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D E C I S I O N
of 8 February 2001

Case Number: T 0188/97 - 3.3.4

Application Number: 88310922.5

Publication Number: 0318216

IPC: C12N 15/00

Language of the proceedings: EN

Title of invention:
NANBV diagnostics and vaccines

Patentee:
CHIRON CORPORATION, et al

Opponent:
(4) Dade Behring Marburg GmbH
(5) The Research Foundation for Microbial Diseases of Osaka University
(6) F. HOFFMANN-LA ROCHE & CO. Aktiengesellschaft

Headword:
NANBV/CHIRON CORPORATION

Relevant legal provisions:
EPC Art. 105, 123(2)(3), 84, 56, 83, 87-89
EPC R. 13, 67, 57a

Keyword:
"Admissibility of the interventions (no)"
"Admissibility of Appellant's II appeal (yes)"
"Main request - added subject-matter (yes)"
"Auxiliary requests A to D - sufficiency of disclosure (no)"
"Auxiliary request E - inventive step (yes)"

Decisions cited:
G 0001/93, G 0009/93, G 0004/97, J 0008/81, J 0002/87, J 0003/87, J 0027/92, T 0201/83, T 0025/85, T 0292/85, T 0081/87, T 0073/88, T 0060/89, T 0905/90, T 0187/91, T 0289/91, T 0288/92, T 0124/93, T 0296/93, T 0412/93, T 0824/94, T 0343/95, T 0460/95, T 0923/95

Catchword:
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Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 0188/97 - 3.3.4

D E C I S I O N
of the Technical Board of Appeal 3.3.4
of 8 February 2001

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 18 December 1996 concerning maintenance of European patent No. 0 318 216 in amended form.**

Composition of the Board:

Chairwoman: U. M. Kinkeldey
Members: F. L. Davison-Brunel
C. Holtz

Summary of facts and submissions

I. European patent No. 0 318 216, with the title "NANBV diagnostics and vaccines" claiming six priorities from 18 November 1987, 30 December 1987, 26 February 1988, 6 Mai 1988, 26 October 1988 and 14 November 1988 was granted with 77 claims for the Contracting States AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE, 53 claims for the Contracting State ES and 72 claims for the Contracting State GR, all on the basis of European patent application No. 88 310 922.5.

II. Six notices of opposition were filed. Opponents 1 to 3 withdrew their oppositions. By a decision within the meaning of Article 106(3) EPC dated 18 December 1996, the Opposition Division maintained the patent in amended form on the basis of the third auxiliary request then on file.

III. Appellants I (Patentees) and Appellants II (Opponents 6) lodged an appeal against the decision of the Opposition Division. Opponents 4 and 5 are parties to the proceedings as of right (Article 107 EPC).

Formal issues

Admissibility of the interventions

IV. On 16 March 1999, an intervener filed a letter which stated that a notice of intervention under Article 105 EPC was enclosed and that this notice was based on seizure proceedings instituted by Appellants I, in Belgium, on 17 December 1998. Accompanying this letter was a copy of the order served by the Judge of Seizures at the Court of First Instance, Ghent, Belgium, under Articles 1481-88 of the Belgian Judicial Code, which

provisions govern said seizure proceedings, as well as an opinion from a Belgian legal counsel explaining why the Belgian seizure proceedings should qualify as an infringement proceeding under Article 105 EPC. It was also requested to file the grounds for the intervention after the admissibility of the intervention had been acknowledged by the Board. The opposition fee and the appeal fee were paid on the same day.

V. In a communication dated 8 April 1999, the Board's registrar informed the Intervener that, since the letter received on 16 March 1999 had not been accompanied by a notice of intervention including a written reasoned statement, it seemed that the intervention was inadmissible.

VI. In their submissions dated 8 June 1999, the Intervener withdrew their request that the seizure proceedings be regarded as a procedure for infringement according to Article 105 EPC and announced their intention to file a new notice of intervention on the basis of the official court proceedings for infringement initiated by Appellants I as a result of the findings of the investigation carried out during the seizure proceedings and served on the Intervener on 23 April 1999.

VII. On 23 July 1999, the Intervener filed a second notice of intervention in a written reasoned statement. The opposition fee and the appeal fee were paid on the same day.

VIII. The Board sent a communication pursuant to Article 11(2) of the Rules of Procedure of the Boards of Appeal, requesting that the Intervener file some

documents and evidence thought relevant for the assessment of the admissibility of the interventions.

IX. Submissions were made as to the admissibility of the intervention(s) by both Appellants I and the Intervener. Together with the Intervener's submissions was a witness statement by the Intervener's representative to the effect that the grounds for the intervention were not filed with the letter dated 16 March 1999 following the advice obtained from a qualified person of the legal department of the EPO during a telephone conversation which took place on 21 January 1999.

X. At the Board's request, this qualified person submitted a written declaration to the effect that the content of the telephone conversation referred to by the Intervener could not be recalled, but that the only advice that could have been given would be that the Intervener should submit a complete notice of intervention in due time, and probably could submit evidence regarding the nature of the Belgian seizure proceedings later on.

XI. At oral proceedings held on 29 February and 1 March 2000 concerning the question of admissibility of the intervention(s), the Board announced their decision that the interventions were not admissible.

XII. The documents relied on by the parties in support of their requests to declare the interventions (in)admissible, which are mentioned in the present decision are the following:

(a) Opinions of the Belgian legal counsel dated

8 February 1999 and 15 November 1999 filed with the Intervener's submissions dated 15 March 1999 and 16 November 1999, as well as

(b) literature on the nature of Belgian seizure proceedings under Articles 1481 - 1488 of the Belgian Judicial Code,

(c) copies of telephone records and written declarations by the representative and others, related to telephone advice purported to have been given by EPO officials, these documents being annexed to the Intervener's submission dated 16 November 1999,

(d) a declaration of Professor Strowel, dated 20 February 2000 submitted on 22 February 2000,

(e) case law on the principle of legitimate expectation from the boards of appeal, from the European Court of Human Rights and from the Court of Justice of the European Communities.

XIII. The arguments by Appellants I with regard to the admissibility of the interventions are summarized as follows:

The seizure proceedings:

- Infringement proceedings qualified a party to file an intervention under Article 105 EPC. They were instituted against an assumed infringer once said assumed infringer was informed for the first time by an order from a court that he was under attack for infringement. This was the information contained in the

order from the seizure judge in the present case. Thus, the seizure proceedings were to be regarded as infringement proceedings for the purpose of Article 105 EPC. This had been confirmed twice by the legal counsel of the Intervener in his letters of 15 March 1997 and 18 February 1999.

- Professor Strowel's declaration about the legal nature of the seizure proceedings was one-sided in that it focused on the discovery part of the seizure proceedings, largely overlooking the possibility for the judge to issue an injunction restraining the assumed infringer.

- An identification of the details of the proceedings for infringement was not required by Article 105 EPC. In Belgium, these rights comprised the right to start seizure proceedings, which empowered the judge to impose heavy restraints on the alleged intervener.

- The fact that the injunctive part of the order issued by the Judge of seizure on 17 December 1998 was discharged on appeal did not mean that the injunction was never ordered or never took place. Even if it were the case that the Court of Appeal judgment could erase the seizure proceedings for the purpose of Article 105 EPC (which they could not), that had not happened because the Belgian Supreme Court was still seized of the matter.

- The Belgian seizure proceedings were infringement proceedings as from the date on which the assumed infringer was served with the judge's order, in the present case, the 17 December 1998. Thus, the three month period under Article 105 EPC for the filing of a

notice of intervention started running from that date and the last day for the filing of this notice was 17 March 1999. In accordance to Article 105(2) EPC, the notice of intervention shall be filed **in a written reasoned statement**. It was therefore beyond argument that it must include a properly substantiated statement of grounds of intervention.

- It was clear law that the date which started the time period for filing an intervention running was the date when the first set of proceedings for infringement of the patent (T 296/93). Accordingly, since the Belgian seizure proceedings initiated on 17 December 1998 were to be considered as infringement proceedings for the purpose of Article 105 EPC, the notice of intervention filed on 23 July 1999 was out of time. In any event, the infringement proceedings initiated on 23 April 1999 were a continuation of the original seizure proceedings, so for that reason as well no new period started to run.

- If, as reasoned by the Intervener, it was enough in order to start a new time period for intervention that the patentee added to his infringement suit another product disclosed in his patent, then an infringer could get a new time period for intervention running simply by informing the court that he was using a product mentioned in the patent but not previously mentioned in the infringement suit, as this would result in the Patentee including the new product in the ongoing proceedings or starting a further infringement suit. This could not have been the intention behind Article 105 EPC.

Legitimate expectations:

- The Intervener could not justify any right of legitimate expectation as a result of telephone conversations with employees of the EPO in inter-partes cases like the present as the rights of the other party would be disregarded. The case Colak v Germany before the European Court of Human Rights, decision of 6 December 1988, showed that no legitimate expectation arose even where a judge of the court itself assured a party (incorrectly) about a legal situation. The court ruled that a judge cannot speak on behalf of his fellow judges.

- The evidence produced by the Intervener was only a reflection of their own opinion. The written declaration of the EPO employee showed that it was very difficult, if at all possible, to establish afterwards what had, in fact, been said. Even if the Intervener was given the advice not to file any grounds for the intervention, they were not entitled to rely on said advice, since the EPC was clear as to the requirements for an admissible intervention, which were the same as for notices of opposition under Article 99(1) EPC in conjunction with Rule 55(c) EPC.

The legitimate expectations of the patentee must also be guaranteed, ie. that an intervention must be filed in time and meets the requirements of the EPC.

XIV. The arguments by the Intervener with regard to the admissibility of the interventions are summarized as follows:

The seizure proceedings

- The proceedings instituted against a third party

which would qualify this party to file an intervention under Article 105 EPC had to be proper court proceedings. Thus, it was only after the Intervener was sued under the Belgian Patents' Act that infringement proceedings could be considered initiated. In contrast, seizure proceedings were organized by Article 1481-1488 of the Judicial Code.

- As seen from the declaration of Professor Strowel, the seizure proceedings also differed from a proceeding for infringement in that they were in essence a general procedure used by a Patentee to gather evidence of patent infringement. Their "evidence gathering" nature was confirmed by the case law (Supreme Court, 3 September 1999, Sanac Belgium/ Variantsystemet, No. C 96 0097.N.).

A number of other characteristics distinguished seizure proceedings from infringement proceedings:

- Although the order may contain in addition to the descriptive part, a restraining or injunctive part, this latter part of the order was only ancillary to the descriptive part as it could not be issued on its own.

- The restraining or injunctive order was at the discretion of the judge.

- If the patentee did not go forward with a court suit within one month of the filing of the report from the descriptive proceedings, the order fell as if it had never existed.

- The judge had no power to decide the merits of the case.

- On 17 December 1998, the Judge of seizure had issued an order to the Intervener which comprised injunctive relief. The Court of Appeal of Ghent had nullified this order insofar as the injunctive relief was concerned, reducing it to a mere description. Consequently, the seizure action in the present case could no longer be fairly described as infringement proceedings.

- Article 105 EPC was not quite clear as to which legal procedure instituted against a third party would make it allowable for this party to file an intervention. The three versions of the article differed; the French and German versions required an "action en contrefaçon" and a "Verletzungsklage" to be instituted, whereas the English version spoke more generally of "proceedings for infringement". Since the seizure proceedings in Belgium could not be characterized as an "action en contrefaçon", or as a "Verletzungsklage", they did not qualify as a legal procedure for the purpose of filing an intervention.

