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Datasheet for the decision of 3 December 2009

Case Number: T 0361/08 - 3.3.08

Application Number: 96916289.0

Publication Number: 0842276

IPC: C12N 15/54

Language of the proceedings: EN

Title of invention:
Method for reproducing in vitro the RNA-dependent RNA polymerase and terminal nucleotidyl transferase activities encoded by hepatitis C virus (HCV)

Patentee:
ISTITUTO DI RICERCHE DI BIOLOGIA MOLECOLARE P. ANGELETTI S.P.A.

Opponents:
Bayer Health Care AG
Tibotec BVBA

Headword:
RNA polymerase/ISTITUTO RICERCHE BIOLOGIA

Relevant legal provisions:
RPBA Art. 12(4), 13(1)
EPC Art. 123(2)(3)

Relevant legal provisions (EPC 1973):
EPC Art. 54(1), 56, 84, 106(3), 111(2)
EPC R. 68(1)(2)

Keyword:
"Main request and auxiliary requests I, II, III, V - admitted into proceedings (no)"
"Auxiliary requests IV, VI - admitted into proceedings (yes)"
"Auxiliary request IV - added subject-matter (no), clarity (yes), novelty (yes), inventive step (no)"
"Auxiliary request VI - inventive step (no)"
"Auxiliary requests VII and VIII - remittal (no)"

Decisions cited:
G 0012/91, J 0042/89, T 0390/86, T 0595/90, T 0762/90, T 0473/98, T 0054/00, T 0090/03, T 0537/05

Catchword:
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Case Number: T 0361/08 - 3.3.08

D E C I S I O N
of the Technical Board of Appeal 3.3.08
of 3 December 2009

Appellant: (Patent Proprietor)
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Decision under appeal: **Decision of the Opposition Division of the European Patent Office posted 17 December 2007 revoking European patent No. 0842276 pursuant to Article 102(1) EPC 1973.**

Composition of the Board:

Chairman: L. Galligani
Members: P. Julià
T. Karamanli

Summary of Facts and Submissions

I. European patent No. 0 842 276 with the title "Method for reproducing in vitro the RNA-dependent RNA polymerase and terminal nucleotidyl transferase activities encoded by hepatitis C virus (HCV)", based on the European patent application No. 96 916 289.0 and published as international patent application WO 96/37619 (referred to in this decision as "*the application as filed*"), was granted with a set of 14 claims.

Claims 1 to 3 and 8 as granted read as follows:

"1. A method for producing *in vitro* the RNA-dependent RNA polymerase activity encoded by hepatitis C virus (HCV), comprising the step of incubating together HCV NS5B, ribonucleotide substrates, and a RNA template, provided that said incubating takes place *in vitro*."

"2. The method of claim 1, wherein said NS5B is the only HCV protein present during said incubating."

"3. The method of claims 1 or 2, wherein said method provides primer independent RNA-dependent RNA polymerase activity."

"8. A method for identifying a HCV RNA-dependent RNA polymerase inhibitor comprising:

(a) incubating *in vitro* a composition comprising HCV NS5B, ribonucleotide substrates, an RNA template, and a test compound, under conditions suitable to produce

NS5B RNA-dependent RNA polymerase activity in the absence of said compound; and
(b) measuring the ability of said compound to affect said NS5B RNA-dependent RNA polymerase activity."

Claims 4 to 7 were directed to particular embodiments of claims 1 to 3: claim 4 defined the NS5B as an extract of an organism expressing nucleic acid encoding NS5B; claim 5 required the NS5B to be purified; claim 6 defined the amino acid sequence of NS5B (SEQ ID NO: 1); claim 7 required the NS5B to be produced from a NS2-NS3-NS4-NS5 polyprotein by means of multiple proteolytic events occurring in an organism expressing a nucleic acid encoding that polyprotein, followed by purification of the NS5B. Claims 9 to 14 related to particular embodiments of claim 8 and read as granted claims 2 to 7.

II. Three oppositions were filed raising grounds for opposition under Article 100(a) to (c) EPC 1973. The second opponent withdrew its opposition with letter dated 21 July 2006.

III. Oral proceedings before the opposition division took place on 24 October 2007. At the beginning of the oral proceedings, the patentee withdrew the main request then on file and submitted as a new main request the claims as granted and maintained the three auxiliary requests then on file (cf. page 1, fourth paragraph of the minutes of the oral proceedings before the opposition division (hereinafter "minutes")). After the opposition division announced that this request did not fulfil the requirements of Article 123(2) EPC, the patentee submitted an amended main request and

"*indicated that he wishes to withdraw all other requests on file*" (cf. page 2, third paragraph of the minutes). In reaction to the announcement that the amended main request did not fulfil the requirements of Article 123(2) EPC the patentee amended the main request again and *"signed this confirming that this was the sole request*" (cf. page 3, third and fourth paragraphs of the minutes). At the end of the oral proceedings the patentee stated that it "*did not wish to file further requests*" (cf. page 6, second paragraph from the bottom of the minutes).

The sole request corresponds to the "*sole request (amended MR)*" referred to in the decision under appeal, and annexed thereto.

Since the opposition division considered the subject-matter of the claims according to this sole request not to fulfil the requirements of Article 56 EPC 1973, the patent was revoked under Article 102(1),(3) EPC 1973 at the end of the oral proceedings before the opposition division.

