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Datasheet for the decision of 25 October 2006

Case Number: T 1399/04 - 3.3.04

Application Number: 99303729.0

Publication Number: 0956861

IPC: A61K 38/21

Language of the proceedings: EN

Title of invention:
Combination therapy comprising ribavirin and interferon alpha in antiviral treatment naive patients having chronic hepatitis C infection

Patentee:
SCHERING CORPORATION

Opponents:
01. Alfa Wassermann S.p.A.
02. Teva Pharmaceutical Industries Ltd.
03. Sandoz GmbH
04. Krauss, Jan B.

Headword:
Combination therapy HCV/SCHERING

Relevant legal provisions:
EPC Art. 52(4), 54, 87-89, 111(1), 113(1), 123(2)
EPC R. 67

Keyword:
"Substantial procedural violation - (yes)"
"Reimbursement of the appeal fee - (yes)"
"Admissibility of late-filed documents - (yes)"
"Added subject-matter - (no)"
"Not patentable invention - (no)"
"Priority, novelty - (yes)"

Decisions cited:
G 0005/83, G 0004/92, G 0002/98, T 0019/86, T 0081/87, T 0133/87, T 0125/91, T 0464/94, T 0808/94, T 0233/96, T 0914/98, T 0893/90, T 1020/03

Catchword:
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Case Number: T 1399/04 **-** 3.3.04

D E C I S I O N
of the Technical Board of Appeal 3.3.04
of 25 October 2006

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Decision under appeal:
Decision of the Opposition Division of the European Patent Office posted 16 December 2004 rejecting the oppositions filed against European patent No. 0956861 pursuant to Article 102(2) EPC.

Composition of the Board:

Chair: U. Kinkeldey
Members: M. Wieser
G. Weiss

Summary of Facts and Submissions

I. Appeals were lodged by Opponents 01 to 04 (Appellants I to IV) against the decision of the Opposition Division wherein their oppositions against European patent No. 0 956 861, claiming priority from US 79566 (15 May 1998), were rejected under Article 102(2) EPC.

II. The patent had been granted with claims 1 to 11. Claim 1 read as follows:

"The use of ribavirin for the manufacture of a pharmaceutical composition for treating a patient having chronic hepatitis C infection to eradicate detectable HCV-RNA wherein the pharmaceutical composition is for administering an effective amount of ribavirin in association with an effective amount of interferon alpha, **characterised in that** the ribavirin in association with the interferon alpha is for administration for a time period of 40-50 weeks, the patient is an antiviral treatment naive patient, and the patient is one having a HCV genotype type 1 infection and a viral load of greater than 2 million copies per ml of serum as measured by HCV-RNA quantitative PCR."

Independent claim 2 referred to the use of interferon alpha for the manufacture of a pharmaceutical composition for treating a chronic HCV patient. Independent claim 3 related to the use of both, ribavirin and interferon alpha, for the same purpose. Dependent claims 4 to 11 referred to preferred embodiments of the subject-matter of claims 1 to 3.

III. The patent had been opposed under Article 100(a) EPC on the grounds of lack of novelty (Article 54 EPC), lack of inventive step (Article 56 EPC) and because it did not relate to a patentable invention according to Article 52(4) EPC and under Article 100(c) EPC on the ground of added subject-matter.

IV. The Opposition Division, at the end of oral proceedings held on 1 December 2004, had decided that claims 1 to 11 as granted met all requirements of the EPC.

Two letters of formal complaint, dated 14 and 16 December 2004, were sent by Opponent 02's representative to the Vice President DG2 of the EPO. Therein it was stated that the Opponents' right to be heard at the oral proceedings before the Opposition had been violated contrary to the requirements of Article 113(1) EPC and that the Opposition Division, therefore, had reached their decision by making a substantial procedural violation. Copies of these letters were submitted to the President of the EPO on 21 December 2004.

A further letter of complaint, concerning the course of events at the oral proceedings before the Opposition Division, was sent by Opponent 02 "To the Customer Services department" on 16 December 2004. This letter was signed by Dr Yehudah Livneh, General Patent Counsel of Opponent 02.

V. Patent proprietor's (Respondent's) representative, in a letter to the Vice President DG2 of the EPO, dated 21 January 2005, argued that the Opponents' right to be heard had not been violated and that the Opposition

Division had not committed a substantial procedural violation at the oral proceedings.

VI. In their respective letters setting out the grounds of appeal, all four Appellants requested to set aside the decision by the Opposition Division, to revoke the patent and to reimburse the appeal fees (Rule 67 EPC).

Appellant II, in addition, requested expedited processing of the appeal procedure.

As an auxiliary request Appellants I, II and IV requested to remit the case to the department of first instance for further prosecution according to Article 111(1) EPC.

VII. The Board expressed their preliminary opinion in a communication dated 7 April 2006.

Oral proceedings were held on 24 and 25 October 2006.

VIII. Appellants I to IV requested that the decision under appeal be set aside, that the patent be revoked and the appeal fees are reimbursed.

The Respondent requested that the decision under appeal be set aside and the case be remitted to the department of first instance for further prosecution.