- Even if the seizure proceedings were to be considered as infringement proceedings, the institution of infringement proceedings on 23 April 1999 started a new time period running under Article 105 EPC. Indeed, the latter proceedings had been extended in scope, by including two further allegedly infringing embodiments in addition to the ones having been the subject-matter of the injunctive part of the order in the seizure proceedings and must, therefore, be seen as procedurally distinct from the seizure proceedings. The situation was analogous to that in the following example: A sues B for infringement by a non-critical product of B who withdraws the product in return for A abandoning its action. Then, A sues B in a new action

for infringement by another product. B decides that it is worth the cost of litigation and, also, to intervene in pending opposition proceedings. It would seem inherently wrong that B would have lost the opportunity to intervene in the opposition proceedings in this scenario.

Legitimate expectations

- In the event the Board was minded to consider the seizure proceedings as infringement proceedings which made it allowable to file an intervention under Article 105 EPC, then, the intervention filed on 16 March 1999 was admissible even if the grounds for the intervention were not filed within the three months period starting from the 17 December 1998. The three month time period was a provision of Article 105(1) EPC, which was solely concerned the filing of the notice of intervention. In contrast, the filing of the grounds of intervention was governed by the provision of Article 105(2) EPC which did not specify any time limits.

The Intervener had required advice on that point from a qualified person of the legal department of the EPO in a telephone conversation which took place on 21 January 1999 and was, then, answered that it was not necessary to file the grounds for the intervention whilst only seizure proceedings were in play. The particulars of the case, such as the patent number of the appeal case number were not given. The Intervener was entitled to rely on the information given by the EPO employee, as often confirmed by the case law of the Boards of Appeal starting with decisions J 2/87 (OJ EPO 1988, 330) and J 3/87 (OJ EPO 1989, 003). This case law was also

applicable in inter partes cases. In J 27/92, (OJ EPO 1995, 288), the Board concluded with regard to the content of a telephone conversation that it was convincing to believe the person who still had a recollection of it.

Admissibility of the opposition

XV. The arguments by Appellants I with regard to the admissibility of the opposition by Appellants II are summarized as follows:

- According to the case law of the Boards of Appeal (see, in particular, T 289/91, OJ EPO 1994, 649) an objection that an opposition was inadmissible could be raised at any stage of the proceedings, including before the Boards of Appeal. Appellants I' submissions in this respect were, thus, to be taken into consideration.

- Appellants I had sued Appellants II in Germany for infringement of the German part of the opposed patent. In these proceedings which were still pending before the German appeal court, Appellants II had argued that they were co-owners of the patent in suit as from January 1998, when a scientist purporting to have a right of co-inventorship in the patent had assigned this right to them. In accordance with the Enlarged Board decision G 9/93 (OJ EPO 1994, 891) that a Patentee is not allowed to oppose its own patent, Appellants II' appeal should be found inadmissible from at least the date of assignment. Alternatively, the proceedings should be suspended until the ownership claim was resolved by a final decision. In this respect, attention was drawn to Rule 13(4) EPC which

provided a procedure -suspension of the proceedings- to be followed in a situation where ownership of an opposed patent was challenged during the course of an opposition. This Rule established the principle of suspension which could be applied in the unusual circumstances of this case. Finally, if the Board was minded to continue with the appeal proceedings, Appellants I requested that the Board consider referring one or more questions of law to the Enlarged Board of Appeal, in particular the question of whether a party pursuing a claim in a national court of an EPC Contracting State for an ownership interest in a patent can oppose in the EPO what may in fact be his own patent.

XVI. The arguments by Appellants II with regard to the admissibility of their opposition are summarized as follows:

- The request by Appellants I that the opposition be found inadmissible was filed too late to be taken into consideration.

- The Enlarged Board decision G 9/93 (OJ EPO 1994, 891, issue of December) which stated that a European patent cannot be opposed by its own proprietor also ruled that this finding should not be applied to notices of opposition filed before the publication of the decision (par. 6.1 of the decision). The opposition was filed by Appellants II in September 1994 and was, therefore, valid quite irrespective of whether Appellants II were co-owners of the patent or not. In this regard, Appellants I' argument that the date which counted was the one from which Appellants II claimed ownership started (ie. January 1998) was not correct in view of

the findings by the Enlarged Board that the date to be considered was the date of filing of the opposition. If one was to accept that the admissibility of an opposition could change with time, it would mean an absence of legal certainty for the parties, which was clearly unacceptable.

- Rule 13(4) was meant as a mean of protection for a party who thought himself deprived of its right of ownership. It stated that if this party consented to the continuation of the proceedings, they could continue. In the present case, Appellants II were such a party and consented to the continuation of the proceedings which, therefore, should not be interrupted.

Procedural abuse

XVII. The arguments by Appellants I with regard to a procedural abuse are summarized as follows:

The fact that Appellants II subauthorized the Intervener's representative as one of their own representative was an attempt to advance the interests of said Intervener despite their exclusion from the case as a party. There were doubts whether the representative was truly representing Appellants II because she had never represented them before and she even filed an opposition to one of their patents which was in the HCV field. This situation amounted to a procedural abuse. A parallel had, thus, to be drawn with the situation dealt with in the Enlarged Board decision G 4/97 (OJ EPO 1999, 270) where the headnote 1(b) made the important point that a liberal view as regards the admissibility of oppositions by so-called

nominee opponents did not extend to allowing an opponent to circumvent the law by an abuse of process. This finding also had to apply to a rejected Intervener, thus, the representative should be prevented from addressing the Board, and the documents and evidence filed by her should be excluded from the proceedings.

XVIII. The arguments by Appellants II with regard to a procedural abuse are summarized as follows:

By appointing the representative of the Intervener as their own representative, Appellants II exercised their right to appoint the representative of their choice.

XIX. The Intervener requested that the intervention be declared admissible, alternatively that a question be referred to the Enlarged Board of Appeal and that the opposition and appeal fees for the notice of intervention filed on 23 July 1999 be reimbursed.

XX. Appellants I requested

(1) that the interventions be rejected as inadmissible, alternatively that a question be referred to the Enlarged Board of Appeal.

(2) that the opposition filed by Appellant II be declared inadmissible or that the proceedings be suspended under Rule 13(4) EPC and that questions be referred to the Enlarged Board of Appeal.

Patentability issues

XXI. Granted claims 1 and 32 read as follows:

"1. A polypeptide in substantially isolated form comprising a contiguous sequence of at least 10 amino acids encoded by the genome of hepatitis C virus (HCV) and comprising an antigenic determinant wherein HCV is characterized by:

(i) a positive stranded RNA genome;
(ii) said genome comprising an open reading frame (ORF) encoding a polyprotein; and
(iii) said polyprotein comprising an amino acid sequence having at least 40% homology to the 859 amino acid sequence in Figure 14."

"32. A polynucleotide in substantially isolated form comprising a contiguous sequence of nucleotides which is capable of selectively hybridizing to the genome of hepatitis C virus (HCV) or the compliment thereof, wherein HCV is characterized by:

(i) a positive stranded RNA genome;
(ii) said genome comprising an open reading frame (ORF) encoding a polyprotein; and
(iii) said polyprotein comprising an amino acid sequence having at least 40% homology to the 859 amino acid sequence in Figure 14."

Dependent claims 2 to 12 were directed to further features of the claimed polypeptide and claim 13 to an immunoassay kit. Claim 14 related to a composition comprising a polypeptide according to claims 1 to 11 and Claim 15 related to a vaccine composition according to claim 14. Independent claim 16 related to an immunoassay for detecting anti-HCV antibody and dependent claims 17 to 31 related to further features of the immunoassay or polypeptide for use in said

immunoassay. Dependent claims 33 to 39 were directed to further features of the polynucleotide of claim 32. Dependent claims 40 to 44 were directed to a probe, PCR and probe kits, and a method of performing a PCR reaction comprising the polynucleotide of 32 to 39. Independent claim 45 related to a method for assaying a sample for the presence or absence of HCV polynucleotides. Independent claim 46 related to a DNA polynucleotide encoding a polypeptide with the features given in claim 1 and dependent claims 47 to 57 were directed to further features of this polynucleotide, to vectors carrying it, host cells transformed by said vector and a method of producing it from these host cells. Claims 58 and 59 were directed to anti-HCV antibody compositions and claims 60 and 61, to an immunoassay kit and method comprising/making use of the anti-HCV compositions. Independent claim 62 related to a polypeptide with the same features as in claim 1 when fused to a non-HCV amino acid sequence and claims 63 to 70 to further features of said polypeptide, composition and vaccine comprising it. Independent claim 71 related to a method of growing HCV and dependent claims 72 to 75 to further features of said method. Independent claim 76 and claim 77 related to an HCV immunoassay antigen.

The corresponding claims were filed for the Contracting States ES and GR.

XXII. The Board sent a communication pursuant to Article 11(2) of the Board's of Appeal giving its preliminary, non-binding opinion on substantive matter.

XXIII. Appellants II submitted observations in answer to the Board's communication. Arguments relative to the

substantive issues to be discussed were also presented by the Intervener's representative acting as newly appointed representative of Appellants II, together with expert reports.

XXIV. Appellants I filed a further submission together with a new main request and auxiliary requests A to D as well as two statements, one declaration, seven affidavits and five documents. The new main request contained 81 claims and claim 1 was identical to claim 1 as granted.

XXV. Oral proceedings took place on 27 to 30 June 2000. As announced with letter of 21 May 2000, Opponents 5 were not present at the oral proceedings. Appellants I replaced auxiliary request A by a new auxiliary request A and filed a further auxiliary request E.

The new auxiliary request A contained 81 claims; claims 1, 31, 67 and 76 for all Contracting States but ES and GR read as follows:

"1. A polypeptide in substantially isolated form comprising a contiguous sequence of at least 10 amino acids encoded by the genome of hepatitis C virus (HCV) and comprising an **HCV** antigenic determinant wherein HCV is characterized by:

a positive stranded RNA genome;
said genome comprising an open reading frame (ORF) encoding a polyprotein; and **the entirety of the** said polyprotein having at least 40% homology to the **entire polyprotein of a viral isolate from the genome of which was prepared cDNAs deposited in a lambda gt-11 cDNA library with the American Type Culture Collection (ATCC) under accession n.**

40394."(amended wording emphasized by the Board).

"31. A polynucleotide in substantially isolated form comprising a contiguous sequence of nucleotides which is capable of selectively hybridising to the genome of hepatitis C virus (HCV) or the complement thereof, wherein HCV is characterized by:

a positive stranded RNA genome;
said genome comprising an open reading frame (ORF) encoding a polyprotein; and **the entirety of the** said polyprotein having at least 40% homology to the **entire polyprotein of a viral isolate from the genome of which was prepared cDNAs deposited in a lambda gt-11 cDNA library with the American Type Culture Collection (ATCC) under accession n. 40394**."(amended wording emphasized by the Board).

"67. An immunoassay method for detecting an HCV antigen in a sample comprising:

(a) providing an anti-HCV antibody composition according to claim 64 and 65;
(b) incubating a sample with said anti-HCV antibody composition under conditions that allow for the formation of an antibody-antigen complex; and
(c) determining whether antibody-antigen complex comprising the anti-HCV antibody is formed."

"76. A method of growing hepatitis C virus (HCV) comprising providing hepatocyte cells infected with HCV, and propagating said cells in vitro, wherein said HCV is characterized by:

a positive stranded RNA genome;
said genome comprising an open reading frame (ORF) encoding a polyprotein; and **the entirety of the** said polyprotein having at least 40% homology to the **entire polyprotein of a viral isolate from the genome of which was prepared cDNAs deposited in a lambda gt-11 cDNA library with the American Type Culture Collection (ATCC) under accession n. 40394**."(amended wording emphasized by the Board).

Auxiliary request E contained five claims. Claims 1 and 5 for all Contracting States but ES and GR read as follows:

"1. A polymerase chain reaction (PCR) kit comprising a pair of primers capable of priming the synthesis of cDNA in a PCR reaction, wherein each of said primers is a polynucleotide comprising a contiguous sequence of nucleotides which is capable of selectively hybridising to the genome of hepatitis C virus (HCV) or the complement thereof, wherein HCV is characterized by:

a positive stranded RNA genome;
said genome comprising an open reading frame (ORF) encoding a polyprotein; and **the entirety of the** said polyprotein having at least 40% homology to the **entire polyprotein of a viral isolate from the genome of which was prepared cDNAs deposited in a lambda gt-11 cDNA library with the American Type Culture Collection (ATCC) under accession n. 40394**."(amended wording emphasized by the Board).