IV. Independent claims 1 and 6 of the request on which the decision under appeal was based read as follows:

"1. A method for producing *in vitro* the RNA-dependent RNA polymerase activity encoded by hepatitis C virus (HCV), comprising the step of incubating together HCV NS5B, ribonucleotide substrates, and a RNA template, provided that said incubating takes place *in vitro*, wherein said NS5B is expressed in either an eukaryotic or prokaryotic heterologous system."

"6. A method for assaying *in vitro* the RNA-dependent RNA polymerase activity encoded by HCV in order to identify, for therapeutic purposes, compounds that inhibit the enzymatic activity and therefore might interfere with the replication of the HCV virus comprising:

(a) incubating *in vitro* a composition comprising HCV NS5B, ribonucleotide substrates, an RNA template, and a test compound, under conditions suitable to produce NS5B RNA-dependent RNA polymerase activity in the absence of said compound, wherein said NS5B is expressed in either an eukaryotic or prokaryotic heterologous system; and
(b) measuring the ability of said compound to affect said NS5B RNA-dependent RNA polymerase activity."

Claims 2 to 5 were embodiments of claim 1 and read as granted claims 4 to 7 and claims 7 to 10 were dependent on claim 6 and read as granted claims 11 to 14, wherein, however, claims 5 and 12 as granted (claims 3 and 8 in the new main request) were amended to read "*said NS5B is purified to apparent homogeneity*" and claims 7 and 14 as granted (claims 5 and 10 in the new main request) were amended to read "*followed by purification of said NS5B to apparent homogeneity*".

V. With letter of 13 February 2008, the patentee (appellant) filed a notice of appeal and, on 24 April 2008, a statement setting out the grounds of appeal together with a main request and an auxiliary request. The main request was identical to the third auxiliary request which was then on file and subsequently withdrawn in the oral proceedings before the opposition

division (cf. page 2, third paragraph of the minutes). The auxiliary request was identical to the sole request considered by the opposition division in the decision under appeal and annexed thereto (cf. point III *supra*).

In the statement setting out the grounds of appeal, neither any objection of substantial procedural violation was raised nor any comments made on the fact that the decision under appeal gave reasons, only and exclusively, for not allowing the appellant's sole request.

VI. In a letter dated 27 August 2008, opponent 03 (respondent II) replied to the appellant's grounds of appeal.

VII. On 7 April 2009, the board sent a communication under Rule 100(2) EPC informing the parties of its preliminary, non-binding opinion on both procedural and substantive issues of the appeal proceedings. Reference was made in that communication *inter alia* to Article 12(4) of the Rules of Procedure of the Boards of Appeal (RPBA) in view of a possible finding of non-admissibility of the appellant's main request.

VIII. On 16 June 2009, the appellant replied to the board's communication. It maintained its main request and filed new auxiliary requests 1, 2 and 3.

IX. On 8 July 2009, the board summoned the parties to oral proceedings. A communication pursuant to Article 15(1) RPBA, annexed to the summons, informed the parties of the board's preliminary, non-binding opinion on issues of the appeal proceedings. Reference was made in that

communication *inter alia* to Articles 12(4) and 13(1) RPBA in relation to the admission of the appellant's main request and auxiliary requests 1 to 3.

X. In a letter received on 3 November 2009, the appellant replied to the board's communication and requested that the patent be maintained as granted (**main request**). It also filed auxiliary requests I to VI of which **auxiliary request VI** was the same as the auxiliary request filed with the statement of grounds of appeal (see Section V *supra*). All auxiliary requests contained 5 claims, except for auxiliary request VI.

Whereas claim 1 of the **auxiliary request I** was a combination of granted claims 1 and 3, claim 1 of the **auxiliary request II** was a combination of granted claims 1 and 2 and claim 1 of the **auxiliary request III** a combination of granted claims 1, 2 and 3.

Claim 1 of the **auxiliary request IV** read as follows:

"1. A method for producing *in vitro* the RNA-dependent RNA polymerase activity encoded by hepatitis C virus (HCV), comprising the step of incubating together recombinant HCV NS5B purified to apparent homogeneity, ribonucleotide substrates, and a RNA template, provided that said incubating takes place *in vitro*."

Claim 1 of the **auxiliary request V** read as claim 1 of auxiliary request IV combined with granted claim 3.

Claims 2 to 5 of the auxiliary requests I to V were dependent on claim 1 and read as granted claims 4 to 7.

XI. Oral proceedings before the board took place on 3 December 2009 in the absence of the duly summoned opponent 01 (respondent I). During these proceedings, the appellant withdrew its auxiliary request IV and replaced it with a new **auxiliary request IV** identical to the withdrawn request except for the deletion of dependent claims 2 and 3 and the renumbering of the remaining dependent claims (cf. Section X *supra*). The appellant also submitted auxiliary requests VII and VIII (cf. Section XV *infra*).

XII. The following documents are cited in this decision:

D3: R.T. Chung and L.M. Kaplan, Hepatology, 1992, Vol. 16, No. 4, abstract 350;

D5: M. Tsutsumi et al., Hepatology, 1994, Vol. 19, No. 2, pages 265 to 272;

D7: A. Takamizawa et al., J. Virol., March 1991, Vol. 65, No. 3, pages 1105 to 1113;

D8: C. Lin et al., J. Virol., December 1994, Vol. 68, No. 12, pages 8147 to 8157;

D11: A. Grakoui et al., J. Virol., March 1993, Vol. 67, No. 3, pages 1385 to 1395;

D14: Y. Matsuura and T. Miyamura, Seminars in Virology, 1993, Vol. 4, pages 297 to 304;

D28: K.L. Neufeld et al., J. Biol. Chem., December 1991, Vol. 266, No. 35, pages 24212 to 24219.