IX. The present decision refers to the following documents:

(OD1) Gastroenterology, vol.111, 1996, pages 1307-1312

(OD2) Hepatology, vol. 26, No. 3, Supplement 1, 1997, pages 108S-111S

(OD5) J. Hepatology, vol. 23, Supplement 2, 1995, pages 8-12

(OD8) EP-A-0 707 855

(OD11) Scand. J. Infect. Dis., vol. 27, 1995, pages 325-329

(OD12) Hepatology, vol. 26, no. 2, pages 500-504

(OD34) Hepatology, vol. 24, 1996, 356A, abstract 917

(OD35) Gastroenterol., vol. 105, 1993, pages 507-512

(OD105) Declaration by Dr T. Berg, 20 April 2005

X. The submissions made by the Appellants, as far as they are relevant to the present decision may be summarised as follows:

The abrupt and unexpected end of the oral proceedings before the Opposition Division took the Appellants by surprise. They were only given the possibility to present their arguments with regard to inventive step in the light of document (OD2). Oral proceedings were scheduled for two days. When the Opposition Division at the evening of day one interrupted the proceedings for a deliberation the Appellants were thoroughly convinced that this deliberation only concerned the argument

submitted so far, namely inventive step in the light of the disclosure in document (OD2). Contrary to this and to the surprise of the Appellants the Opposition Division after resuming the proceedings gave a final decision with regard to inventive step in the favour of the Opponent. The Appellants have had no possibility to bring forward their remaining arguments in the light of the disclosure in other prior art documents. Their right to be heard had thus been violated contrary to the requirements of Article 113(1) EPC. According to the case law of the Boards of Appeal such violation had to be considered as a substantial procedural violation which justified the reimbursement of the appeal fee according to Rule 67 EPC. However, as the factual situation of the present case had not significantly changed and a remittal to the department of first instance would significantly delay a final decision and create a period of legal and commercial uncertainty, a final decision should be taken by the Board.

Appellants I, II and IV, at the oral proceedings, formally withdrew their auxiliary request for remittal to the department of first instance for further prosecution (see section VI above).

If the Board would nevertheless follow Respondent's request and remit the case, Appellant III argued that it should not examine the question of inventive step (Article 56 EPC) at all. A partial consideration of this issue by the Board, for instance only with regard to the question whether or not the claimed subject-matter was inventive in the light of the disclosure in document (OD2) alone, could create problems for the

department of first instance when considering to combine document (OD2) with another prior art document.

In the present case the results of the clinical trials on file were all in the hand of the Respondent. This created a very difficult situation for the Appellants. They had to consult experts in the here relevant technical field and to ask them for their interpretation of these data. These interpretations, which were filed during the appeal procedure in the form of expert declarations, reflected the understanding of the disclosure in the prior art by a person skilled in the art at the relevant date. It was therefore considered to be fair to admit these declarations, and further documents cited therein, into the proceeding.

In case the Board intended to base its decision to remit the case to the department of first instance upon the filing of 46 documents during the appeal procedure (documents (OD75) to (OD120)), Appellant II offered not to refer to any of these documents in his pleadings at the oral proceedings before the Board of Appeal.

The term "antiviral treatment naïve patients" was given a precise meaning in section [37] of the application as published. The same term when used in the claims was not restricted by the precise definition given in the description, which resulted in a violation of the requirements of Article 123(2) EPC (Appellant I).

The subject-matter of the claims was excluded from patentability according to the requirements of Article 52(4) EPC.

The claimed invention was defined in the priority document in respect to an effect measured at a specific point in time, which effect was not part of the present claims. The subject-matter of the claims as granted was thus a generalization of the invention disclosed in the priority document, which had a different conceptualisation. The claims therefore were not entitled to the priority date.

The alleged invention lacked novelty in view of a public prior use (Appellant III). Evidence therefore had to be taken from in Dr Berg's declaration (document (OD105)). Moreover, the claimed subject-matter lacked novelty in view of the disclosure in prior art documents (OD2), (OD8) and (OD12) contrary to the requirements of Article 54 EPC.

XI. The submissions made by the Respondent, as far as they are relevant to the present decision may be summarised as follows:

The Appellants had been given ample opportunity, both during the written procedure and at the oral proceedings before the Opposition Division, to present their arguments. At the oral proceedings they were repeatedly invited by the Chairman of the Opposition Division not to restrict their argumentations to the disclosure in document (OD2) alone, but to also consider other prior art documents already discussed in the written procedure. Accordingly, there was no reason why the Appellants should have been taken by surprise when the Opposition Division at the end of the first day of the hearings announced a final decision with

regard to the requirements of Article 56 EPC and rejected the Oppositions.

During the appeal procedure the Appellants had filed 46 additional documents. This massive filing at a late stage of the procedure had the effect that, with regard to the issue of inventive step, the present case had substantially changed. Especially the filing of a number of declarations by Appellant II exactly two months before the oral proceedings, wherein the Appellant's technical experts, by referring to a number of additional documents, presented their interpretation of the experimental data and the disclosure in the most relevant prior art on file, had put an immense pressure on the Respondent who had not sufficient time to counter argue these new lines of argumentation. It was of no importance whether or not the Appellants would refer to these documents during the oral proceedings, as the content of these documents had already come to the Boards attention and it could not be excluded that it played some role in the present decision finding process.