"5. A method for assaying a sample for the presence or absence of HCV polynucleotides comprising:

(a) contacting the sample with a probe under conditions that allow the selective hybridisation of said probe to an HCV polynucleotide or the complement thereof in the sample, wherein said probe comprises a polynucleotide comprising a contiguous sequence of nucleotides which is capable of selectively hybridising to the genome of HCV or the complement thereof, wherein HCV is characterized by:
a positive stranded RNA genome;
said genome comprising an open reading frame (ORF) encoding a polyprotein; and **the entirety of the** said polyprotein having at least 40% homology to the **entire polyprotein of a viral isolate from the genome of which was prepared cDNAs deposited in a lambda gt-11 cDNA library with the American Type Culture Collection (ATCC) under accession n. 40394** and

(b) determining whether polynucleotide duplexes comprising said probe are formed, and further wherein said polynucleotide is a DNA polynucleotide and optionally comprises a detectable label.

Claims 2 and 3 were directed to further embodiments of the kit of claim 1 and claim 4 was directed to a method of performing a PRC reaction using the primers defined in claims 1 and 2, respectively.

XXVI. In the course of the procedure, more than 280 documents were filed in relation to substantive matters, of which the following are mentioned in this decision:

(37): Bradley, D. and Maynard, J., Seminars in Liver Disease, Vol. 6, No. 1, pages 56 to 66, 1986,

(101): EP-A-O 388 232,

(104): Jacob, J. et al., The Journal of Infectious Diseases, Vol. 161, pages 1121 to 1127, 1990,

(107): Okamoto, H. et al., Japan. J. Exp. Med., Vol. 60, No. 3, pages 167 to 177, 1990,

(114): Choo, Q. et al., Proc. Natl. Acad. Sci. USA, Vol. 88, pages 2451 to 2455, 1991,

(126): GB 2 239 245,

(128): Gowans, E., Today's Life Science, pages 30 to 37, October 1992,

(137): Chan, T. et al., Hepatology, Vol. 17, No. 1, pages 5 to 8, 1993,

(144): Simmonds, P. et al., J. of Clinical Microbiology, Vol. 31, No. 6, pages 1493 to 1503, 1993,

(156): Patents Court of the UK: Chiron Corporation v. Organon Teknika Ltd (no.3), Fleet Street Reports, pages 202 to 251, 1994,

(162): Yoo, B. et al., J. of Virology, Vol. 69, No. 1, pages 32 to 38, 1995,

(194): Statement of Prof. Dr, H.J. Thiel, dated 26 May 2000, filed with Appellants I' submissions of 26 May 2000,

(211): Expert's report of Prof. H. Varmus filed by Appellants I in answer to the grounds of opposition before the first instance,

(212): Expert's report of Prof. W. Brammar filed by Appellants I in answer to the grounds of opposition before the first instance,

(213): Expert's report of Prof. H. Thomas filed by Appellants I in answer to the grounds of opposition before the first instance,

(214): Expert's report of Dr. M. McGarvey filed by

Appellants I in answer to the grounds of opposition before the first instance,

(215): Annex 1 to the Witness Statement of Prof. M. Houghton filed by Appellants I in answer to the grounds of opposition before the first instance,

(219): Supplementary report by Professor H. Thomas filed by Appellants I in answer to the grounds of opposition before the first instance,

(624): Honda, M. et al., J. of Virology, Vol. 73, No. 2, pages 1165 to 1174, 1999,

(625): Comparisons of DNA sequences filed by Appellants II with their submissions dated 25 May 2000,

(635): Ezzel, C., Nature, Vol. 333, page 195, 1988,

(640): Statement of Dr. P. Simmonds dated 25 May 2000 filed by Appellants II with their submissions dated 25 May 2000,

(642): Statement by Dr. G. Maertens dated 24 May 2000 filed by Appellants II with their submissions dated 25 May 2000,

(646): Joyce, C., New Scientist, issue of 26 May 1988.

XXVII. The submissions by Appellants I in writing and during the oral proceedings which took place from 27 to 30 June 2000, insofar as they are relevant to the present decision on substantive matter are summarized as follows:

Main request

Rule 57a EPC

In opposition proceedings, claim 32 was denied novelty. The granted claims which were directly or indirectly dependent on claim 32 were redrafted as independent

claims in reaction to this finding. The amendment which was allowable under Rule 57a EPC was one of the reasons why the number of claims had increased from 77 to 81.

Article 123(2) EPC; claim 1 (claim 1 as granted)

- According to the case law (T 201/83, OJ EPO 1984, 481; T 288/92 of 18 November 1993; T 187/91, OJ EPO 1994, 572), the disclosure of a patent application as filed was not limited to the expressis verbis content of the description but also comprised what the skilled person would objectively derive from it. In the present application, it was stated that putative HCV strains were identifiable by their homology at the polypeptide level. The skilled person would, thus, have understood that homology should be used to identify new HCV strains. Figure 14 was a sensible sequence to choose to carry out the homology comparison for the identification of HCV isolates as the polypeptide sequence given therein was large enough to serve as fingerprint for the virus. It was not controversial that HCV strains exhibited at least 77% homology in their amino-acid sequence (document (194), par. 21).

- It was not so that the application as filed, page 9, lines 50 to 56 taught that the homology should exist over the entire polyprotein because the polyprotein was not mentioned in the application and it was taught on page 9, lines 54 to 56 that the amino-acid sequence may be compared to the sequence**s** provided, which sequences did not comprise that of the polyprotein. Furthermore, on page 9, the HCV strains were defined as more than about 40% homologous **at the polypeptide level** and on page 12, lines 2 to 5, it was stated that the term polypeptide did not refer to a specific length of the

product.

- On page 52, example IV. H.3, a sequence comparison was carried out between a non-structural protein of the Dengue virus and the HCV polypeptide of Figure 26. If the Board felt it appropriate, the reference to Figure 14 in claim 1 could be replaced by a reference to Figure 26.

- The homology feature was added to the claim at the request of the Examining Division but it was not an essential feature as HCV was a defined taxonomic entity easily identifiable by those skilled in the art.

Auxiliary request A

Article 123(2) EPC

Claim 1

- Support could be found in the application as filed for the fact that the 40% homology existed over the entire of the polyprotein, on page 9, lines 16 to 20 and lines 52 to 54 taken together with the passages on page 20, line 52, page 21, lines 4 to 16 and lines 38 to 40.

- A viral isolate was disclosed as the product of the isolation step, page 5, lines 44 and 56.

Claim 31

- The skilled person would understand the term "capable of selectively hybridising" as meaning "capable of hybridising not at random under appropriate conditions". Such an hybridisation was disclosed in the application as filed on page 10, lines 12 to 14,

page 19, lines 18 to 30, 39 to 44, page 22, line 57 to page 23, line 3, page 26, lines 38 to 51.

- That the claimed polynucleotide was capable of selectively hybridising to **the genome** of HCV was disclosed on pages 28 to 36, 42, 43, 52 to 53.

Article 123(3) EPC

Claim 1
No evidence had been provided that there existed viruses other than HCV, the entire polyprotein of which would have at least 40% homology to the entire HCV polyprotein. Appellants II' objection was without any basis.

Claim 31
This claim corresponded to granted claim 32 which was directed to polynucleotides which were capable of selectively hybridising to the genome of an HCV virus. There, thus, could not be an extension of the scope of protection, quite irrespective of the features used to define HCV. And, anyhow, the extension of the 40% homology feature to the whole of the polyprotein amounted to a restriction of the scope of the claim.

Other claims
Writing a dependent claim in an independent form by spelling out the subject-matter of the claim, it was originally dependent from, did not amount to an extension of scope. Thus, none of Appellants II' objections against claims 39, 40 to 44, 46, 47, 50 and 51 had any basis.

Article 84 EPC

Claim 1

- The skilled person would have no difficulty in understanding that a polypeptide carrying an HCV antigenic determinant was a polypeptide which contained an epitope encoded by the HCV genome which epitope was recognized by antibodies (Abs) present in individuals infected with HCV.

It could occasionally happen that the serum of HCV infected patients did not bind the HCV antigenic determinant because the patient had not yet developed a sufficient amount of Abs. Yet, this was a problem known to the skilled person which did not distract from the fact that it was always possible to test a polypeptide for comprising an HCV antigenic determinant against a panel of available sera known to contain Abs against HCV. As for the false positives obtained in document (137) (page 6, Results, lines 1 to 4), they were obtained with a fusion SOD-HCV polypeptide and could be due to a reaction with anti-SOD Abs.

- The skilled person would give to the term "homology" its generally accepted meaning: two polypeptides chains are said to be homologous when they carry **the same** amino acids in a certain number of positions in the two polypeptides chains.

- There was no difficulty in obtaining the whole of the protein sequence as admitted by Appellants II themselves in their submission of 26 May 2000. Accordingly, the skilled person would not have any problem to decide which polypeptide fell within the claim.

Claim 31

- The wording "contiguous sequence of nucleotides which is capable of selectively hybridizing to the genome of hepatitis C virus" was already present in the granted claim 32 and, thus, was not opened to an objection for lack of clarity.

- The cloning of the HCV viral genome was acknowledged by the scientific community as being of immense importance (documents (211), par. 97 and (219), par. 37). The viral agent had been elusive for years and all subsequent research flowed from the contribution made by Appellants I. According to the Guidelines for Examination in the European Patent Office, part CIII, 6.2, an invention which opened up a new field was entitled to more generality in the claim. Decision T 292/85 (OJ EPO 1989,275) was also of relevance in this context.

- It was not correct that document (114) suggested that more than one HCV virus was present in the sample from which the cDNA bank was made. Document (114) only suggested that the sequence provided in the patent in suit was a portion of the entire HCV genomic sequence and that, when different HCV isolates were studied, they showed significant genome diversity.

Article 83 EPC

In relation to the subject-matter of claim 31

- The application as filed only provided part of the sequence of the HCV genome because it had been Appellants I' strategy to file early. They had deliberately filed a second patent application (document (101)) including further HCV sequences before

the publication date of the patent in suit because this latter patent could thus not be used as a prior art document for the purpose of Article 56 EPC. This implied that Appellants I themselves considered that cloning the rest of the sequence was a routine matter. The reason why a scientific paper (document (107)) was published by another group disclosing the 5' end sequences of another (Japanese) HCV isolate was that the further understanding of HCV required that the sequence of many isolates from different parts of the world be known.

- The skilled person could carry out the invention as claimed in a routine manner for the following reasons:

- in respect of completing the genomic sequence of the HCV isolate:

- Documents (126), (107) and the document cited in paragraph 43 of document (219) showed that within months of the publication of the patent in suit, other groups using the techniques disclosed in said patent were able to obtain further sequences. Even Appellants II admitted it in their submissions of 26 May 2000, par. 8.6.

- The whole HCV genome was present in the DNA library. The reason why new libraries were constructed in the work described in document (101) was to try and obtain longer DNA fragments which would lead to a quicker identification of the whole genome. Many scientists, including the alleged Intervener, had accessed the deposited library, apparently without complaints. Furthermore, the cloned HCV isolate was prevalent in patients and, therefore, the skilled person could also

make use of libraries which they would construct themselves to retrieve further HCV sequences.

- in respect of isolating further HCV genomes:

- In Section IV of the patent, it was taught that the conserved regions of the HCV genome were at the 5' end. On the basis of this information, the sequences at the 5' end (once characterized) were used without any difficulties to isolate other genotypes (document (640), par. 22 and 23).