XIII. The appellant's arguments, insofar as relevant to the present decision, may be summarized as follows:

Admissibility of the main request (claims as granted) and the auxiliary requests I, II, III and V filed on 3 November 2009

The requests filed on 3 November 2009 were a direct *bona fide* reply to the communications of the board pursuant to Rule 100(2) EPC and Article 15(1) RPBA. The jurisprudence acknowledged that an appeal against the revocation of a patent was the final opportunity for a patentee (appellant) to save something from the wreckage of the patent and that, in this case, a patentee (appellant) was normally allowed to revert to the granted claims as its main request. This was actually the present situation in which the requests filed on 3 November 2009 were the claims as granted (main request) or, in auxiliary requests I, II, III and V, straightforward combinations thereof. None of these requests could surprise the respondents (opponents) since the essential features of these requests were already discussed at first instance and decided upon by the opposition division.

Although the opposition division did not commit a substantial procedural violation, an error of judgment was nevertheless committed by failing to issue a written decision on those requests upon which a decision was announced during the oral proceedings, in particular regarding the patentee's first main request (claims as granted). The fact that, as accurately reported in the minutes, a decision on the claims as granted was given orally during the oral proceedings

put that request immediately out of the patentee's hand. Consequently, the patentee was no longer in a position to withdraw this request from the opposition proceedings. In other words, once a decision on a request was announced by the opposition division, it was no longer legally and procedurally open to the patentee to withdraw that request.

Moreover, when the opposition division gave a decision orally on a particular request and its subject-matter in the course of the oral proceedings, that decision terminated the opposition proceedings with respect to that request. Although such a decision was not final, it was nevertheless a procedural decision that terminated the debate or legal hearing with respect to the subject-matter of the request which was previously discussed. In the present case, since the debate on the patentee's main request was closed once a procedural decision was announced, it was no longer in the patentee's power to withdraw this request from the proceedings.

According to the minutes, the opposition division "*announced*" that the patentee's first main request (claims as granted) "*did not fulfil the requirement of ...*" (page 2, lines 1 and 2 of the minutes). Thus, there could be no doubts that the opposition division took a decision on that request. Therefore, this first main request (claims as granted) remained in the opposition proceedings, it was a factual part thereof and the opposition division had to provide a written decision on its subject-matter. The patentee was entitled to have a written decision on that request. Thus the fact alone that, by an error of judgment, it

was deprived of that decision in the first instance proceedings, could not be used in appeal proceedings to its further disadvantage. That was unfair and totally unjustified. The same applied to a further main request which, according to the minutes, was withdrawn after the opposition division had announced that claim 11 comprised added subject-matter (page 3, third paragraph of the minutes).

The minutes were never contested because they were accurate, only the legal conclusions and the consequences that the opposition division drew from the facts that took place during the oral proceedings were not correct. There was no need to raise an objection of substantial procedural violation since it was only an error of judgement that could be corrected in appeal proceedings.

Since it was the appellant patentee's final opportunity to save its patent, the requests filed on 3 November 2009 should be admitted into the appeal proceedings and remitted to the opposition division for correcting its error, if the board had any doubts on the actual facts of the oral proceedings at first instance and considered the appellant's arguments to have some merit.

Admissibility of the auxiliary request IV filed during the oral proceedings on 3 December 2009 and of the auxiliary request VI filed with the statement of grounds of appeal

The auxiliary request VI was the same request filed at the beginning of the appeal proceedings with the appellant's statement of grounds of appeal, said

request being identical to the request considered by the opposition division in its written decision. Also auxiliary request IV read essentially as the request decided upon by the opposition division in the decision under appeal. It was only amended by the introduction and combination of features that were already discussed and decided upon in the opposition proceedings. In terms of complexity, it did not add anything more to the present case. The subject-matter of auxiliary request IV was similar to that of auxiliary request VI and thus, even if it were to be considered as late-filed, the board could in the exercise of its discretion admit it into the appeal proceedings.

Auxiliary request IV
Articles 123(2),(3) EPC

The features "*recombinant*" and "*purified to apparent homogeneity*" introduced into claim 1 had a basis on page 4 of the application as filed and their introduction did not result in a novel selection. The term "*recombinant*" embraced eukaryotic and prokaryotic expression systems. The proteolytical processing of a HCV polyprotein was mentioned in the application as filed and original claim 1 referred to the polyprotein of SEQ ID NO: 1 as a sequence containing HCV NS5B. The expression of a nucleic acid sequence encoding a HCV polyprotein was also exemplified in the application. The claimed subject-matter was thus supported by the examples and by the application as filed taken as a whole and represented a limitation of the granted claims.

Article 84 EPC 1973

The feature "*recombinant*" was known in the art and required the HCV NS5B protein to be produced by recombinant DNA technology rather than by purification of a native or wild-type HCV NS5B protein. This feature qualified only the HCV NS5B protein but not the claimed method, it did not introduce any (method) step in the claimed method. The feature "*purified to apparent homogeneity*" was clear to the skilled person and, in the context of the patent-in-suit, it was understood as meaning the purification of HCV NS5B from other HCV proteins, such as exemplified in the patent. The patent-in-suit also showed the RNA-dependent RNA polymerase (RdRp) activity to be associated with the HCV NS5B protein.