The documents filed at a late stage of the procedure should therefore not be allowed into the proceedings. In case the Board would decide that these documents were admitted into the procedure, it should, in order to allow a fair hearing of the present case in two instances, after having heard the parties and after having decided on all formal and substantial issues except inventive step (Article 56 EPC), remit the case to the department of first instance for further prosecution.

The term "antiviral naive patients" appeared in the claims as originally filed. The same term, unchanged, was used in the claims as granted. An objection under Article 123(2) EPC, which was concerned with amendments extending beyond the content of the application as filed, could not be of any merit.

The independent claims 1 to 3 were formulated as "Swiss-type-claims" and referred to the use of a substance known per se for a specific second or further medical use. According to the established case law of the Boards of Appeal the subject-matter of these claims was not excluded from patentability according to the requirements of Article 52(4) EPC.

The priority document was not restricted to a method causing a specific effect to be measured at an exact point in time. This embodiment rather was designated in the priority document as being "yet another aspect of the invention". The specification of the priority document when read as a whole contained a direct and unambiguous teaching of the claimed subject-matter.

Neither document (OD105), referring to an alleged public prior use, nor documents (OD2), (OD8) or (OD12) disclosed all features of the presently claimed invention. Therefore, novelty of the subject-matter of claims 1 to 11 (Article 54 EPC) had to be acknowledged.

Reasons for the Decision

Right to be heard - Substantial procedural violation - Reimbursement of the appeal fee
Article 113(1) EPC - Rule 67 EPC

1. Summons to attend oral proceedings before the department of first instance were sent to the parties on 16 March 2004 together with a detailed communication (11 pages) summarising the written procedure. Oral proceedings were scheduled for 1 and 2 December 2004 (the originally planned date, 15 and 16 November 2004, was changed upon request of the present Respondent).

2. In the communication, amongst other issues, the Opposition Division analysed the present Appellants' arguments with regard to the question of inventive step (Article 56 EPC) and identified at least seven different documents which the Appellants had identified as representing the closest state of the art. The parties were reminded that during oral proceedings strict compliance with the "problem-and-solution approach" would be enforced.

3. The evidence on file upon which the Board has to decide whether or not a substantial procedural violation by the Opposition division has happened are the minutes of the oral proceedings before the Opposition Division and the submissions by the parties.

   According to this evidence the following picture can be drawn:

After having heard the parties on the requirements of Articles 123(2) and 52(4) EPC (points (2) and (3) of the minutes) and after deciding on the validity of the claimed priority date (points (4.1) to (4.4) of the minutes), the parties were invited to present their arguments with regard to novelty (Article 54 EPC) of the claims as granted. Upon request of the Patent Proprietor's representative he was given "the opportunity to reply to the submissions of each opponent individually, since in view of the huge number of prior art documents cited in the written procedure, he would find it extremely difficult to reply to all objections in one step" (point (4.6) of the minutes).

4. Having reached a decision with regard to Article 54 EPC, the Opposition Division turned to the requirements of Article 56 EPC. "For the discussion of inventive step it was agreed to follow the modus already applied for the discussion of novelty, i.e. to hear the proprietor with respect to the individual submissions of the opponents" (point (5.1) of the minutes).

Opponent 01's representative presented her arguments wherein she identified document (OD2) as closest state of the art. She was supported by Opponent 02's representative before the Patent Proprietor's representative was heard (points (5.2) to (5.4) of the minutes). The Chairman of the Opposition Division interrupted the representative of the Patent Proprietor and suggested, in view of the late time, to adjourn oral proceedings and to continue on the next day. However, the Proprietor "**preferred to finish the point he was dealing with"** (point (5.4) of the minutes).

5. It seems to the Board that at this point in time during the oral proceedings before the Opposition Division a crucial misunderstanding took place between the Opposition Division and the Opponents with regard to the question what was actually meant by the Proprietor when referring to "**the point**" he wished to finish before an adjournment of the proceedings.

While the Opposition Division seems to have been of the opinion this **"point"** was the question of inventive step in total, the Opponents obviously were of the opinion that **"the point**" to be finished was the assessment of inventive step starting from document (OD2) as closest state of the art only. In the light of the agreement on the modus of the discussion as set out in point (5.1) of the minutes of the proceedings (see above) they obviously were of the opinion that they will be allowed to present other arguments concerning the issue of inventive step, starting from other documents as closest state of the art, after an adjournment of the proceedings and the resumption on the following day.

6. The further course of the oral proceedings, as described in points (5.5) to (5.14) of the minutes and in the submissions of the parties, seems to support this impression of crucial misunderstanding described above. Although the Primary Examiner (point (5.6) of the minutes) and the Chairman of the Opposition Division (point (5.14) of the minutes) invited the parties not only to consider document (OD2) as closest state of the art, but also to argue in the light of other documents, all parties, the Opponents and the Patent Proprietor solely argued with regard to document (OD2).