- in respect of specific cloning difficulties:

- The patent (page 35, example IV.A.22) taught how to overcome the problem due to RNA secondary structure which may be encountered while cloning the entire genome, and how to clone the 3' end of the genome. There was no evidence on file that this teaching could not be followed nor that any specific, hitherto undisclosed measure had to be taken to get to the 3' end.

- The objection that the toxicity of HCV polypeptides to the cells, they were expressed in, may cause difficulties in cloning was not relevant as the expression of said polypeptides was not the screening method of choice as DNA probes could be made starting from the sequences provided in the patent in suit.

The situation was quite different to that encountered in the case dealt with in decision T 412/93 of 21 November 1994, where the disclosure was found insufficient with regard to a claim to Epo cDNA, which molecule had only been obtained some years after the

publication date of the patent in suit. Indeed, the priority date of the instant invention was 1987 rather than 1983 and, in between time, the PCR technique had been made available, rendering obsolete the cloning problems earlier encountered. The situation was rather alike to that which led the then competent Board to acknowledge sufficiency of disclosure in relation to a claim to Epo DNA (par. 112 of the decision) because although a lot of time and effort may be involved into obtaining Epo genomic sequences, this did not amount to undue burden.

In relation to the subject-matter of claims 1 and 67

- Claim 1 did not raise the same issue as claim 31 as it was concerned with polypeptides. The DNA sequences encoding said polypeptides were found in the open reading frame, of which it was never argued that it was not sequencable without undue burden.

- The patent specification gave instructions on how to proceed to identify an HCV antigenic determinant on pages 37, 39, 58 and 59. Documents (144) and (212), pages 68 to 69 showed that it was possible to test antigenicity without undue burden. The same evidence was also given in document (213), par. 91 and 92. Sufficiency of disclosure was, thus, achieved in relation to the subject-matter of claims 1 and 67.

In relation to the subject-matter of claim 76

The patent specification provided information to use the hepatocyte cell lines to grow the virus, on the way to transfect said cells with HCV and to detect the presence of HCV in said cells. These teachings were

followed in document (162) where it was disclosed that it was possible to maintain cells transfected with HCV. In document (128), viral multiplication was not observed but the authors did not discard the hypothesis that they may not have been able to detect the DNA replication.

Auxiliary request E

Article 84 EPC; claim 5

Claim 5 corresponded to granted claim 45 and, thus, was not opened to an objection under this Article and, besides, the patent specification, page 40, Example IV.C.I provided ample support for the workability of the claimed method.

Articles 87 and 88 EPC

- In the fourth priority document, the agent responsible for NANB hepatitis (page 4, lines 16 to 18) was identified as a positive strand RNA virus (page 100) and characterized by its hybridisation properties (page 16, lines 11 to 14). By virtue of the natural capability of RNA genomes to mutate, this agent was necessarily the representative of a family of NANBH causative agents. A deposited cDNA library made it available. As the agent was the same entity as the HCV virus disclosed in the patent in suit, it was irrelevant that it was named differently (causative agent and HCV) in the priority document and in the patent in suit and priority rights were valid as from the filing date of the fourth priority document.

In accordance with the case law (T 73/88, OJ EPO 1992,

557), it was allowable to introduce the 40% homology feature in the claim although it was not disclosed in the fourth priority document as this feature only served to restrict the scope of the claim.

- The notion of using DNA from the isolated HCV virus in a PCR reaction was present in the fourth priority document page 39, page 40 and page 41, lines 26 to 31. Diagnotic kits were disclosed on page 42.

Article 56 EPC

- Never before had a pathogen been cloned before it was identified by classical methods. No-one succeeded to get one positive clone without using the invention as disclosed in the patent in suit (documents (214), par. 11 and (156), page 236). Indeed, obtaining the first HCV clone was extremely difficult as there was little HCV DNA available to construct the library with and no primers for its amplification, no reliable sera or Mabs for screening the recombinant clones and identifying the true positive clones above background. In contrast, once the first clone was isolated and sequenced, the task of obtaining further clones and, eventually, the whole genome, became a routine task.

- In accordance with the case law of the Boards of Appeal, what was said during an oral disclosure such as Dr. Houghton's seminar on 6 Mai 1988 had to be proven beyond doubt. Here, there were no pre- or post-published abstract available. Dr. Houghton's evidence in document (215), par. 118 and 119 was that he gave a very general disclosure of how HCV DNA was cloned. This disclosure may have given the skilled person a hope to succeed but did not amount to a reasonable expectation

of success as understood in the case law (T 60/89, OJ EPO 1992, 268; T 296/93, OJ EPO 1995, 267).

- Even assuming that Dr. Houghton disclosed lambda gt11 as the cloning vector, this did not make the cloning task any more obvious as this vector was known from the state of the art to be a suitable vector when a good antigen was to be recombinantly expressed and a well-characterized source of Mabs was available to test it. Neither of these conditions were fulfilled in the case of HCV.

- The objection by Appellants II that inventive step did not exist in relation to claim 1 because of its wide scope was not valid as the inventive step lay upstream of the isolation of entire HCV genomes ie. in the isolation of the first HCV clone.

XXVIII. The submission in writing and during oral proceedings by Appellants II and Opponents 4, insofar as they are relevant to the present decision on substantive matter can be summarized as follows:

Main request

Rule 57a EPC

- The increase in the number of claims was not achieved in answer to any grounds of opposition and, therefore the new main request was not allowable.

Article 123(2) EPC

- The standards to be applied for the assessment of whether the requirements of Article 123(2) EPC were

fulfilled were summarized in decision T 824/94 of 18 November 1999 (point 2). They were quite strict as the legal security of third parties relying on the content of the original application was a most important concern (G 1/93, OJ EPO 1994, 541).

- There was no disclosure in the application as filed that a new viral isolate was an HCV new strain if its polyprotein sequence comprised an amino-acid sequence which was at least 40% homologous to the 859 amino-acid sequence of Figure 14. Document (194) may have disclosed that it was the case but it could not be used to supplement the faulty disclosure in said application.

- If the passage on page 9, lines 51 to 56 of the published version of the application as filed was interpreted as implying that the 40% homology should exist over the whole protein, then, this would clearly contradict the wording of claim 1, feature (iii).

- As for the example IV.H.3 wherein the sequence of a Dengue virus protein was compared to part of the sequence shown in Figure 26, it did not amount to a disclosure of identifying a new HCV isolate by the degree of homology of part of its polyprotein to the sequence of Figure 14.

Auxiliary request A

Article 123(2) EPC

The artificial combination of parts of the application as filed which were clearly independent from each other could not be used as a mean to justify fulfilling the

requirements of Article 123(2) EPC. On the contrary, in accordance with the case law (T 824/94, see supra), the claimed subject-matter should be clearly and unambiguously disclosed in said application.

Claim 1

- Nowhere was it written in the application as filed that the 40% homology had to be between the entire polyprotein of the HCV isolate and the entire polyprotein of the viral isolate present in the deposited gene bank. This combination was an arbitrary choice. Taking together the passages on page 9, lines 51 to 54 and on page 12 lines 2 to 5, one came to the opposite conclusion that the homology could involve polypeptides of any length.

- The term "viral isolate" was not to be found in the application as filed.

Claim 31

- The application as filed disclosed neither a polynucleotide comprising a contiguous sequence capable of **selectively hybridizing** nor a polynucleotide capable of selectively hybridising **to the genome of HCV.** One could find references to hybridisation and to the genome of HCV but **selective hybridisation** and **the genome** were not combined in one teaching.

Article 123(3) EPC

Claim 1

- The viral isolate referred to in the claim needed not be an HCV virus. It could also be a virus, the polyprotein of which happened to have 40% homology to the polyprotein encoded by the viral isolate from the

genome of which the cDNA bank was prepared. Therefore the claim comprised polypeptides from such viruses. Its scope had been enlarged compared to that of the granted claim.

- The claim covered polypeptides from a virus, the polyprotein of which had more than 40% homology to the HCV entire polyprotein but not necessarily 40% homology to the polypeptide of Figure 14. Its scope had therefore been enlarged.

Claim 31

In documents (624) and (625), it was shown that substantial homology existed between the 5' untranslated HCV sequence and hog cholera sequences or HGBa and HGBc sequences, respectively. This meant that sequences from viruses other than HCV were capable of selectively hybridising to the genome of hepatitis C virus ie. that the scope of the claim had been enlarged.

Other claims

Claim 39 corresponded to granted claim 40 when dependent on granted claim 32. Leaving out the dependency could be considered as an enlargement of the scope of the claims. Furthermore, claims 40 to 44, 47 and 51 had no equivalent in the granted claim request. The dependency of claims 46 and 50 was directed to claims different from those, the equivalent granted claims were dependent on. This also amounted to an enlargement of the scope of protection.

Article 84 EPC

Claim 1

- The term HCV antigenic determinant was unclear in the absence of any definition in the patent specification. In particular, such questions arose as to whether it was an antigen which should be conserved in all HCV strains or whether it was enough that it should be present in one of them, and how much reactivity should be expected with non-HCV antibodies. The patent specification provided the antigen C100-3 which was not recognized by some sera of infected patients but was recognized by sera of some uninfected patients (patent in suit, page 57, lines 50 and 51 and document (137), respectively).

- Example IV.H.3 showed a study of the homology between the non structural protein of Dengue virus and the HCV polypeptide of Figure 26, comprising data on exact homology as well as conservative replacement. This made it doubtful which kind of homology was meant in the term "at least 40% homology" used in the claim to define the polyprotein of the HCV virus. And besides, the specification was silent as to which method to use to measure the level of homology. Accordingly, the skilled person would have difficulty in knowing on which criteria to identify HCV.

- The sequence of the whole polyprotein had not been disclosed and, therefore, one could not know, when working with one polypeptide, whether this polypeptide fell under the claim or not. The situation was further complicated by the fact that the claimed polypeptide needed not have the same sequence as the sequence of polypeptides contained within the polyprotein of reference but needed only to have 40% homology to it.

Claim 31

- It was unclear from the wording of the claim if the selective hybridisation to the genome of the hepatitis C virus was to take place with the polynucleotide itself or with the contiguous sequence contained within said polynucleotide. In addition the term "genome of hepatitis C virus" was also unclear as the sequences of different hepatitis C viruses were all different.

- The scientists who acknowledged the cloning of the HCV genome as a breakthrough did not themselves work with HCV. In fact, the situation was that 76% of the genome had been provided. In contrast, the claim was extremely large covering not only the disclosed sequence but all other sequences of the HCV isolate as well as sequences of other isolates. The balance between the contribution to the art and the scope of the claim was not respected.

- The genome of the HCV viral isolate was defined by reference to a deposited gene bank. In view of the information given in document (114) (Figure 1) regarding clonal heterogeneity of some of the cDNA clones, it was not sure whether one or more HCV isolates had been present in the sample used to prepare the cDNA bank. Thus, it could be that no HVC virus had such a genome as was disclosed in the patent specification.

Article 83 EPC

In relation to the subject-matter of claim 31

- There was doubt whether the entire sequence could be obtained without undue burden as Appellants I did not provide it in the patent in suit. They also filed

another patent application (document (101)) in respect of further HCV sequences, which implied that they themselves considered the further isolation of these sequences as worth patenting. A scientific paper was also published by another group describing 5' HCV sequences (document (107).

- The skilled person wanting to carry out the invention as claimed was faced with many difficulties:

- in respect of obtaining the whole genomic sequence of the HCV isolate:

- A great number of additional clones would have to be isolated and their inserts identified. This was already undue burden.

- There was no evidence that the deposited gene bank contained the whole of the HCV genome (document (640), par. 14 to 16). In document (101), page 13, Appellants I admitted that they had used **a number** of other cDNA libraries for the isolation of further clones. These libraries were not available to the skilled person. And besides, had the skilled person made their own library, there was a likelihood that the cloned viral isolate would not have been the same as the viral isolate in the patent in suit, which meant that it was not possible to obtain the missing sequences.

