed in the patent in connection with hepatitis B virus could be extended to hepatitis C virus. The burden of proof for demonstrating that the claimed use was also possible for hepatitis C virus rested with the proprietor of the patent in suit. Since evidence to this effect had not been filed by the proprietor, the disclosure of the invention had to be regarded as insufficient because the invention could not be carried out over the whole scope claimed.

VI. The patent proprietor (appellant) lodged an appeal against the interlocutory decision of the opposition division.

VII. The respondent (opponent) did not respond to the appellant's statement of grounds of appeal.

VIII. Oral proceedings took place on 27 March 2006 in the absence of the respondent who had previously announced that he would not be attending.

IX. The following documents are referred to in this decision:

D19:Rehermann, B. et al., Journal of Virology, vol. 70, no. 10, 1996, pages 7092-7102; abstract

D24: "Viral hepatitis and liver disease; proceedings of the 1990 International Symposium on Viral Hepatitis and Liver Disease: Contemporary Issues and Future Prospects"; Editors: Hollinger, F. B. et al., 1991

D37: Rothbard, J.B. and Taylor, W.R., The EMBO Journal, vol. 7, no. 1 1988, pages 93-100

X. The arguments of the appellant submitted in the context of Article 83 EPC and as far as they are relevant for the present decision may be summarized as follows:

The burden of proof in opposition proceedings rested with the opponent and not with the proprietor. Therefore, it was not correct that the opposition division denied sufficiency of disclosure for the reason that the proprietor had not provided evidence that the invention worked for all claimed embodiments.

The difference in the molecular structures of hepatitis B virus and hepatitis C virus was not of relevance for the assessment of whether the teaching in the patent how to treat a chronic hepatitis B virus infection could be extended to the treatment of a chronic hepatitis C virus infection. Rather, the nature of the immunological response to the viruses in the liver of infected subjects was decisive for determining whether chronic infections caused by either of hepatitis B or C virus could be treated in the same way. The available evidence in the post-published documents pointed to the fact that stimulating the T-cell response was an effective treatment for hepatitis caused by hepatitis C virus.

The invention contributed a new general principle to the art. It was held for example in decisions T 694/92 and T 636/97 that in such a situation claims of a broad scope were allowable even in view of only a limited number of actually exemplified embodiments.

XI. The arguments of the respondent submitted in writing in the context of Article 83 EPC during the opposition proceedings and as far as they are relevant for the present decision may be summarized as follows:

Claim 1 did not only cover the use of the compounds referred to in the claim in the manufacture of a medicament for the treatment of hepatitis B virus infection, but also of hepatitis C virus infection. Hepatitis B and C viruses were members of different virus families, i.e. while hepatitis B was a member of the hepadnaviridae family of viruses which were DNA viruses with a partially double stranded DNA genome,

hepatitis C virus was a member of the flaviviridae family which were single-stranded (+) stranded RNA viruses. Thus, both viruses had different molecular structures. Therefore, at the priority date of the patent in suit the way how an infection progressed to the chronic state was believed to be different for hepatitis B and C virus. Indeed, it had been shown in post-published document D19 that cytotoxic T lymphocytes were hard to detect in patients chronically infected with HBV. In contrast, in the case of a chronic hepatitis C infection a strong response of cytotoxic T lymphocytes was detected. Therefore, the disclosure in the patent in suit of results of a treatment with a compound covered by claim 1 of an hepatitis B infection did not enable the skilled person to achieve the same successful treatment for an hepatitis C infection.

XII. The appellant (patentee) requested that the decision under appeal be set aside and that the patent be maintained on the basis of the main request filed with the statement of the grounds of appeal, such main request being the same as the main request before the opposition division.

The respondent (opponent) made no explicit written requests.

Reasons for the decision

1. The opposition division refused the main request pursuant to Article 100(b) EPC. Other objections were not raised with respect to this request. Therefore, the

sole question at issue is whether or not the main request fulfils the requirements of Article 83 EPC.