The Chairman finally interrupted the proceedings and announced after a deliberation of the Opposition Division and a resumption of the proceedings that the oppositions were rejected (points (5.15) to (5.17) of the minutes. This decision included that claims 1 to 11 as granted were based on an inventive step in accordance with the requirements of Article 56 EPC.

7. The immediate reaction of all Opponents to the announcement of this decision was surprise and they also immediately complained that their right to be heard has been violated contrary to the requirements of Article 113(1) EPC, as they were not given the opportunity to present all their arguments with regard to the issue of inventive step (see point (6) of the minutes).

8. The provision of Article 113(1) EPC, requiring that the decisions of the EPO may only be based on grounds or evidence on which the parties concerned have had an opportunity to present their comments, is one of the most important guarantors for the parties that proceedings before the EPO will be conducted openly and fairly. It is of fundamental importance for ensuring a fair procedure between the EPO and the parties conducting proceedings before it (cf. decision of the Enlarged Board of Appeal G 4/92, OJ EPO 1994, 149; point (2) of the reasons).

9. The opportunity to present comments must be a genuine and realistic one in the circumstances of the case and not merely theoretical (cf. decision T 914/98 of 22 September 2000; point (2)). As an express right to

oral proceedings is enshrined in Article 116 EPC, failure to adequately hear the parties at such an oral proceedings cannot be cured by referring to the fact that the parties could have presented all their arguments in the written procedure.

10. In the present case the Opponents in the written procedure have presented various lines of argumentation attacking the inventive step of the claimed subject-matter and starting from different documents as closest state of the art. The protests of the Opponents after the oral proceedings before the Opposition Division are a strong indicia that they intended to present and to further substantiate these different lines of argumentation at the oral proceedings.

11. The decision under appeal deals in point (6) with the requirements of Article 56 EPC. In point (6.1) the Opposition Division reasons its decision with regard to an inventive step of the claimed subject-matter starting from document (OD2) as closest state of the art.

12. According to point (6.2) "the same conclusion would be reached if one started from document OD8 as the closest prior art document, ...". Considering the course of events as described above, the Board is convinced that the Appellants (Opponents) were not given the possibility at the oral proceedings before the Opposition Division to present their comments on this issue and were thus taken by surprise by the announcement by the Opposition Division that their oppositions were rejected and the reasons based on document (OD8).

13. Therefore the Board arrives at the judgement that the (Opponents') Appellants' right to be heard as defined in Article 113(1) EPC has been violated in the procedure before the Opposition Division. This constitutes a substantial procedural violation in view of which the Board considers it as being equitable to refund the appeal fees, as provided for under Rule 67 EPC.

Admissibility into the procedure of documents (75) to (120)

14. The decision under appeal contains as Annex I a list of 74 cited documents (documents (OD1) to (OD74)). In the appeal procedure 46 additional documents have been filed by the Appellants (see "List of cited documents", submitted by the Respondent with letter dated 16 October 2006; documents (OD1) to (OD119) plus document (OD120) filed by Appellant III with letter dated 19 October 2006).

All these newly filed documents have been referred to by the Appellants in their written submissions with regard to the requirements of Article 56 EPC.

15. The Board has decided that the decision under appeal with regard to the question of inventive step has been taken by the Opposition Division by violating the requirements of Article 113(1) EPC.

The Board takes the view that for the hearing of this issue in order to arrive at a fair and justified decision it should consider all pieces of evidence

which the Appellants have brought forward to substantiate their arguments.

Documents (OD75) to (OD 120) are therefore admitted into the procedure.

Amendments - Article 123(2) EPC

16. The application as originally filed reads on page 12, lines 27 to 29:

"The term "antiviral naïve patients" in the context of the present invention means that the patients have never been treated with ribavirin or any interferon including, but not limited to an interferon-alpha."

Claim 1 as originally filed refers to "[t]he use of ribavirin for the manufacture of a pharmaceutical composition for treating an antiviral treatment naïve patient having chronic hepatitis C infection ...".

The same formulation is used in claim 1 as granted (see section (II) above).

17. Article 123(2) EPC requests that a European patent application or a European patent may not be amended in such a way that it contains subject-matter which extends beyond the content of the application as filed.

Appellant (I) argues that claim 1 as granted violates the requirements of Article 123(2) EPC as it does not contain the exact interpretation of the term "antiviral naïve patients" as given in the application as filed.

18. Claim 1 as granted, as regards the term in question, is identical to claim 1 as originally filed. For this reason alone, no violation of Article 123(2) EPC is seen.

Moreover, a patent specification shall be used to interpret the claims, that is to say the patent itself is its own dictionary. In the present case, the meaning of the term "antiviral naïve patients" is given in the description of the patent in suit (paragraph [37]) and, identically, in the application as filed. Thus, there is no room for a different, broader definition of this term.

Patentable inventions - Article 52(4) EPC

19. According to Article 52(4) EPC methods for treatment of the human or animal body by surgery or therapy and diagnostic methods practised on the human or animal body are not considered to be patentable inventions.

Claims 1 to 3 refer to the use of ribavirin, interferon-alpha or both for the manufacture of a pharmaceutical composition for treating an antiviral naïve patient having hepatitis C (HCV) genotype 1 infection having a viral load of greater than 2 million copies per ml of serum for a time period of 40 to 50 weeks.