- in respect of isolating other HCV genomes:

The patent in suit provided no useful information as to which part of the disclosed sequence should be used as a probe to obtain the genomes of further HCV isolates. On page 69, it even suggested using a region which was

not conserved amongst HCV isolates. The teaching that the 5' sequences would be conserved would not be taken into account by the skilled person who knew that these sequences could be very small in Flaviviridae. In fact, it was only in 1990, that primers were described which were sufficiently conserved between different genotypes of HCV that they could be used to isolate other HCV strains (document (640), par. 22 and 23).

- in respect of special cloning difficulties:

- These comprised secondary structures in the RNA which may lead to low efficiency of reverse transcription as well as the potential toxicity of HCV polypeptides to the cells, they were expressed in. The patent in suit provided no helpful teachings how to overcome these problems.

- The cloning of the 3' end beyond the polyU region of the genome was only achieved in 1995 using special measures and took a considerable amount of ingenuity. Appellants II had provided experimental evidence (document (642)) that indeed it was not possible to extend the sequence disclosed in the patent specification towards the 3' end.

In relation to the subject-matter of claims 1 and 67

- The same objections as raised in relation to claim 31 were valid in relation to claim 1 since both claims were equally wide. In particular, it was necessary to clone the entire genome before the sequence of the polyprotein could be determined.

- The patent specification did not provide sufficient

guidance to be able to determine whether a given polypeptide contained an HCV antigenic determinant. Indeed, new HCV strains were regularly isolated which may or may not contain the same antigenic determinant as the reference strain so that the panel of pedigreed sera used in the patent specification to determine the presence of an HCV antigenic determinant in the reference strain would not necessarily allow the detection of HCV antigenic determinants of new serotypes.

- For the same reason, sufficiency of disclosure was also not achieved with regard to the subject-matter of claim 67 which was directed to an immunoassay involving sera from HCV infected patients.

In relation to claim 76

The patent specification provided no examples of cultivation of the virus in hepatocyte cells. It was stated in documents (128) and (104) that attempts at HCV cultivation in such cells had not succeeded. In document (162) a very specific approach was used to obtain infectious virus, which approach was not disclosed in the patent in suit.

The situation was alike the one which led the Board in the case T 412/93 (supra) to refuse sufficiency of disclosure in relation to a claim to Epo cDNA whereas this cDNA was only obtained some years after the publication date of the patent then in suit.

Auxiliary request E

Article 84 EPC; claim 5

The step of DNA amplification was an essential step without which it was impossible to detect HCV in a sample. It was not mentioned in the claim, nor was any example provided of probing a DNA sample without first amplifying the DNA, it contained. Thus, the claim was unclear and not supported by the description.

Articles 87 and 88 EPC

Priority document IV disclosed the causative agent of a family of diseases (page 4, line 16 to 18) but this agent was not identified as being a virus, let alone the representative of a viral species. It did not disclose the existence of a polyprotein. PCR kits were not mentioned. In fact, the identification of the causative agent as a flavivirus named HCV was only done in the fifth priority document.

Priority document V failed to disclose that at least a 40% homology feature existed between the whole polyprotein of HCV viruses. The patent in suit enjoyed priority rights from the filing date of said application.

Article 56 EPC; inventive step

The closest prior art was a lecture delivered by Dr. Houghton on 6 Mai 1988, the content of which he described in document (215). This content was also summarized in two news reports (documents (635) and (646). Dr. Houghton declared in document (215) that he had given a seminar where he had announced the successful identification of clones of HCV, described the route taken for creating the library of HCV clones and for identifying said clones.

Evidence that he must have talked about using lambda gt11 as cloning vector was provided in document (213), the author of which acknowledged in paragraph 69 that he had switched to using this vector once he had heard of Dr. Houghton's presentation. Thus, the Houghton's seminars pointed the way in which the skilled person should work. Furthermore, a source of HCV DNA was available at the filing date, to construct the cDNA library (document (37) as well as Abs panels to screen the recombinants.

For all these reasons, the skilled person had a reasonable expectation of success to achieve the invention of claim 1 which was very wide in scope. The requirements of Article 56 EPC were not fulfilled.

XXIX. Appellants I requested that the decision under appeal be set aside and that the patent be maintained on the basis of either of the main request or auxiliary request A filed on 28 June 2000 or auxiliary requests B, C, or D, all filed on 26 May 2000, or auxiliary request E filed on 30 June 2000, each request consisting of three sets of claims for Greece, Spain and 10 Designated States.

XXX. Appellants II and Opponents 4 requested that the decision under appeal be set aside and that the patent be revoked.

XXXI. At the end of the oral proceedings which took place on 27 to 30 June 2000, the decision was announced that auxiliary request E meets the requirements of the EPC and Appellants I were requested to file an adapted description within two months. The adapted description was filed in due time. Appellants II and Opponents 4

did not raise any objections thereto.

Reasons for the Decision

Formal issues:

Admissibility of the intervention filed on the basis of the Belgian seizure proceedings

1. To decide on the admissibility of this intervention, two questions need to be answered: firstly, whether the Belgian seizure proceedings which led to the order of 17 December 1998 are infringement proceedings for the purpose of Article 105(1) EPC and, thus, started the three months time limit for filing an intervention and secondly, whether a written reasoned statement has to be filed within this same time limit.

2. According to the established practice of the boards of appeal, the assessment of the nature of a procedural act taken by a party before the EPO is to be made with consideration of its actual substance rather than with consideration of its form or of the name by which it is labelled (see eg. decision J 8/81, OJ EPO 1982, 10). This Board finds it appropriate to apply this principle also to national infringement proceedings, having regard to the object behind the Article 105 provision of the EPC. Thus, what matters to decide whether or not the Belgian seizure proceedings which led to the order of 17 December 1998 are infringement proceedings for the purpose of Article 105 EPC is the actual substance and potential results of these proceedings.

3. The order served by the Judge of Seizures to the

Intervener on 17 December 1998 contained two parts. The first part allowed the petitioner, Appellants I in the present case, to search the premises of the Intervener in order to describe polynucleotides, recombinant vectors, host cells, production methods, polypeptides and immunoassays that were alleged to infringe European patents No. 0 318 216 (the patent in suit) and 0 450 931, which polypeptides and immunoassays were manufactured, kept in stock, offered for sale and sold by the intervener, as well as -in accordance with Article 1481 of the Judicial Code- documents, calculations and reports showing the alleged infringement. For this purpose an expert was appointed to carry out the necessary investigations. The second part of the order prohibited the Intervener from (according to the English translation) 'releasing or alienating' in any way the infringing articles described by the expert, and the polypeptides, the immunoassays with the name 'LIA-HCV-3' and the PCR HCV amplification and detection kit called 'INNO-LIPA HCV II', upon penalties of fines.

4. In the Board's judgment, the second part of the order has all the features of an injunctive order as would be served to an alleged infringer under Article 52(4) of the Belgian Patent Act of 1984 in infringement proceedings.

5. The Intervener highlighted the procedural specificities of the Belgian seizure proceedings (see Section XIV, above). In the Board's judgment, however, these procedural features of the Belgian seizure proceedings do not affect the injunctive nature of the order taken on 17 December 1998 in the course of these seizure proceedings.

6. The Board agrees with Appellants I' position (see Section XIII above) that the fact that the injunctive part of the order issued by the Judge of seizure on 17 December 1998 was discharged on appeal does not mean that the injunction was never ordered or never took place. Further, the fact that in the English version of Article 105 EPC, the term "proceedings for infringement" may be a reference to a wider concept of the kind of procedure which can be the basis of an intervention than the terms "action en contrefaçon" or "Verletzungsklage" in the French and German versions has no bearing on the nature of the order.

7. The conclusion is, thus, reached that the Belgian seizure proceedings instituted against the Intervener on 17 December 1998 started the three months time limit under Article 105 EPC. This time limit expired on 17 March 1999.

8. The Board sees no reason to refer a question to the Enlarged Board of Appeal, as the question of whether these proceedings are infringement proceedings for the purpose of Article 105 EPC could be resolved in accordance with the principle of the established case law of the EPO to look to the substance of a procedural act to determine its nature.

9. The next step in assessing the admissibility of the intervention based on the seizure proceedings is to answer the question of whether the grounds of intervention mentioned in Article 105(2) EPC have to be filed within the three months time period for filing the notice of intervention according to Article 105(1) EPC.

10. The French and German versions of Article 105(2) EPC state that: "La déclaration d' intervention doit ètre présentée par écrit et motivée." and " Der Beitritt ist schriftlich zu erklären und zu begründen." which, according to the Intervener, allows that the grounds for intervention can be filed after the three months time limit. In the English version, however, Article 105(2) EPC states that "Notice of intervention shall be filed **in** a written reasoned statement" (emphasis added by the Board). In the Board's judgment, this clear wording leaves no room for interpretation. Therefore, the grounds for intervention are part of the notice of intervention.

11. The Intervener argued that a qualified person from the EPO provided them in a telephone conversation with the advice that the grounds for intervention could be filed at a later date. In their view, this entitled them to the legitimate expectation that a late filing of the grounds of intervention would not affect the admissibility of said intervention.

12. A number of decisions have been issued by the Boards of Appeal on legitimate expectations in inter partes cases: T 25/85 of 18 December 1985, T 124/93 of 10 August 1995, T 343/95 of 17 November 1997, T 923/95 of 12 November 1996, T 905/90 (OJ EPO 1994,306), T 460/95 of 16 July 1996. Those concerning ex parte cases are in this Board's view not of relevance to the present case. The facts dealt with in T 460/95 (see supra) appear to have most similarities with those of the present case: the Appellants explained in a request for restitutio in integrum (Article 122 EPC) that their belated filing of grounds of appeal was due to their reliance on the information obtained during a telephone

call to a registrar of the Boards of Appeal that they could have an extended period of time for the filing of the grounds of appeal. The registrar in question could only vaguely recall the telephone conversation but could not exclude that there had been a misunderstanding due to language difficulties. When the Appellants filed their request for prolongation in writing, the Registrar failed to make them aware of the misunderstanding. The then competent Board decided that the Appellants should not be penalized for having received an erroneous information from the European Patent Office.

13. The decisive difference with the facts of the present case, however, is that, here, the qualified person from the EPO, who was not in any way involved in the case, declared on 15 February 2000 that she did not remember the telephone conversation referred to by the Intervener, and that the only advice which could *reasonably* have been given would be that the Intervener should submit a complete notice of intervention in due time with the grounds for it, and could probably submit evidence regarding the nature of the Belgian seizure proceedings later, on invitation by the Board.

14. Since the facts cannot be established with sufficient certainty and taking into account the conclusion reached in point 10 above that there is no ambiguity in Article 105 EPC as to when the grounds for intervention must be filed and the fact that the parties before the EPO are supposed to know the dispositions of the EPC likely to affect their case, the Board concludes that there is no room for legitimate expectations and decides that the intervention based on the seizure proceedings is not admissible.

Admissibility of the intervention filed on 23 July 1999

15. The question has to be answered whether or not the court proceedings for infringement initiated by Appellants I against the Intervener on 23 April 1999 can be said to relate to new court proceedings different from the earlier seizure proceedings, which would allow a new time period of three months to start for the filing of a notice of intervention. Article 105(1) EPC must be interpreted to mean that if a patentee would attack the infringer with regard to the same patent a second time, e.g. by referring to another part of the patent than what it did in the first infringement proceedings as in the present case, a new period for intervention would start.

16. The seizure proceedings and the following proceedings for infringement differ in that more products are included as allegedly infringing products in the second action. However, all of the products which were the object of the seizure order are included in the second action as allegedly infringing products and the proceedings of 23 April 1999 were initiated as a *continuation* of the seizure proceedings. Thus, as the infringement proceedings of 23 April 1999 as a whole are a direct follow up of the seizure proceedings, they cannot be regarded as new and separate different court proceedings for infringement.