Article 54(1) EPC 1973

Document D3 referred to extracts of HCV infected cells and to a partially purified RdRp activity. There was no reference in that document to a HCV NS5B protein let alone to a recombinant one purified to apparent homogeneity in preference to other HCV proteins. There was nothing in document D3 linking the RdRp activity to a HCV NS5B protein nor any evidence showing the RdRp activity to be provided by a HCV NS5B protein alone.

Document D5 showed that, in cellular extracts similar to those used in document D3, the RdRp activity was associated with a protein of a higher molecular weight (86 kDa) than that of a recombinant HCV NS5B protein (66-68 kDa). Thus, the proteins were clearly different and since there was no indication in document D3 of the protein or proteins responsible for the RdRp activity,

it was not clear what was actually partially purified in document D3. Whereas in the patent-in-suit a protein (a biological product) was purified (HCV NS5B protein), in document D3 only an enzymatic (RdRp) activity (a biological activity) was partially purified. Thus, the patent-in-suit and document D3 followed completely different pathways.

Article 56 EPC 1973

Document D3, the closest prior art, disclosed the partial purification of a RdRp activity from naturally HCV-infected human liver cells. Reference was made to the interest in developing an HCV RdRp assay for identifying compounds of possible therapeutic interest that could inhibit the HCV RdRp activity and interrupt the viral replicative cycle. Starting from that prior art, the technical problem to be solved was to provide isolates of the HCV RdRp activity.

Document D3 referred to these isolates as being complexes containing the HCV RdRp activity. This was in line with other prior art documents that showed the HCV NS5B protein to be necessary for the HCV RdRp activity but not sufficient, i.e. that something more was required to obtain the RdRp activity. Document D5 showed that the HCV NS5B protein detected in naturally HCV-infected cells had a larger molecular weight (86 kDa) than that of a recombinant HCV NS5B protein (66-68 kDa). Thus, the skilled person was taught not to expect the HCV RdRp activity to be provided by the HCV NS5B protein alone but to look for complexes of a molecular weight higher than that of the HCV NS5B protein.

Although, based on the identification of a low degree of homology and of a conserved (GDD) motif in the sequence of the HCV NS5B protein when compared with other viral (RdRp) polymerases, there were documents on file (*inter alia* D8 and D11) speculating on the possible role of the HCV NS5B protein in the HCV RdRp activity, none of these documents was supported by experimental evidence. Moreover, even if these documents suggested the NS5B protein to be necessary to obtain the RdRp activity, there was no suggestion that the HCV NS5B protein alone was sufficient to obtain that activity. The combination of these documents with document D3 was not direct and required to ignore the references in document D3 to the presence of complexes as well as the disclosure of document D5, both leading the skilled person to look for something more (complexes) than just the sole presence HCV NS5B protein.

In view of that prior art, the path followed in the patent-in-suit (purification of the HCV NS5B protein to homogeneity) was not obvious because the skilled person was led by that prior art to expect HCV NS5B complexes to be responsible for the HCV RdRp activity but not the HCV NS5B protein alone. The system used in the patent-in-suit (Sf9 cells infected by recombinant baculovirus Bac5B) showed the HCV RdRp activity to be associated only and exclusively with the HCV NS5B protein alone.

Although HCV, pestiviruses and flaviviruses were classified as three genera in the family *Flaviviridae*, their degree of homology in the NS5 region was so low (Table 2 of document D7) that no conclusions could be drawn from these distantly related viruses and the less

so for a poliovirus, a picornavirus that was even less related to HCV and with a lower similarity in the NS5 region. Thus, the conclusions drawn in document D28 for the RdRp activity of polioviruses could not be extrapolated to the HCV NS5B protein. Nor was the combination of documents D3 and D28 straightforward, since they were concerned with very distantly related viruses with a low degree of homology, particularly in the NS5 region.

XIV. The respondent II's arguments, insofar as relevant to the present decision, may be summarized as follows:

Admissibility of the main request (claims as granted) and the auxiliary requests I, II, III and V filed on 3 November 2009

It was the respondent's recollection of the events of the oral proceedings at first instance that the opposition division did not announce any decision during these proceedings but only a final decision at the end of the oral proceedings. The patentee was given the opportunity to file new requests and to reintroduce, if so wished, subject-matter of previous requests. According to the minutes, the patentee was expressly asked for further requests and he chose, nevertheless, to maintain only a sole main request. Thus, the opposition division took a single (final) decision, as shown on the last sheet of the decision under appeal. Both the minutes and the decision under appeal were accurate and reflected the facts and the decision taken at the first instance proceedings.

During the oral proceedings at first instance, the opposition division announced only opinions but no decisions. Since no final decisions were announced during these oral proceedings, the patentee was not prevented from withdrawing those requests on which an opinion was announced. If other than mere opinions had been announced, the patentee could have contested the minutes but it never did. If the appellant's argument was correct, and even though no objection of substantial procedural violation was raised in the appellant's grounds of appeal, the subject-matter of the granted claims had to be reintroduced by the appellant at the earliest possible stage of the appeal proceedings, i.e. with its grounds of appeal, and not at the latest stage just shortly before the oral proceedings.