20. The Appellants have argued that the use of these substances for the treatment of (HCV) was known in the art and that the claims amounted to no more than an extension of a known regimen of 24 weeks to 40 to 50 weeks. The continuation of treatment must be based

on a decision of the physician. Therefore, as the claimed subject-matter related to no more than a physician's decision, it was not a patentable invention according to Article 54(2) EPC.

21. According to the decision of the Enlarged Board of Appeal G 5/83 (OJ EPO 1985, 64) a claim which takes the form of use of a compound for the preparation of a medicament for a specific therapeutic use, will avoid being in conflict with Article 52(4) EPC, irrespective of the degree of detail with which the therapeutic use is stated (cf. decision T 1020/03 of 29 October 2004, point (18) of the reasons).

If a claim is drafted such to avoid the prohibited method of therapy of Article 52(4) EPC first sentence, as in the Board's judgement is the case for present claims 1 to 3 which are in the approved "Swiss" form, compliance with this provision does not need to be considered further. The decisive question to be answered in accordance with decision G 5/83 is then whether the intended method of treatment for which the medicament was manufactured was novel and inventive, and not any further considerations under Article 52(4) EPC (cf. decision T 1020/03 supra, points (26) and (34) of the reasons).

22. Accordingly, the argument of the Appellants must fail. The requirements of Article 52(4) EPC are met.

Priority - Articles 87 to 89 EPC

23. The priority document, on page 4, lines 15 to 24, refers to "yet another aspect of the invention". This aspect relates to the treatment of the patient group of claims 1 to 3 (antiviral treatment naïve, chronic HCV genotype 1, virus load greater than 2 million copies) for the time period as stated in the claims (40 to 50 weeks). The treatment is said to be "such that about 23-31% of the patients having no detectable HCV-RNA at the end of said 40-50 week period also have no detectable HCV-RNA for at least 24 weeks after the end of said administration." The same wording can be found in claim 52 of the priority document.

The Appellants argued that claims 1 to 3 did not contain the specifically disclosed effect which was measured at a defined point in time (23-31% have no HCV-RNA at the end of the treatment and 24 weeks thereafter). They concluded that the subject-matter of the claims 1 to 3 was a generalization of the invention disclosed in the priority document, which had a different conceptualisation.

24. Claims 1 to 3 refer to the use of ribavirin, interferon alpha, or both for the manufacture of a pharmaceutical composition for **treating** a patient having chronic HCV. The claims do not refer to a method for healing a certain percentage of the treated patients. As can be seen from tables 6, 14, 16 and 17, which are contained in the priority document, in the application as originally filed and in the patent as granted in an unmodified way, a number of patients treated responded to the treatment in a positive way.

On page 5, lines 14 to 33 of the priority document it is stated that two to three times more patients of the target group as defined in claims 1 to 3, when treated for an extended time period of 40 to 50 weeks, had no detectable HCV-RNA in their serum at least 24 weeks after termination of combination therapy, compared to those who had been treated for 24 weeks only.

25. Article 87(1) EPC provides that a European patent application may claim the priority of an earlier application only for the same invention. This means that the subject-matter of the European patent application's claims must be clearly identifiable in the previous application as a whole. However, identical wording is not required (cf. decision T 81/87 OJ EPO 1990, 250, point (6)).

The Board is convinced that the priority in respect of present claims 1 to 11 in accordance with Article 88 EPC is to be acknowledged as the skilled person can derive the subject-matter of the claims directly and unambiguously, using common general knowledge from the previous application as a whole, in detail from page 5, lines 14 to 33 and tables 6, 14, 16 and 17 (cf. decision of the Enlarged Board of Appeal G 2/98 OJ EPO 2001, 413; point (9)).

Novelty - Article 54 EPC

Public prior use

26. Appellant III argued that the patent in suit lacked novelty in view of public prior use. Evidence therefore

was to be taken from a declaration by Priv.-Doz. Dr Thomas Berg signed on 20 April 2005 and submitted with letter dated 26 April 2005 (document (OD105)).

Dr Berg declares that he has treated a patient having chronic HCV genotype 1 infection in the time between 31 May 1996 and March 2000. The patient, who had a virus load of 24 million copies by millilitre of serum, was treated by combination therapy, i.e. 3 x 3 million units interferon per week plus 400 mg ribavirin per day (points 2 to 6 of the declaration).

27. The patient received his/her first liver transplant on 24 December 1993 and did not receive interferon or ribavirin before the start of the combination therapy on 31 May 1996.

Regarding the time before 24 December 1993 it is said in document (OD105) that it is assumed ("Es ist daher anzunehmen, ...") that the patient had not received interferon (point (8)). This assumption is based on the facts that the patient suffered from liver cirrhosis, which is considered to be an exclusion criterion for the application of interferon, and that interferon in the early 90ies was used rarely and mainly for clinical studies. A treatment with ribavirin before 24 December 1993 is excluded because this medicament was not approved before this date and there were no data available as to its efficacy (point (9)).