17. The seizure proceedings initiated on 16 December 1999 are infringement proceedings for the purpose of Article 105 EPC and the grounds for intervention must be filed within the three months period starting with the date on which infringement proceedings were instituted (see points 7 and 10 above). Here the grounds for

intervention were filed with the submissions of 23 July 1999, that is after the time period had elapsed. The conclusion is, thus, reached that the intervention filed on 23 July 1999 is not admissible.

The request for reimbursement of the opposition and appeal fees

18. Since the Board declared the second intervention inadmissible, there is no legal basis for reimbursement of the appeal fee for that intervention under Rule 67 EPC. An intervention when admissible is to be treated as an opposition hence the payment of an opposition fee is required. In analogy with an opposition which is declared inadmissible, this fee is only to be reimbursed if the opposition-intervention is deemed not to have been filed. This is not the case here. None of the appeal or opposition fee paid for the second intervention can therefore be reimbursed.

Admissibility of Appellants'II appeal

19. On the day before the oral proceedings, Appellants I challenged the admissibility of Appellants'II appeal. In accordance with the case law of the Boards of Appeal (T 289/91, OJ EPO 1994,649, point 2.1) that an objection regarding the admissibility of an opposition can be raised at any stage of the proceedings, the Board considers this issue.

20. Appellants I drew the Board's attention to the fact that in an appeal which was still pending before the German appeal court, Appellants II were arguing that they were co-owners of the patent in suit. In Appellants I' opinion, this implied that the present

appeal by Appellants II was inadmissible in accordance with the Enlarged Board decision G 9/93 (see supra) that a Patentee is not allowed to oppose its own patent.

21. In point 6.1 of G 9/93, it is stated that this *"ruling ...that self-opposition is inadmissible should,..., not be applied to notices of opposition filed before the publication of the present decision."*. Appellants II' notice of opposition was received by the European Patent Office on 15 September 1994, whereas the decision G 9/93 was published in the 1994 December issue of the Official Journal, thus, the prohibition of self-opposition ruled in the decision G 9/93 does not apply here.

22. All other criteria for admissibility being fulfilled, it is concluded that Appellants II' opposition is admissible. In view of this finding, Appellants'I request to refer a question to the Enlarged Board of Appeal on the matter is rejected.

23. Appellants I put forward the further request that the proceedings be stayed until Appellants II' status with respect to the patent in suit was decided by the German court. The situation was argued to be analogous to that which led to the ruling in Rule 13(4) EPC that "if a third party provides proof to the European Patent Office during opposition proceedings or during the opposition period that he has opened proceedings against the proprietor of the European patent for the purpose of seeking a judgment that he is entitled to the European patent, the European Patent Office shall stay the opposition proceedings unless the third party consents to the continuation of such proceedings."

24. Although the status of Appellants II with respect to the patent in suit is irrelevant to the admissibility of their opposition (see point 21 above), the Board observes that since Appellants II are not a third party, Rule 13(1) does not apply to them. For the case the Board accepted the analogy of the present situation to the one envisaged in Rule 13(4) EPC, Appellants II gave their consent that the proceedings be continued (see section XVI). Thus, Appellants'I request is refused.

Procedural abuse

25. Shortly before the oral proceedings, Appellants II sub-authorized as one of their representatives the patent attorney initially representing the Interveners, whose interventions were decided inadmissible (see points 1 to 17 above). Appellants I argued that this may in fact be an attempt to advance the interests of the Intervener despite their exclusion from the proceedings, which attempt amounted to an abuse of procedure.

26. It is the Board's view that appellants may authorize any representative of their choice to represent them before the EPO. The Board sees no procedural abuse in this course of action. Only submissions by the newly sub-authorized representative which the Board will take into account for reaching a decision are those which were made as from the date of the sub-authorisation.

Patentability issues

Main request

Rule 57a EPC

27. The main request for all Contracting States but ES and GR contains four more claims than the granted claim request. Appellants I pointed out that this difference was due to the fact that claims which were hitherto directly or indirectly dependent on granted claim 32 were redrafted as independent claims. They explained that these changes were introduced in reaction to the finding of the Opposition Division that claim 32 was not novel. The Board agrees and, thus, considers the main request allowable under Rule 57a EPC.

Article 123(2) EPC; added subject-matter, claim 1

28. The objection was raised against claim 1 that the definition of the HCV virus as having a "polyprotein comprising an amino acid sequence having at least 40% homology to the 859 amino acid sequence in Figure 14" was not disclosed in the application as filed.

29. On page 9 of the published version of said application (which has the same wording as the patent as originally filed), lines 51 to 54, it is stated: *"...Putative HCV strains are identifiable by their homology at the polypeptide level. Generally, HCV strains are more than 40% homologous... at the polypeptide level".*
Furthermore, on page 12, lines 2 to 4, the following definition is given: *"The term "polypeptide" refers to a molecular chain of amino acids and does not refer to a specific length of the product; thus, peptides, oligopeptides, and proteins are included within the definition of polypeptide"*. Taking together both these definitions leads to the conclusion that, irrespective

of its length, a polypeptide of a given HCV strain is 40 % homologous to the corresponding polypeptide of any other HCV strain. Thus, the polyprotein of a given HCV strain (admittedly being the polypeptide of greatest length) is 40 % homologous to the polyprotein of any other given strain. This conclusion can be reached starting from the definition of the polypeptide given on page 12 quite irrespective of the polyprotein of the reference strain ever being mentioned in the application as filed since, according to the definition, said polyprotein like that of all other HCV strains is included within the definition of the term polypeptide.

30. On page 9, lines 55 and 56, one way is suggested for determining amino acid sequence homology, which involves comparing the amino acid sequence of a strain to be identified *"to the sequence**s** provided herein"* (emphasis added). The use of the term "sequences" in the plural is indicative that a strain can be defined as an HCV strain if the 40% homology exists **irrespective of which polypeptide is taken as reference polypeptide** (all other criteria being fulfilled). This implies that all corresponding polypeptides of different HCV strains share this level of homology. If all do, then the polyproteins of different HCV strains which comprise them all, also necessarily exhibit 40% homology.

31. In contrast, the definition of HCV in the claim requires that the 40% amino acid homology be observed between a polypeptide of 859 amino acids corresponding to that disclosed by its sequence in Figure 14 and the 859 amino-acid long polypeptide of Figure 14. Thus, this definition comprises viruses, the polyprotein of

which has less than 40% homology to the reference polyprotein outside of this region. Consequently, the claim comprises polypeptides from such viruses. These polypeptides are not disclosed whether implicitly or explicitly in the application as filed.

32. It was suggested to replace the reference to Figure 14 in the claim by a reference to Figure 26, as the application as filed (page 52) contained one example of the homology of part of a non-structural protein of the Dengue virus to part of the amino acid sequence disclosed in Figure 26. However, this change would not cure the deficiency under Article 123(2) EPC for the reason given above with regard to the reference to Figure 14, that the claim would comprise polypeptides of viruses, the polyprotein of which did not have 40% homology to the polyprotein of the reference virus over its whole length, such polypeptides not being originally disclosed.

33. Finally, it was also argued that the 40% homology to Figure 14 was a feature which could be dispensed with and, thus, that it could not affect allowability under Article 123(2) EPC. The reasons why it could be dispensed with was that HCV was a well defined taxonomic entity and, that, as pointed out in document (194), point 21, the skilled person would know that the polyproteins of all HCV viruses isolated up till now were at least 77% homologous. It is, however, not disputed by Appellants I that HCV was not a defined taxonomical entity at the filing date of the application (patent in suit, page 5, lines 1 to 2), nor that establishing the level of homology between the polyproteins of different HCV strains could only be achieved after the filing date, once further HCV viral

strains had been isolated.

34. In the Board's judgment, the line of arguments developed in point 33 above essentially confuses different questions, namely what the person skilled in the art would understand the claimed subject-matter to be on the basis of a knowledge acquired in the years after the application was filed and what the claimed subject-matter would be understood to be, then as now, on a straightforward reading of the claim. Only the second question is of relevance to the assessment of whether the requirements of Article 123(2) EPC are fulfilled.

35. In accordance with the case law of the Boards of Appeal (see section XV, Main request, Article 123(2) EPC, claim 1, supra), an amended claim is allowable under Article 123(2) EPC if the claimed subject-matter is clearly and unambiguously derivable from the application as filed, whether explicitly or implicitly, the whole teachings of this application including description, claims and figures being taken into account. As explained in point 31 above, it is not the case here that polypeptides are disclosed in the application as filed which originate from viruses, the polyproteins of which are 40% homologous solely over the 859 amino-acid sequence specifically disclosed in Figure 14.

36. The main request is refused for failing to fulfill the requirement of Article 123(2) EPC.

Auxiliary request A

Article 123(2) EPC

Claim 1

37. Polypeptides comprising an HCV antigenic determinant are disclosed in example IV.B.3 of the application as filed (see, in particular, page 38, lines 36 and 37). The basis for the characterisation of the HCV polyprotein as now found in the claim is in the following passages in the application as filed:

- page 9, lines 51 to 56 combined to page 12, lines 2 to 4 describes that the "at least 40% homology" should be found at the polyprotein level (see points 30 and 31 above). The combination of these informations is not considered to be artificial as it is achieved as a simple matter of logic in the technical context by replacing the term "polypeptide" on page 9 by its definition provided on page 12.

- on page 5, lines 44 to 45, the invention is said to pertain to the isolation ... of hepatitis C virus (HCV). On lines 55 to 56, it is stated: "*Portions of the cDNA sequences...are useful...to isolate naturally occurring variants of the virus".* Although the term "viral isolate" is not found expressis verbis, it is accepted that the product of the isolation of a virus will ultimately be the viral isolate.

- on page 15, the deposited cDNA library is identified by its accession number.

Claim 31

38. In the passage bridging pages 42 and 43 of the

application as filed, primers derived from clones 81, 36 and 37b are identified by their sequences. As these primers are used for amplifying the HCV genome in a sample and the amplified sequences hybridize to RNA of infected chimpanzees but not to that of uninfected chimpanzees (page 43, lines 34 to 43), the application as filed indeed discloses polynucleotides which are capable of selectively hybridising to the HCV genome.

39. For these reasons, it is concluded that claims 1 and 31 fulfil the requirements of Article 123(2) EPC. The Board is satisfied that this conclusion can be extended to all other claims, against which no other objections were raised under this Article.

Article 123(3) EPC

Claim 1

40. It was argued that the scope of claim 1 was wider than that of granted claim 1 as the claim comprised polypeptides from viruses other than HCV which would happen to have 40% homology to the whole HCV protein. No evidence was provided that such viruses existed. The argument having no technical basis, it is not considered relevant for the assessment of whether the requirements of Article 123(3) EPC are fulfilled.

41. The argument that the claim now covers polypeptides from HCV viruses which would have at least 40% homology at the polyprotein level but would fail to exhibit this degree of homology in the 859 amino acid long polypeptide fragment of Figure 14 cannot be accepted in view of the definition of the HCV strains in the patent specification as being 40% homologous at the

polypeptide level, the polypeptide being defined as a chain of amino acids of any length. As already mentioned in points 29 and 30 above, these definitions imply that the homology feature is valid for HCV polypeptides in general including that disclosed in Figure 14.

42. In the Board's judgment, the scope of the claim has been restricted by defining the level of homology as being over the whole of the HCV polyprotein rather than over the 859 amino acid long polypeptide fragment of Figure 14.

Claim 31

43. This claim corresponds to granted claim 32, the definition of the HCV virus having been restricted in scope (see point 42). The scope of the claim has not been enlarged.