Since the patentee (appellant) did not contest the minutes, did not raise an objection of substantial procedural violation and did not file the requests now on file with the grounds of appeal, the introduction of these requests at such a late stage of the appeal proceedings amounted to an abuse of procedure and they should not be admitted. It would be unfair and unjustified to punish the respondents for the appellant's wrong understanding of the actual intentions of the opposition division to give an opinion and not a decision and for the appellant's wrong interpretation of the term "*announced*" in the minutes.

Admissibility of the auxiliary request IV filed during the oral proceedings on 3 December 2009 and of the

auxiliary request VI filed with the statement of grounds of appeal

Auxiliary request IV was late filed and it could have been filed with the appellant's grounds of appeal. There was no reason for the board, exercising its discretion, to admit this request into the appeal proceedings. According to the RPBA, the parties should have a complete case at the beginning of appeal proceedings. That was not so for the appellant in the present appeal and the filing of auxiliary request IV at a late stage of the appeal proceedings was an abuse of procedure. Moreover, the subject-matter of auxiliary request IV was not the same as that of auxiliary request VI and represented a broadening or extension thereof, thereby adding further complexity.

Auxiliary request IV
Articles 123(2),(3) EPC

There was no basis in the application as filed for the introduction of the features "*recombinant*" and "*purified to apparent homogeneity*" into claim 1. Although both features were present on page 4 of the application as filed, that disclosure comprised several combinations (by using the term "*or*" with multiple alternatives) and, in claim 1, these features were taken out of context. The combination of claim 1 represented a particular selection from all other possible combinations, for which no direct basis was found in the application as filed. The subject-matter of the dependent claims was taken from the examples of the application, which could not be used as a basis for

a generalization. The less so when in combination with the feature "*recombinant*" introduced into claim 1.

Article 84 EPC 1973

The feature "*purified to apparent homogeneity*" in claim 1 was not clearly defined in the prior art nor in the patent-in-suit. The meaning given to that feature by the patentee showed it to be ambiguous and open to interpretation. The term "*recombinant*" in claim 1 referred to a method of production. The introduction of a process-feature in a method claim rendered the scope of that claim unclear and ambiguous. According to the jurisprudence, the claims were to be clear by themselves, without a need to refer to the description. If there was any ambiguity, they were not to be allowed.

Article 54(1) EPC 1973

Document D3 disclosed the purification of a HCV RdRp activity, which was known in the art to be provided by the HCV NS5B protein. Although there was no reference in that document to a recombinant HCV NS5B protein, the recombinant production of a HCV NS5B protein did not confer a characteristic technical feature to the resulting recombinant protein so as to differentiate it from a native or a wild-type HCV NS5B protein. The (slight) difference found in document D5 between the molecular weight of a recombinant HCV NS5B (66-68 kDa) and that of a HCV NS5B protein detected in human liver (86 kDa) was explained in that document as being associated with the expression system used. More importantly, document D5 clearly identified the RdRp activity to the HCV NS5B protein.

Document D3 referred to the purified RdRp activity as being primer-dependent. Since in the patent-in-suit a primer-dependent RdRp activity was shown only for a purified HCV NS5B protein but not for cellular extracts or unpurified HCV NS5B, it was to be concluded that the HCV NS5B of document D3 was also pure. In line with the jurisprudence, once a product was made available to the art by a purification method, the product was made available with all degrees of purity. The fact that document D3 (purification of RdRp activity) and the patent-in-suit (purification of a HCV NS5B protein) followed different pathways was irrelevant since the result obtained was the same in both cases.

Article 56 EPC 1973

Document D3, the closest prior art, disclosed the partial isolation of a HCV RdRp activity and provided a motivation to develop a RdRp assay for identifying inhibitors of that activity. Starting from that prior art, the technical problem to be solved was the provision of the RdRp assay as suggested in document D3. There were prior art documents on file (*inter alia* documents D8 and D11) which, based on the presence of a critical GDD motif (known to be essential for the RdRp activity of other related viral RdRp enzymes) in the sequence of the HCV NS5B protein, identified the HCV RdRp activity with the HCV NS5B protein. Although there was a low degree of homology between the HCV NS5B protein and the corresponding NS5 regions of those related viruses, this was irrelevant since, for enzyme activity, it was known that only particular residues (active centre) were essential and not the complete

sequence. These prior art documents disclosed suitable expression systems for easily obtaining a recombinant HCV NS5B protein. Document D3 provided a clear guidance leading the skilled person in an obvious manner to the HCV NS5B protein disclosed in those documents. The patent-in-suit followed that guidance and filled only evident gaps without any effort and without encountering any real technical difficulties. Nothing prevented the combination of the teachings of document D3 with those of the prior art documents.

Although document D3 referred to complexes containing the RdRp activity, the nature of these complexes was completely undefined and unknown. In view of the prior art on file, which identified the HCV RdRp activity with the HCV NS5B protein, it would take the skilled person's imagination to guess the nature of such complexes. Even though document D5 stated that the NS5B protein of naturally HCV-infected cells had a slightly larger molecular weight than the recombinant HCV NS5B protein, there was no experimental measure of the HCV RdRp activity in that document nor a suggestion that any other protein was required to obtain that RdRp activity. Document D5 did not identify the product of higher molecular weight with any complex but it merely attributed the detected molecular weight discrepancy to the different systems used (natural infected vs. host cells), assuming that the associated differences were known to the skilled person. Thus, the disclosure of document D5 did not amount to a prejudice preventing the skilled person to consider the HCV NS5B protein alone as the sole responsible for the HCV RdRp activity. The less so since the skilled person knew that in other related viruses (and even in the less related

poliovirus) the polymerase had the very same conserved GDD motif and was the sole enzyme responsible for the RdRp activity.