28. Appellant III argued that no obligation for secrecy existed with regard to the treatment of the patient as described in document (OD105). Documents existed at the Charité, Berlin, which had not been disclosed in the

present procedure for reasons of privacy of the patient (letter dated 24 August 2006; page 20).

29. In ascertaining the facts relating to an alleged prior use a strict standard of proof has to be applied (see Case law of the Boards of Appeal of the EPO, 4th Ed. 2001, VI.J.5(b)). A European patent should not be refused or revoked unless the grounds for refusal or revocation are fully and properly proved.

30. The period of treatment described in point (2) of document (OD105) runs from 31 May 1996 to March 2000, thus roughly 200 weeks. Appellant III argues that a patient being treated for 200 weeks, at a certain point in time has been treated for 40 to 50 weeks, as required by the claims.

The Board does not agree that the subject-matter of claims 1 to 3, which explicitly refers to an administration period of 40 to 50 weeks, encompasses a therapy wherein the medicaments in question have been administered for about 200 weeks. Thus, even in the assumption that the public prior use was proven as required by the case law of the Boards of Appeal (see above), it was not novelty destroying.

31. Moreover, when indicating why the treated patient is considered to be antiviral treatment naïve, the declaration relies on assumptions ("Es ist daher anzunehmen, ..."; point (8) of document (105)).

In the Board's view it is not justifiable to decide whether a public prior use is prejudicial to novelty on the basis of **probability**. When a patent is revoked for

lack of novelty, the Board has to be **sure**, having taken all the facts and arguments put foreward during the proceedings into consideration, that the revocation is justified (cf. decision T 464/94 of 21 May 1997; point 16)).

32. At least for the reasons given in points (30) to (31) above, the Board judges that the evidence on file is not sufficient to prove beyond reasonable doubt that document (OD105) discloses a novelty destroying public prior use of the claimed subject-matter.

Written evidence

33. The Appellants objected to the novelty of the claimed subject-matter in the light of the disclosure in documents (OD2), (OD8) and (OD12).

34. Document (OD2) is a review article published about eight months before the priority date of the patent in suit and refers to therapy of HCV.

Starting at the bottom of the left column on page 109S the document contains a chapter dealing with combination therapy, i.e. the administration of ribavirin and interferon alpha. In the right hand column on the same page the document contains a summary of clinical studies carried out in Italy, Sweden, Japan and Taiwan and reports of the first randomized double-blind, placebo-controlled study of combination therapy with 100 interferon naïve patients with chronic HCV. (These studies are published in documents (OD1), (OD5), (OD11), (OD34) and (OD35)). The administration time in all these studies is 24 weeks. The results of some

studies are shown in tables 2 and 3 on page 110S. The tables show biochemical (alanine aminotransferase level) and virological (absence of detectable HCV-RNA by PCR) "end-of-treatment" response (ETR) and "sustained response (SR). The results are indicated as percentages of successfully treated patients.

In the chapter titled "Discussion" on page 110S, right column, it is said that it is difficult to recommend combination therapy as the first approach to treatment for interferon naïve patients. Especially patients with a favourable clinical profile (young age, low viral load or infection with HCV genotype 2 or 3) respond equally well to interferon alone. The sentence bridging pages 110S and 111S reads as follows:

"In this respect, patients with high HCV RNA levels, genotype 1, high degrees of viral genomic diversity, **or** histological evidence of advanced fibrosis or cirrhosis would be candidates to receive combination therapy initially." (emphasis added by the Board).

Page 111S, left column, second full paragraph reads:

"At present several multicenter and multinational randomized controlled trials comparing interferon alone to the combination with ribavirin are under way in Europe, North and South America, Asia and Australia. These studies will compare 24 and 48 weeks of therapy and will include large enough samples of patients to evaluate whether the combination is helpful in patients with all genotypes, all levels of HCV-RNA, and all histological stages of disease."

The patients of claims 1 to 3 of the patent in suit are defined as being antiviral treatment naïve **and** having a chronic HCV genotype 1 infection **and** a viral load of greater than 2 million copies per ml measured by quantitative PCR. This patient group is not disclosed in document (OD2).

The sentence bridging pages 110S and 111S (see above) lists several parameters of a clinical profile that would make an interferon naïve patient a candidate for receiving combination therapy initially. The first three of these parameters are separated by commas, the third and fourth parameters are separated by the word **"or"**. The Board concludes that the authors of document (OD2) considered a patient having a high HCV RNA level, **or** genotype 1, **or** a high degree of viral genomic diversity, **or** histological evidence of advanced fibrosis or cirrhosis, to be a candidate for combination therapy.

The passage on page 111S, left column (see above) refers to clinical studies which either will have to be carried out in the future, or whose results will become available in the future. The announcement that these studies will compare 24 and 48 weeks of therapy and will investigate the effectiveness of combination therapy for patients with all different genotypes, all levels of HCV RNA and all histological stages of the disease makes it **probable but in no case sure** that the exact clinical set up of claims 1 to 3 will be covered (antiviral naïve patients, chronic HCV genotype 1 infection, virus load greater than 2 million copies per ml, administration for 40 to 50 weeks).