Other claims

44. Consideration of the newly filed claims leads to the conclusion that:

- Claim 39 has the same subject-matter as granted claim 40 dependent on claim 32.
- New claims 40 to 44 dependent on claim 39 have the same subject-matter as granted claims 33 to 39.
- New claim 45 dependent on claims 39 to 43 has the same subject-matter as granted claim 41.
- New independent claim 46 has the same subject-matter as granted claim 42 dependent on claim 32.
- New claims 47 to 49 dependent on claim 46 have

the same subject-matter as granted claims 42 to 44.
- New independent claim 50 has the same subject-matter as granted claim 45 when dependent on claim 32.
- New claim 51 has the same subject-matter as granted claim 45 when dependent on granted claim 40.

There is no extension of scope resulting from the changes in dependency.

45. The claims of Auxiliary request A fulfil the requirements of Article 123(3) EPC.

Article 84 EPC, clarity

Claim 1

46. The clarity of the term "polypeptide carrying an HCV antigenic determinant" was challenged by Appellants II. In the Board's judgment, the skilled person would give this term the meaning, common general knowledge would have it to be, that is, that the polypeptide is identifiable by its ability to react with anti HCV-antibodies. Appellants II pointed out that the sera of some HCV infected patients do not recognize the HCV antigen c100-3 disclosed in the patent in suit (false negative, patent in suit, page 57, lines 50 to 51) whereas c100-3 is recognized by the sera of some uninfected patients (false positive, document (137), page 6, Results, lines 1 to 4), which, in their opinion, leads to confusion.

47. The weak reliability of anti-HCV sera appears to have

been well- known at the filing date. In practice, samples from patients suspected to suffer from NANBH were tested not only against sera from chronic and acute phase NANBH patients but also against sera from negative controls and other disease controls (ie. qualified panels for putative NANBH assays, patent in suit page 57, Table 7). Thus, the skilled person was aware of the problem and knew which measures to take to alleviate it. Accordingly, the Board does not consider the difficulties which the testing of HCV determinants may cause as introducing a lack of clarity into the claim.

48. The objection under Article 84 EPC (see section XXVIII) that the term "homology" in the definition of the HCV virus is not clear in view of the alternative meanings given to this term in example IV.H.3 is not an objection which results from an amendment carried out after grant. Thus, it cannot be considered.

49. Finally, the Board wants to point out that the knowledge of the whole polyprotein sequence of the HCV virus is not required to perform immuno-assays with a qualified panel for putative NANBH assays. Thus, a partial lack of knowledge of this sequence creates no uncertainty when trying to determine whether or not a polypeptide carries an HCV antigenic determinant.

Claim 31

50. The wording "contiguous sequence of nucleotides which is capable of selectively hybridising to the genome of hepatitis C virus" is already present in the corresponding claim 32 as granted. It is not opened to an objection for lack of clarity.

51. The objection was also raised under Article 84 EPC that the scope of the claim is not commensurate with the technical contribution in the patent specification. As Article 84 EPC is not a ground for opposition, the objection is rejected.

52. The objection for lack of support that the cDNA bank was flawed will be addressed under the heading "Sufficiency of disclosure".

Article 83 EPC; sufficiency of disclosure

53. All the objections raised under Article 83 EPC against claims 31, 1 and 76 are discussed here. The conclusions reached with regard to claims 31 and 76 are relevant to the corresponding claims in auxiliary requests E and B to D, respectively (see points 81 to 85, below).

In relation to the subject-matter of claim 31

54. The issues to be decided are whether the disclosure in the patent in suit of 77% of the genome of one HCV strain is sufficient to enable the isolation and characterisation, firstly, of the rest of the genome and, secondly, of further HCV variants, without undue burden or the exercise of inventive skills.

- Isolating and characterising the full genome of HCV

55. In the patent specification, it is taught that the cDNAs corresponding to the entire HCV genome may be isolated by "genome walking". The method is explained on page 14, lines 6 to 10 and exemplified in Section IV.A.1 to IV.A.19. The cDNA library on which to carry

out the method was deposited and the necessary primers can be devised starting from the sequences which are provided. The Board, thus, concludes that the skilled person had at his/her disposal the tools necessary to carry out genome walking over the whole length of the genome and that enough technical information was made available to carry out said method.

56. There is evidence on file to back up this conclusion. In the post-published document (101), 99% of the HCV genomic sequence is determined by walking the genome in the manner described in the patent in suit, using the deposited cDNA library (named "c" library on page 12, line 33) as well as further cDNA libraries prepared from the same source as the "c" library. On page 12, lines 34 to 36, it is stated: *" Several of the clones containing HCV cDNA reported herein were obtained from the "c" library. Although other clones reported herein were obtained from other HCV libraries, the presence of clones containing the sequences in the "c" library was confirmed."* In particular, 5' and 3' end sequences are shown to be present in the deposited cDNA library on page 27, lines 18 and 19 and page 28, lines 25 to 27. In document (642), an experimental report filed on 26 May 2000, Appellants II describe a failure to retrieve 5' or 3' DNA sequences from the deposited library. Yet, in view of the positive results published in 1990 (document (101)), these latter data cannot be taken as proof that these sequences are not present in the library.

57. In document (640), par. 15 and 16 it is disclosed that the sequences obtained in document (101) lack 98 base pairs at the extreme 3' end of the genome and the authors express the opinion that identifying these 98

base pairs took a considerable amount of ingenuity. The difficulties associated with obtaining the 98 bp fragment are said to be an extensive internal base paring in this region as well as the fact that the sequence at the 3' end is not known so that the primer necessary to initiate reverse transcription of said 3' end into cDNA cannot be synthesized.

58. The Board notices that the problem of obtaining the cDNA representative of the extreme 3' end of the genome is addressed in the patent in suit (Example IV.A.22). It is advised to denature the RNA to remove the secondary structures and to attach a polyA tail to said 3' end which permits polyT to be used as primer of the reverse transcriptase reaction. In the absence of any experimental evidence on file that this method fails to work, document (640) which, as stated above, only provides the opinion of its author is not considered as casting doubts on sufficiency of disclosure.

59. Appellants II also drew the Board's attention to the disclosure in document (101), Figure 17 that the sequence of the same DNA fragment obtained from more than one clone isolated from the above mentioned cDNA libraries is not always exactly the same. Their position was that these variations could be due to the presence of more than one HCV virus in the plasma pool used as HCV cDNA source, and that, therefore, the whole of the HCV DNA sequence disclosed in the patent in suit could well not be that of one virus but a mosaic of DNA fragments from many HCV viruses. In document (114), the scientific publication corresponding to document (101), these variations which are only observed at a few positions were attributed to clonal heterogeneity (see Legend to Figure 1). Thus, in the absence of any

experimental evidence that more than one virus was present in the plasma pool, the above argument which implies that the disclosure in the patent in suit is insufficient with regard to isolating the genome of one HCV virus is not convincing.

60. The Board concludes from the findings in points 55 to 59 above that the skilled person could have isolated the whole of the HCV genome without undue burden or exercise of inventive skills.

- *Isolating other HCV strains*

61. The patent specification, page 70, lines 31 to 39 teaches how to obtain new HCV isolates using the HCV cDNA disclosed in the patent in suit. Post-published document (107) (page 171, Results) shows that indeed using 16 oligonucleotide primers copied from said DNA allowed the amplification of further genomes. The cloning and sequencing of two further HCV strains HC-J1 and HC-J4 was, thus, achieved.

62. In addition, the information is given on page 69, Example IV.M of the patent in suit that the 5' region of flaviruses is conserved and it is suggested to use DNA primers from the 5' end of the flaviruses genome to amplify and clone further HCV DNA sequences. HCV being known as a flavivirus, the skilled person would deduce therefrom that sequences derived from the 5' end of the HCV genome would be particularly suited as probes and/or primers to isolate further HCV strains. In this respect, Appellants II filed document (640) (paragraphs 21 to 23) as evidence that further HCV isolates could not be detected by amplification using PCR primers designed from the NS3 region of the HCV genome

disclosed in the patent in suit. Yet, document (128), Figure 1 shows that this region is not at the 5' end. The observed negative result is, thus, no proof that it would undue burden or even impossible to isolate further HCV strains by following the teaching in the patent specification.

63. An argument was also made that the potential toxicity of HCV polypeptides to the cells in which they would be expressed would be detrimental to isolating further HCV clones. The Board cannot see any relevance to this argument because, contrary to the experiment destined to obtain the first HCV DNA clone, genome walking starting with primers and probes disclosed in the patent specification does not require that the HCV polypeptides be expressed.

64. Finally, Appellants II considered the fact that further work relating to DNA sequences from the HCV isolate of the patent in suit and of other HCV isolates was thought worthy of publication as proof that the teachings of the patent in suit were deficient in this respect. The Board rather considers that this is a proof that the patent in suit opened the way to a full investigation of the etiologic agent of NANB hepatitis.

65. The present situation is comparable to that dealt with in the case T 412/93 of 21 November 1994 relating to the cloning of the DNA encoding erythropoietin. Sufficiency of disclosure was then acknowledged in respect of isolating the DNA (other than cDNA) encoding said protein although the Board came to the conclusion (point 112 of the decision) that the skilled person would have to invest a lot of time and effort. In the same manner, it is accepted here that much time and

effort may be requested to obtain the complete genomic sequence of the HCV virus of the patent in suit and to isolate further HCV genomes. Yet, as the sequences of probes and primers useful for these purposes are disclosed in the patent in suit, this time and effort will be spent in the framework of routine experimentation. Thus, it is concluded that no undue burden or exercise of inventive skills is involved.

66. The patent in suit provides a sufficient disclosure in relation to the subject-matter of claim 31.

In relation to the subject-matter of claims 1 and 67

67. Claim 1 comprises any HCV antigenic polypeptide, be it natural or obtained by chemical synthesis or by expression in a recombinant organism (patent in suit, page 12, lines 32 to 34), from polyproteins of all HCV viruses, with conformational as well as linear epitopes, containing an epitope which may be as small as 5 amino-acids (patent in suit, page 12, lines 21 to 22).

68. The patent in suit provides the examples (Examples IV.B.3 and IV.B.5) of how a 131 and a 363 amino acid long HCV polypeptides obtained by recombinant means may be tested for containing a NANBH associated epitope(s) using the serum from a patient with chronic NANBH.

69. Appellants I introduced documents (212) and (213) as evidence that, at the filing date, it would be considered an easy matter to synthesize short polypeptides and to test their antigenicity. Both documents point out to the so-called PEPSCAN method published in 1987 (Annexure 5 to document (212)) which,

according to document (212) (point 144) made it possible to synthesize 2000 short peptides per ten working days. The patent in suit does not make reference to this method. Assuming for the sake of argument that the PEPSCAN method was common general knowledge, its efficiency is to be appraised in relation to the task at hand. As shown in post-published document (128), Fig. 1, the HCV polyprotein, in fact, is 2759 amino-acids long and there are as many polyproteins as HCV strains, which implies that the number of 10 amino-acid long polypeptides to be synthesized is considerable (for example, it is disclosed in Annexure 5 that no less than 208 overlapping hexapeptides are needed to cover a 213 amino acid long sequence).

70. Once the peptides are made, they must be tested for antigenicity against qualifying panels of sera from infected patients, which ought to contain antibodies against said peptides. In document (213), point 92, it is disclosed that at least two qualifying panels were available at the filing date (one of them being the one used in Example IV.I.3 of the patent in suit) and that others could be made when necessary. The patent in suit teaches neither the necessity to, nor the way of, building up new qualifying panels which is contrary to the requirement of Article 83 EPC that the disclosure has to be "complete".

71. Only some conformational epitopes will be characterized by the above mentioned technique as acknowledged in document (213), page 50. No guidance is provided by the patent in suit for identifying conformational epitopes in general.

72. Finally, it must be kept in mind that producing HCV polypeptides from other HCV strains than the one sequenced in the patent in suit requires the preliminary isolation and characterisation of the genomes of said strains, which step in itself already necessitates much time and effort.