XV. The appellant (patent proprietor) requested that the decision under appeal be set aside and the patent be maintained on the basis of the main request (claims as granted) filed with letter of 3 November 2009, or in the alternative, that the patent be maintained in amended form on the basis of one of auxiliary requests I, II, III (all filed with letter of 3 November 2009), IV (filed during oral proceedings of 3 December 2009), V (filed with letter of 3 November 2009) or VI (filed with the statement of the grounds of appeal). As auxiliary request VII, it requested that the case be remitted to the opposition division should the main request, the auxiliary requests I, II, III, and V not be admitted into the appeal proceedings. As auxiliary request VIII, it requested that the case be remitted to the opposition division for further prosecution on the basis of auxiliary request IV filed during oral proceedings of 3 December 2009.

XVI. Respondent II (opponent 03) requested that the appeal be dismissed.

XVII. No requests were on file from respondent I (opponent 01).

Reasons for the Decision

1. The appeal is admissible.

Admission of the main request (claims as granted) into appeal proceedings

2. According to Article 13(1) RPBA, any amendment to a party's case after it has filed its grounds of appeal may be admitted and considered at the board's discretion. The discretion shall be exercised in view of *inter alia* the complexity of the new subject-matter submitted, the current state of the proceedings and the need for procedural economy.

3. The board notes that it was only after the board's communication under Article 15(1) RPBA and shortly before the oral proceedings, that the appellant reverted to the granted claims as its main request (cf. Sections IX and X *supra*). Hence the present main request was filed after the filing of the statement of grounds of appeal. Thus it is an amendment to the appellant's case within the meaning of Article 13(1) RPBA. Accordingly, it lies within the board's discretion to admit this request into the appeal proceedings.

4. When exercising its discretion under Article 13(1) RPBA, the board cannot ignore what happened during the oral proceedings before the opposition division.

5. The board considers that the minutes correctly reflect the course of the oral proceedings before the opposition division since there is no reason for the board to doubt the completeness or correctness of the minutes. Firstly, no request for correction of the minutes has been filed by any of the parties. In fact, the appellant explicitly submitted in the oral

proceedings before the board that the minutes were correct as to what happened during the oral proceedings before the first instance but only the legal conclusions and the consequences that the opposition division drew therefrom were wrong. Secondly, there is no indication in the first instance decision given orally and subsequently put in writing that the minutes could be wrong or incomplete.

6. According to the minutes, after a discussion on the main request which was then on file, namely on the claims as granted, and a short break of the oral proceedings it was announced that the main request did not fulfil the requirement of Article 123(2) EPC (cf. page 1 to page 2, first paragraph of the minutes) and the patentee was also informed that this objection applied - at least partly - to all the auxiliary requests then on file (cf. page 2, second paragraph of the minutes). In reaction to this objection under Article 123(2) EPC, the patentee submitted an amended main request and "*indicated that he wishes to withdraw all other requests on file*" (cf. page 2, third paragraph of the minutes). The discussion continued on the basis of the amended main request. In response to a further objection under Article 123(2) EPC, the patentee deleted claim 11 of the amended main request and confirmed that this was its "*sole request*"(cf. page 3, fourth paragraph of the minutes). After the discussion on this sole request and the announcement of the chairman that the opposition division "*found claims 1 and 6 to lack inventive step*" the patentee was asked whether it would file further requests. After a short break the patentee stated that it "*did not wish to file further requests but intended to appeal*" (cf. page 6,

third and fourth paragraphs of the minutes). According to the last page of the minutes (EPO Form 2309.2) a decision revoking the patent was announced at the end of the oral proceedings and the oral proceedings were closed.

7. The appellant argues that, during oral proceedings, the opposition division announced an "oral" decision on the main request being the claims as granted which terminated the debate with respect to this request and that, once the decision was announced, it was no longer possible for the patentee to withdraw this request from the opposition proceedings.

8. It is true that the opposition division was not precluded from giving a substantive interlocutory decision within the meaning of Article 106(3) EPC 1973 in the course of opposition proceedings (see for example T 390/86, OJ EPO 1989, 30 and T 537/05 of 29 March 2007). Indeed, had the opposition division taken a decision on the main request being the claims as granted, the appellant would have been barred from withdrawing them later (cf. T 54/00 of 19 December 2000, Reasons, point 4; also T 537/05, *supra*, Reasons, point 1.6).

However, the board does not concur with the appellant's argument that the chairman announced such a decision during the oral proceedings before the opposition division for the reasons that follow.

It is clear from the minutes and the EPO Forms 2309.2 and 2339 that at the end of the oral proceedings a decision revoking the patent was announced. This was in

accordance with Rule 68(1), first sentence EPC 1973 which was then in force and stipulates that where oral proceedings are held before the EPO, the decision may be given orally. The minutes also clearly indicate that this decision was based on the sole remaining request which did not encompass claims 2,3,9 and 10 as granted.