As already mentioned in point (31) above, when a patent is revoked for lack of novelty, the Board has to be **sure**, having taken all the facts and arguments put foreword during the proceedings into consideration, that the revocation is justified (cf. decision T 464/94, supra)

Thus, document (OD2) does not anticipate the subject-matter of claims 1 to 11.

35. Document (OD8), a European patent application filed by the present Respondent, discloses the use of ribavirin, interferon alpha or both in the manufacture of a pharmaceutical composition for treating chronic HCV infections (claims 1 to 3). The patients may be previously untreated, thus antiviral treatment naïve (column 3, line 36), and the duration of the treatment is from 6 to 12 months (claim 11).

The document does not refer to a specific HCV genotype and does not mention the virus load of the patients.

The Appellants argued that a skilled person following the teaching in document (OD8) and treating chronic HCV patients in general, automatically treats patients with HCV genotype 1. In fact a very high percentage, at least more than 50%, of all HCV infections were genotype 1 infections, which were known to be associated with a high virus load. The subject-matter of present claims 1 to 3 was therefore the selection of a specific patient group, which, for a big part, overlapped with the patient group disclosed in document (OD8).

The Appellants pointed to the relevant case law of the Boards of Appeal with regard to inventions referring to a selection from a broader range and especially to overlapping ranges.

This case law, which is summarised on pages 80 to 83 of the English version of the Case law of the Boards of Appeal, 4th Ed. 2001, explicitly refers to "a selection of a sub-range of **numerical values** from a broader range" and to "overlapping **numerical ranges"**. The patent in suit does not refer to numerical values or ranges, but to the treatment of a specific sub-group of human patients within all human beings suffering from HCV infection.

The Board considers the difference in complexity between an human organism and the one-dimensional structure of a numerical value or a numerical range to be so fundamental that the case law mentioned above does not apply in the present case.

Moreover the Appellants referred to the case law of the Boards of Appeal with regard to novelty of claims referring to a second or further medical use of a substance for the preparation of a medicament to be applied to different groups of subjects.

If the use of a compound was known in the treatment or diagnosis of a disease of a particular group of subjects, the treatment or diagnosis of the same disease with the same compound could nevertheless represent a novel therapeutic or diagnostic application, provided that it is carried out on a new group of subjects which is distinguished from the

former by its **physiological or pathological** status (cf. decisions T 19/86, OJ EPO 1989, 24; point (8) of the reasons and decision T 893/90 of 22 July 1993 (point (4.2) of the reasons).

The patient group according to present claims 1 to 3 is defined as being infected by a specific genotype of HCV, genotype 1, which is a **pathological** characteristic allowing to differentiate members of this group from all other HCV patients, **and** it is further defined by a viral load of greater than 2 million copies per ml of serum, which is a **physiologically** characterising feature. Both features are not disclosed in document (OD8).

According to the established case law of the Boards of appeal, cf. decisions T 19/86 and T 893/90 (supra), the subject-matter of claims 1 to 3 represents a new therapeutic application as the patient group concerned is distinguishable from the patient group of document (OD8) by its **physiological and pathological** status.

The Appellants referred to decision T 233/96 of 4 May 2000. In this decision the competent Board, in point (8.7) of the reasons, interpreted decisions T 19/86 and T 893/90 such that the conclusion reached in these decisions, namely that the treatment or diagnosis of the same disease with the same compound could represent a novel therapeutic or diagnostic application provided it is carried out on a new group of subjects, does not apply, if the group chosen overlaps with the group previously treated or the choice of the novel group is arbitrary which means that no functional relationship does exist between the

particular physiological or pathological status of this group of subjects (here humans who are unable to exercise adequately) and the therapeutic or pharmacological effect achieved.

The present Board does not see a basis for this interpretation in the relevant parts of decisions T 19/86 (points (5) to (8)) and T 893/90 (points (4.2) to (4.6)).

Claim 1 of the second auxiliary request considered by the Board in decision T 233/96 referred to the use of adenosine in the preparation of a diagnostic agent for detecting a vascular disease of coronary arteries in a human patient **"who is unable to exercise adequately"**. Claim 1 of the main request and of the first auxiliary request, which did not refer to this patient group, had been found to lack an inventive step (points (3) to (7.7) of T 233/96). In point (8.8) it is stated that the feature **"who is unable to exercise adequately"** is very vague and general and embraces at best a subgroup of those patients having coronary artery disease already being treated with adenosine according to a prior art document. Moreover, there did not exist "... any functional relationship between the incapability of a patient to exercise adequately and the pharmacological effect achieved by the administration of adenosine in the diagnosis of various types of coronary disease. In fact, no evidence or argument was provided by the appellant to show any interaction between the physical hindrance and the hyperemic effect caused by adenosine."

The Board in decision T 233/96 did not regard the feature in question to be capable of distinguishing the subject-matter of the claim from the disclosure in the prior art and came to the conclusion that the claim lacked inventive step.

The technical situation underlying the present case differs obviously from the situation underlying decision T 233/96.