73. In the Board's judgment, the sheer amount of time and effort necessary to carry out the claimed subject-matter over its whole scope is well beyond what the average skilled person would consider as undue burden although potentially useful techniques existed. And the patent in suit fails to give adequate information on how to isolate conformational epitopes and how to produce qualifying panels. Thus, the description is not sufficient for the subject-matter of claim 1 to be reproduced without undue burden or exercise of inventive skills.

74. The present situation is comparable to that dealt with in the case T 412/93 (see supra) where sufficiency of disclosure was denied in relation to the subject-matter of a claim directed to a cDNA encoding erythropoietin. The then competent board came to the conclusion that although there were methods available to attempt the cloning of said cDNA and that, therefore, it could be envisaged that the task would be performed in years to come, the patent in suit did not provide sufficient and complete information for the skilled person to accomplish this task without undue burden or exercise of inventive skills.

75. The patent in suit does not provide a sufficient disclosure in relation to the subject-matter of claim 1.

76. Claim 67 is directed to an immuno-assay for detecting HCV antigen which requires, on the one hand, the HCV antigens and, on the other, the antibody compositions for testing them. Sufficiency of disclosure is not fulfilled in relation to the subject-matter of this claim for the same reasons as given in relation to the subject-matter of claim 1.

- In relation to the subject-matter of claim 76

77. Claim 76 relates to a method of growing hepatitis C virus in hepatocyte cells in vitro. On page 24, lines 1 to 10 of the patent in suit, it is taught that primary hepatocytes may be infected with HCV in vivo, then passaged in vitro to obtain a culture of NANBH infected hepatocytes, alternatively that cultures of hepatocytes may be transformed by the virus or transforming genes in order to create permanent or semi-permanent cell cultures. No examples are provided.

78. Document (104) published in 1990 makes use of the first of the above mentioned methods. It discloses that HCV DNA replication takes place in the cultured hepatocyte cells, yet the conclusion is reached on page 1126 that: *"the NANBH-infected hepatocytes could not be maintained for extended periods in culture."*. In document (128) published in 1992, it is stated: *"Despite many undocumented attempts, early attempts at in vitro culture of the parenteral form of NANBH were unsuccessful"*. In document (162) published in 1995, the opinion is expressed that *"...one of the major impediments to the structural analysis of the HCV genome...has been the lack of a reliable cell culture system permissive for HCV replication."* The establishment of a long term persistently infected

culture of the differentiated human hepatoma cell line HUH-7 by transfection of HUh-7 with HCV RNAs transcribed in vitro from a full length cDNA clone is then described.

79. These post-published documents provide evidence that despite many attempts at setting up a culture method according to the patent in suit, it took seven years after the filing date of the patent before one specific cell line could be transformed with HCV and stably maintained in vitro, which cell line is not disclosed in the patent in suit. Therefore, sufficiency of disclosure is not achieved in relation to the subject-matter of claim 76.

80. Auxiliary request A is refused because claims 1, 67 and 76 do not fulfil the requirements of Article 83 EPC.

Auxiliary requests B to D

81. Claims 70, 77 and 69 of auxiliary requests B to D respectively are directed to a method of growing HCV in hepatocyte cells comprising the same steps as claim 76 of Auxiliary request A. Said requests are not allowable under Article 83 EPC for the same reason as given in relation to said claim 76.

Auxiliary request E

82. All claims of the main request and of auxiliary request A which were found unallowable by the Board have been deleted from this request.

83. No objections were raised under Article 123(2) and (3) EPC. The Board is also of the opinion that the

requirements of this article are fulfilled.

84. Claim 5 corresponds to granted claim 45. The objection for lack of clarity raised by Appellants II on the ground that the essential step of DNA amplification is not mentioned in the claim does not result from any amendments carried out after grant and, therefore, will not be taken into consideration, considering that Article 84 EPC is not a ground for opposition.

85. The reproducibility of the subject-matter of claims 1 to 5 depends on the reproducibility of isolating and characterising the full genome of HCV, and of isolating other HCV strains. This has already been acknowledged in points 55 to 65 above. The requirements of Article 83 EPC are fulfilled.

Article 87 to 88 EPC; priority rights

86. According to Article 88(3) and (4) EPC, the right of priority shall cover those elements of the application which are specifically disclosed as a whole in the application whose priority is claimed. In decision T 81/87 (OJ EPO 1990, 250), it was made clear that the disclosure of the essential features must be either express, or be directly and unambiguously implied by the text, and that missing elements which are to be recognized as essential only later on are thus not part of the disclosure.

87. Claim 1 is directed to a polymerase chain reaction (PCR) kit comprising a pair of primers. In priority document IV, there is no express disclosure of a PRC kit. In fact, the only polynucleotide kit which is disclosed comprises a probe containing a nucleotide

sequence from HCV (page 42, lines 11 to 14). On page 41, lines 26 to 31, it is emphasized that the hybridisation signal of the probe will be enhanced if the NANB sequence present in the sample before probing is amplified before probing. It is stated: *"This* (the amplification) *may be accomplished, **for example**, by the technique of Saiki et al."* (emphasis added by the Board) ie. by the PCR technique. Nowhere else in priority document IV is any further reference to the PCR technique to be found. In the Board's judgment, the mere mention of the PCR technique as one possible technique to amplify HCV DNA as a preliminary step in an experiment aimed at probing DNA does not amount to a disclosure of a PCR kit in terms of "the same invention" as required by Article 88(3) EPC. Accordingly, it is concluded that priority document IV does not provide a basis to acknowledge priority rights to the subject-matter of claim 1.

88. In priority document V, PCR kits are not disclosed expressis verbis. However, the use of HCV cDNA fragments as primers for the PRC reaction is mentioned on page 51, lines 2 to 5. In example IV:C.3, IV:H.2 and IV:K, primers are used in a PCR reaction to amplify HCV sequences potentially present in a sample with the aim of detecting them, or to clone uncharacterized HCV cDNA sequences. It is accepted that this disclosure amounts to an implicit disclosure of PCR kits. Priority document V, however, fails to disclose that HCV strains are identifiable by their property of having a polyprotein which is at least 40% homologous to the polyprotein of the reference virus. Contrary to Appellants' I position, the Board does not consider this feature as having the sole function to restrict the scope of the claim but as an essential feature as

it provides the necessary information to isolate all primers derived from such strains. As priority document V fails to disclose an essential feature of the claimed subject-matter, it does not provide a basis on which to acknowledge priority rights.

89. Priority document VI contains the same information as the patent in suit regarding primers, PCR reactions, and the identification of the HCV virus. It also comprises a method for assaying a sample for the presence of HCV polypeptides which is identical to the method of claim 5. Priority rights are, thus, derivable from the sixth priority document.

Article 56 EPC; inventive step

Claim 1

90. The closest prior art document to the subject-matter of claim 1 being a polymerase chain reaction kit is document (635), a news report on the talks given by Dr. Houghton on 6 May and 24 August 1988, ie. before the filing of the sixth priority application, which discloses that HCV had been characterised as an RNA virus with a genome of approximately 10000 base pairs, 30 to 40% of which have been sequenced.

91. Starting from this closest prior art, the problem to be solved is to detect HCV viruses in a sample.

92. The solution consists in providing primer sequences which enable the amplification of the HCV sequences in said sample using the PCR techniques, thus, allowing the subsequent identification of the HCV viral genomes by hybridisation to a probe. The Board is satisfied

that the above mentioned problem has been solved.

93. In order to isolate such primers, it is necessary to know the DNA sequence of the HCV virus. As this sequence is not available neither from document (635) nor from any of the documents of the state of the art, the first task of the skilled person wanting to solve the above problem will be to isolate the HCV virus de novo. In his witness statement on file as document (215), par. 118 and 119, Dr. Houghton acknowledges that he gave seminars on 6 May and 24 August 1988 where he announced the successful identification of HCV clones, discussed the number of clones screened, described how to create libraries containing HCV cDNA, how to screen them and verify the identity of any potential HCV clone. He apparently has disclosed lambda gt11 as the cloning vector of choice (document (213), par. 69). Yet, Dr. Houghton specifically mentions in his testimony that he did not disclose any of the HCV DNA sequences.

94. There are, however, no pre- or post-published documents available to confirm what was really said at these meetings. In fact, the only report of the relevant time period (other than document (635)) on what was disclosed in the seminar of 6 May 1988 is found in document (646), a short article of the New Scientist dated 26 May 1988. It is stated therein: ""*I believe, it was the first example of cloning a virus without seeing it first*", *says Houghton. Houghton's colleagues,..., spent two years screening millions of separate copies of the clones searching for the one that produced the right viral protein. The protein had to bind an antibody that Houghton assumed must exist in blood infected with non-A non-B hepatitis. "We took a*

gamble, says Houghton, because no-one had ever identified such an antibody"".

95. Taken at its face value, such an information would rather discourage the average skilled person from attempting to isolate HCV DNA sequences by the method described by Dr. Houghton, even under the assumption that some technical details were provided at the seminars so that it would be considered at least theoretically feasible to do so.

96. A few other groups nonetheless attempted to reproduce these teachings. Professor Thomas recalls in document (213), par. 70 that his attempt failed until the HCV cDNA sequences were made available in the patent in suit. In the same manner, evidence is given in document (156), pages 235 to 236, and in document (214), par. 11 that, even after knowing of Appellants' I method, at least three other groups were unable to obtain HCV clones until HCV DNA sequences were available.

97. In the Board's judgment, the route chosen by Appellants I which led to the cloning HCV DNA in absence of a known infectious agent, of an antibody to titer it or even of any sera which could be thought to contain significant quantities of such antibodies was not obvious. And, therefore, the provision of HCV DNA sequences was inventive.

98. The further argument was brought up by Appellants II that claim 1 lacked inventive step because of its very wide scope. This argument, however, is not convincing because the inventive step lay not in identifying all possibly existing HCV viruses but in obtaining the first HCV clone.

99. Claim 1 and claims dependent thereof are inventive.

Claim 5

100. Claim 5 relates to a method for assaying a sample for the presence of HCV polynucleotides which makes use of a probe comprising a polynucleotide capable of hybridising to the genome of HCV. The reasoning developed in points 90 to 99 above which led to the acknowledgement of inventive step with regard to HCV primers equally applies to the isolation of HCV probes. Thus, the claimed method which makes use of said probes is also inventive.

101. Auxiliary request E fulfills the requirements of the EPC.

Adapted description

102. With their submissions dated 29 August 2000, Appellants I provided an amended version of the description. No observations were received from the Appellants. The Board is satisfied that the proposed amendments are suited to adapt the description to the claims of auxiliary request E.

Order

For these reasons it is decided that:

1. The interventions are rejected as inadmissible.

2. The request of the Intervener for questions to be referred to the Enlarged Board of Appeal is refused.

3. The request for the reimbursement of the opposition and appeal fees for the notice of intervention filed on 23 July 1999 is refused.

4. The request that the proceedings be suspended is refused.

5. The request by Appellants I that the opposition of Appellants II be declared inadmissible is refused.

6. The request by Appellants I for questions to be referred to the Enlarged Board of appeal is refused.

7. The decision under appeal is set aside.

8. The case is remitted to the first instance with the order to maintain the patent on the basis of

   - claims 1 to 5 of Auxiliary Request E for Contracting States AT,BE,CH,DE,FR,IT,LI,LU,NL and SE, filed on 30 June 2000,

   - claims 1 to 12 of Auxiliary Request E for Contracting State GR, filed on 30 June 2000,

   - claims 1 to 9 of Auxiliary Request E for Contracting

State ES, filed on 30 June 2000,

- pages 1 to 5, 8, 10 to 12, 14 to 23, 25, 26, 28 to 71 as granted,

- pages 5a, 5b, 6, 7, 9, 9a, 13, 24 and 27 as filed with the submissions dated 29 August 2000, pages 5a and 5b being inserted between pages 5 and 6, pages 9a and 9b being inserted between pages 9 and 10,

- Figures 1 to 47-8 as granted.

The Registrar: The Chairwoman:

A. Townend U. Kinkeldey