2. The reason for the opposition division's finding of lack of sufficient disclosure was that the patent proprietor, who according to the opposition division had the burden of proof, had not submitted evidence to dispel the opposition division's serious doubts as regards the possibility of extending the results disclosed in the patent for the treatment with the combination recited in claim 1 of chronic HBV infection to the treatment of chronic HCV infection.

3. It is established case law, that in opposition proceedings the burden of proof for an assertion regarding facts submitted for substantiating grounds of opposition rests on the opponent (for example T 182/89 of 14 December 1989 or T 548/91 of 7 February 1994). Consequently, in the present case, the burden of proof is not with the proprietor. Therefore, the board is not convinced by the reason given by the opposition division to justify finding a lack of sufficiency of disclosure.

4. Nevertheless, the board cannot set aside the decision of the opposition division because it agrees with the decision for the reasons set out below:

5. Claim 1 is directed to the use of a composition as defined in claim 1 for the production of a medicament for the treatment of chronic hepatitis caused by a hepatitis virus. According to page 2 of the patent in suit infections by hepatitis B, C and D virus can progress to a chronic state. Hence, embodiments of

claim 1 are the use of a composition as defined in the claim for the production of a medicament for the treatment of chronic viral hepatitis caused by either of hepatitis B, C and D virus, the latter not being an issue here because it neither had been dealt with by the respondent nor considers the board it necessary to do so in view of the negative decision, see below.

6. It has been established by the case law in the context of Article 83 EPC that **substantially any embodiment** of the invention as defined in the broadest claim must be capable of being realised (Case Law of the Boards of Appeal of the European Patent Office, 4th edition 2001, II.A.3). Hence, the skilled person must be able to successfully treat chronic hepatitis caused by hepatitis C virus.

7. In the respondent's view this is not the case. He argues that hepatitis B and hepatitis C viruses are members of distinct virus families and consequently have different molecular structures. Therefore, the mechanism of infection of the two viruses is believed to be different, as is the immunological response to their infection. Hence, results specifically related to chronic hepatitis B in the patent in suit cannot be extrapolated to chronic hepatitis C. In other words, the disclosure in the patent in suit of compositions suitable for the treatment of a chronic hepatitis B virus infection is not sufficient to enable the skilled person to achieve treatment for a chronic hepatitis C virus infection.

8. However, according to established case law, whether the disclosure of an invention as claimed is sufficiently

clear and complete to be carried out by the skilled person has to be judged having regard to the teaching made available to the skilled person on the basis of **the whole description in combination with the common general knowledge** (Case law of the Boards of Appeal of the European Patent Office, II.A.1 and II.A.2). Therefore, the issue is not, as implied by the respondent's argument, whether the disclosure in the patent in suit related to the treatment of chronic hepatitis B virus infection is sufficient to enable treatment of hepatitis C virus infection, but rather whether treatment of chronic hepatitis C virus infection can be achieved on the basis of the whole disclosure in the patent in suit supplemented by the common general knowledge of the skilled person.

9. Furthermore, according to the case law, the disclosure should be such as to enable the skilled person to carry out the invention **without undue burden and inventive skill** (Case law of the Boards of Appeal of the European Patent Office, II.A.4). Thus, in the following it will be evaluated whether the skilled person, without undue burden and exercise of inventive skill, was in a position to arrive at hepatitis C T-cell epitope-containing compounds as defined in the claim to be used in the manufacture of a medicament for the treatment of chronic hepatitis caused by hepatitis C virus.

10. The patent in suit contains a general teaching that a combination of at least a polypeptide sequence derived from a polypeptide of the hepatitis virus to be treated and having one or more antigenic T-cell activating epitopes in combination with a carrier capable of

presenting said epitopes is useful to treat chronic hepatitis caused by that virus.