The board also notes that the minutes contain, with regard to the main request being the claims as granted and which was discussed at the beginning of the oral proceedings, the following statement:

"*The proceedings were reopened at 10.50 and it was announced that the MR* (main request, added by the board) *did not fulfill the requirement of Article 123(2) EPC* (cf. page 1 to page 2, first paragraph of the minutes).

However, the board considers that it can not reasonably be understood from this statement and the circumstances of the present case that the opposition division had taken an oral decision on the main request which was then on file. In contrast to case T 537/05 (*supra*), the wording of this statement does not comprise words such as "decide" or "decision" which could possibly - but not necessarily (see T 473/98, OJ EPO 2001, 231, Reasons, point 2.4) - imply that a decision had actually been taken. The wording of this statement rather indicates that the opposition division gave a mere opinion on the non-compliance of the claims as granted with the requirements of Article 123(2) EPC. Moreover, after the announcement in question the opposition division informed the patentee that the objection under Article 123(2) EPC also applied to the auxiliary requests then on file and, subsequently, it

gave the patentee the opportunity to submit a new request (cf. page 2, second paragraph of the minutes). The board regards this as a further indication that the opposition division announced a mere opinion which was not intended to terminate the proceedings on this issue but to continue the discussion on it. In fact, the patentee withdrew all his requests then on file and filed an amended main request as his sole request (cf. page 2, third paragraph of the minutes).

9. In addition, the board deems it appropriate to take into account the statement of grounds of appeal which was filed by the appellant's professional representative who had attended the oral proceedings before the first instance. Had the appellant understood the announcement in question as a substantive oral decision within the meaning of Rule 68(1), first sentence EPC 1973 it could have legitimately expected reasons for that decision in writing (Rule 68(2), first sentence EPC 1973). However, although the reasons of the decision under appeal were based exclusively on the patentee's single request maintained at the end of the oral proceedings, no submission was made in the statement of grounds of appeal that the decision under appeal was not fully reasoned, let alone an incorrect legal conclusion or procedural violation alleged. Moreover there is no submission with regard to Article 123(2) EPC under which the opposition division objected to the claims as granted and to the claims according to the auxiliary requests. The appellant merely disputed the finding of the opposition division on inventive step. However, according to the minutes, inventive step was only discussed with regard to the

subject-matter of the claims according to the sole request on which the decision under appeal is based.

In view of these facts, the board is of the opinion that the appellant and his professional representative had understood that the opposition division announced an opinion on the main request being the granted claims which did not amount to an oral substantive decision and that this request was not part of the decision since it was subsequently withdrawn by the patentee during the oral proceedings before the first instance. The board further notes that it was not until its reply to the board's communication under Article 15(1) RPBA that the appellant submitted that the opposition division took a decision on the request being the claims as granted and that therefore this request remained in the opposition proceedings with the consequence that the opposition division should have provided a written decision on the subject-matter of this request.

10. In view of the above, the board comes to the conclusion that the announcement in question was a mere opinion of the opposition division relating to a request which was subsequently withdrawn and not a decision within the meaning of Rule 68(1), first sentence EPC 1973.

11. Turning now to the appellant's argument that the main request being the granted claims could also not have been withdrawn in oral proceedings before the first instance since the opposition division had closed the debate on this request by announcing the statement in question.

The board is not persuaded by the appellant's argument for the reasons that follow.

Where oral proceedings are held, the decision may be given orally and becomes effective by virtue of its being pronounced (cf. decision of the Enlarged Board of Appeal G 12/91, OJ EPO 1994, 285, Reasons, point 2). The point in time at which a decision given orally enters into force, i.e. the moment it is pronounced, is not the last moment at which parties may still submit observations (cf. G 12/91, *supra*, Reasons, point 3). In oral proceedings submissions can be made until the closing of the debate which is fixed by the decision-making department - having first heard the parties' submissions - to allow itself time to consider its decision (cf. G 12/91, *supra*, Reasons, point 3; J 42/89 of 30 October 1991; T 762/90 of 29 November 1991; T 595/90, OJ EPO 1994, 695, Reasons, point 1). Once the debate has been closed in oral proceedings no submissions may be made by the parties unless the decision-making department decides to re-open this debate.

In the board's view, the opposition division did not close the debate on all issues with the announcement of its opinion. However, even if the board accepted the appellant's argument that the opposition division, by announcing its opinion on all the requests then on file, had closed the debate on the main request being the claims as granted, the opposition division re-opened this debate immediately after the announcement by giving the patentee explicitly the opportunity to submit a new request (cf. page 2, second paragraph of the minutes). Hence the board comes to the conclusion

that the debate was not closed at the time when the patentee withdrew its main request being the claims as granted in the first instance proceedings.

12. On the basis of the foregoing the board concludes that the appellant was not barred from withdrawing its main request being the claims as granted in oral proceedings before the opposition division. Since no decision was announced on this main request and the appellant validly withdrew this request during the oral proceedings before the opposition division, this request was no longer existing in first instance proceedings. Consequently, the opposition division acted correctly in giving no decision on this request at the end of the oral proceedings and no reasons in writing. The same applies to the further requests which, accordingly to the reasons set out above, the appellant validly withdrew during the oral proceedings before the opposition division.