While in case T 233/96 no evidence was on file for the existence of a functional relationship between the feature distinguishing the patient group of the claim from the patient group treated according to the prior art and the pharmacological effect achieved by the active compound of the manufactured composition, this is not so in the present case. The patent in suit contains studies which convincingly show that it is exactly the patient group according to claims 1 to 3, namely antiviral treatment naïve chronic HCV genotype 1 patients with a virus load greater than 2 million copies per ml serum, which profits most from an extension of the combination therapy from 24 weeks to 48 weeks (see tables 6, 14 16 and 17 of the patent).

For this reason alone the present Board considers that the conclusion drawn in decision T 233/96 (supra) do not apply in the present case.

Therefore, in line with the case law of the Boards of Appeal as shown in decisions T 19/86 and T 893/90 (supra), the subject-matter of claims 1 to 11 is novel over the disclosure in document (OD8).

36. Document (12) reports the results of a pilot study of the combination therapy of recurrent HCV infection after liver transplantation. Twenty-one interferon treatment naïve patients with detectable HCV RNA in their serum before transplantation, twenty thereof infected with HCV genotype 1, were treated with ribavirin and interferon alpha after transplantation for six months. Thereafter the patients received ribavirin monotherapy for another six months. Three of the patients had a biological relapse during ribavirin monotherapy. These three patients received a second course of combination therapy which was instituted six months after the first course (see document (OD12), page 501 to 502).

The Appellants argued that claims 1 to 3, referring to an administration period of 40-50 weeks, encompassed a "split treatment" of a patient, which consisted of six months combination therapy, an interruption of six months and a second course of combination therapy.

The Board decides that neither the wording of the claims nor any passage in the description of the patent in suit, especially in the part describing the studies, allows such an interpretation. Thus, as the subject-matter of the claims does not cover a "split-treatment" as disclosed in document (OD12), this documents is not detrimental to the novelty of claims 1 to 11.

37. The Board decides that claims 1 to 11 are novel and meet the requirements of Article 54 EPC.

Remittal - Article 111(1) EPC

38. According to Article 10 of the Rules of procedure of the Boards of Appeal, a Board shall remit a case to the department of first instance if fundamental deficiencies are apparent in the first instance proceedings, unless special reasons present themselves for doing otherwise.

39. According to the case law of the Boards of Appeal the violation of the principle of the right to be heard is considered as a fundamental deficiency of first instance proceedings (cf. decisions T 125/91 of 3 February 1992 and T 808/94 of 26 January 1995, for example).

It is, however, also acknowledged that there is no absolute right for a party to have every aspect of a case examined in two instances (cf. decision T 133/87 of 23 June 1988, point (2), for example). Other criteria, e.g. the general interest that proceedings are brought to a close within an appropriate period of time, have also to be taken into account.

40. In the present case the Appellants' right to be heard has been violated in the procedure before the department of first instance (see points (1) to (13) above). However, for reasons of economy of procedure, Appellants I, II and IV withdrew their requests for remittal of the case at the oral proceedings before the Board as they did not wish an undue delay, which would prolong the period of legal and commercial uncertainty.

The Respondent, arguing that the present case with regard to the issue of inventive step had substantially changed as a result of the fact that the Appellants had filed 36 additional documents in the appeal procedure. He requested remittal of the case to the department of first instance in order to have this new evidence examined by two instances and in order to allow him to prepare counterarguments especially with regard to the complex expert declarations filed by Appellant II two months before the date of the oral proceedings.

41. As a result of a procedural violation, the Appellants, at the oral proceedings before the department of first instance, were able to present only one specific line of argumentation with regard to an alleged lack of inventive step (Article 56 EPC). During the appeal procedure they have not only relied on arguments which had been already raised in the written procedure before the department of first instance, but they have also filed new evidence that opened the door for new lines of argumentation not yet heard by the Opposition Division.

In this respect, the Board agrees with the Respondent that Appellant's II suggestion, not to refer at the oral proceedings before the Board to any of the additional documents filed late in the appeal procedure, was of no help. These documents have been read by all parties and by the members of the Board. As it is not possible to fade out their teaching from a persons mind this could influence the present decision finding process.

42. The Board, has to weigh up the Appellants' arguments with regard to economy of procedure and the Respondent's wish to have all facts and evidence considered by two instances.

Being confronted with this situation, the Board arrives at the decision that the right to a fair procedure and a fair hearing, which is one of the most important principles of procedural law generally recognized in the Contracting States and which has to be taken into account by the EPO under Article 125 EPC, is served best upon remittal of the case to the department of first instance.

Thus, in the present case the Respondent's request should have precedence over apprehensions regarding an undue delay of the procedure.

43. Appellant III has argued that the Board, in the case it decided to remit the case, should not examine the question of inventive step at all. The Board agrees that a partial consideration of this issue, for instance only with regard to the question whether or not the claimed subject-matter was inventive in the light of the disclosure in document (OD2) alone, could create problems for the department of first instance when considering to combine document (OD2) with another prior art document.

Therefore, the Board sustains from such partial examination of inventive step and remits the case to the department of first instance for further prosecution according to Article 111(1) EPC.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the department of first instance for further prosecution.

3. The reimbursement of the appeal fees is ordered.

Registrar: Chair:

P. Cremona U. Kinkeldey