The description of the patent in suit describes in detail the structural proteins of the hepatitis B virion on page 2, lines 28 to 41 and identifies compounds containing T-cell epitopes derived from hepatitis B virus for targeting chronic hepatitis B carriers in Tables I, II and III. Examples 10 and 11 disclose the administration of one such compound containing parts from the S1 and S region of hepatitis B virus to hepatitis B virus-infected chimpanzees and humans.

11. The only passages in the patent specifically related to hepatitis C virus are found on page 2 of the patent in suit:

"There is relatively little data available on hepatitis C and D, on methods for the diagnosis and their treatment and on the respective viruses. [...] Only very recently the hepatitis C virus has been detected and an antibody test (anti-HCV) facilitating the diagnosis of chronic hepatitis C infections has been developed."

12. Thus, while the patent provides extensive disclosure about hepatitis B polypeptides and their T-cell epitopes, there is no explicit disclosure of a single hepatitis C viral polypeptide or T-cell epitope in the patent in suit. The teaching about hepatitis B virus polypeptides and T-cell epitopes does not assist the skilled person to fill this gap because, as known at the priority date of the patent (document D24, page 6),

hepatitis B and C are taxiconomically unrelated viruses with a different genomic structure.

13. At the priority date of the patent in suit a skilled person knew of methods for predicting open reading frames, i.e. amino acid sequences coding for a protein, on the basis of certain sequence patterns in the amino acid sequence and for predicting T-cell epitopes in polypeptides (document D37). The appellant argues that these methods could easily be used for determining the polypeptides expressed by the hepatits C virus genome and the sequence stretches therein representing T-cell epitopes.

14. However, at the priority date of the patent in suit hepatitis C virus had only just been discovered (see page 2 of the patent in suit). None of the prior art documents available to the board and published before the priority date discloses which proteins are actually expressed from the hepatits C virus genome. Hence, nothing was yet known about any viral polypeptide. The board considers that under these circumstances the skilled person could easily make predictions on a theoretical level. However, since such predictions are fraught with uncertainty in the absence of any tangible knowledge about, for example, the actual mode of translation of the viral nucleic acid into proteins, the theoretical determination of open reading frames or of T-cell epitopes with such methods can only be a starting point requiring practical testing of what has been determined on a theoretical level. In view of the apparent lack of information about the synthesis and replication of hepatitis C virus at the priority date of the patent in suit - the only data available being

an antibody test for determining the presence of hepatitis C virus (see the patent in suit on page 2) and the RNA sequence of the genome of HCV (see document D24, page 6) - the board judges that the amount of work to be performed before arriving at the means enabling the claimed use to be carried out was so high as to constitute an undue burden for the skilled person.

15. Moreover, decisions T 694/92 of 8 May 1996 and T 636/97 of 26 March 1998 do not support the appellant's case. These decisions are concerned with the allowability of a broad claim when the patent only discloses a small number of examples. It was held a broad claim is only allowable pursuant to Article 83 EPC, if the intended effect of the invention can be achieved in the broad area claimed without exercising inventive skill. However, as set out above, the skilled person needed inventive skill before it could proceed to the claimed invention and achieve the desired effect.

16. In view of points 10 to 15 above, the board thus concludes that it was only with undue burden that the skilled person could prepare polypeptide sequences comprising T-cell activating epitopes of hepatitis C virus necessary for the use according to claim 1 on the basis of the teaching in the patent and/or the common general knowledge. Hence, the embodiment of claim 1 relating to the manufacture of a medicament for the treatment of chronic hepatitis caused by hepatitis C virus is not disclosed in a manner sufficiently clear for it to be carried out by the skilled person.

17. Consequently, since an invention as claimed is only considered as disclosed in a manner sufficiently clear

and complete for it to be carried out by a person skilled in the art if substantially all of its embodiments can be performed, the invention is not sufficiently disclosed in the present case.

18. The main request does not fulfil the requirements of Article 83 EPC.

Order

For these reasons it is decided that:

The appeal is dismissed.

Registrar: Chair:

P. Cremona G. Alt