13. In view of the particular circumstances of the first instance proceedings, the board considers it appropriate, when exercising its discretion under Article 13(1) RPBA, to take into account also the provisions of Article 12(4) RPBA.

According to Article 12(4) RPBA, the board has the discretionary power to hold inadmissible requests which could have been presented or were not admitted in the first instance proceedings. In the board's view this applies all the more to requests that were filed and subsequently withdrawn in the first instance proceedings, since such a course of events clearly

shows that these requests could have been presented in the first instance proceedings.

In the present case, the appellant validly withdrew his request being the claims as granted in the oral proceedings before the opposition division (cf. points 4 to 12 above). If the appellant had filed such a request with its statement of grounds of appeal, the board would have exercised its discretion according to Article 12(4) RPBA and would have most likely not admitted this request into the appeal proceedings as can be seen from the board's communication pursuant to Rule 100(2) EPC. In this communication, the board clearly indicated that in its preliminary opinion the main request then on file, which had been filed with the statement of grounds of appeal, would not be admitted into the appeal proceedings in accordance with Article 12(4) RBPA since it was submitted on 21 September 2007 as a third auxiliary request and subsequently withdrawn in the first instance proceedings (cf. Sections V and VII *supra*).

In the board's view, the above criteria, which are applied by the board when exercising its discretion under Article 12(4) RPBA, can also be applied by the board when exercising its discretion under Article 13(1) RPBA. The fact that the appellant had chosen to file the present main request after it filed its grounds of appeal should not put the appellant in a better position than if it had filed this request with the statement of grounds for appeal. Otherwise it would be easily possible for the appellant to circumvent the provisions of Article 12(4) RPBA.

Consequently, the fact alone that the present main request was submitted and subsequently withdrawn in the first instance proceedings is for the board a sufficient reason not to admit this request into appeal proceedings, exercising its discretion in accordance with Article 13(1) RPBA. In addition the present main request was submitted at a very late stage of the appeal proceedings and new substantive issues could well arise due to the presence of granted claims for which a decision of the first instance was not given because of the patentee's withdrawal. Therefore the board takes the view that the patentee's behaviour counteracts procedural economy.

14. The appellant further argues that it is always the patentee's right to revert to the granted claims in opposition appeal proceedings against the revocation of a patent.

It is established jurisprudence that the function of appeal proceedings is to give a judicial decision upon the correctness of a separate earlier decision taken by a department of the European Patent Office (cf. "Case Law of the Boards of Appeal of the EPO", 5th edition 2006, VII.D.1). However, it is not the purpose of appeal proceedings to give the patent proprietor the opportunity to recast its claims as it sees fit and to have all its requests admitted into the appeal proceedings. This principle is mirrored in Articles 12(4) and 13 RPBA.

It follows from the above that it is certainly not the appellant patentee's right to revert to the granted claims in appeal proceedings if these claims did not

form a basis for the decision under appeal because the request comprising these claims was withdrawn in the first instance proceedings. Rather it lies within the board's discretion to admit such a request.

15. For the above reasons the board, exercising its discretion under Article 13(1) RPBA, decided not to admit the appellant's main request being the claims as granted into the appeal proceedings.

Admission of auxiliary requests I, II, III and V filed on 3 November 2009 into the appeal proceedings

16. Auxiliary requests I, II, III and V were filed after the board's communication under Article 15(1) RPBA and shortly before the oral proceedings. Since these requests were filed after the filing of the statement of grounds of appeal, they are an amendment to the appellant's case within the meaning of Article 13(1) RPBA. It lies consequently within the board's discretion to admit these requests into the appeal proceedings.

17. When exercising its discretion under Article 13(1) RPBA regarding the admission of said auxiliary requests, it is again appropriate in the present case to take into account what happened during the oral proceedings before the first instance.

It is clear from the minutes that, after the patentee had validly withdrawn all requests then on file which comprised *inter alia* claims 2-3 and 9-10 as granted, it maintained only its sole request at the end of the oral proceedings (cf. Section III above). This sole request,

on which the appealed decision is based, does not comprise granted claims 2-3 and 9-10.

18. In view of the course of the oral proceedings before the opposition division, the criteria which are applied by the board, when exercising its discretion under Article 12(4) RPBA, can also be applied by the board, when exercising its discretion under Article 13(1) RPBA in the present case (cf. also point 13 above).

It is evident that a request which comprises *inter alia* claims 2-3 and 9-10 as granted could have been filed in first instance proceedings, since all requests comprising these claims were filed and subsequently withdrawn during the oral proceedings before the opposition division. Hence, in its communication under Rule 100(2) EPC, the board clearly indicated that in its preliminary opinion the appellant's main request, which comprised said granted claims and was filed with the statement of grounds of appeal, was considered not to be admissible into the appeal proceedings in accordance with Article 12(4) RPBA.

The board considers that the same would have applied if the present auxiliary requests I, II, III and V had been filed with the appellant's statement of grounds of appeal. It is true that claim 1 of auxiliary request I is a combination of granted claims 1 and 3, claim 1 of auxiliary request II a combination of granted claims 1 and 2, claim 1 of auxiliary request III a combination of granted claims 1, 2 and 3 and claim 1 of auxiliary request V a combination of amended claim 1 with granted claim 3 (cf. Section X *supra*). However, by combining the granted or amended claim 1 with granted dependent

claims 2 and/or 3 does not alter the board's view as far as its power under Article 12(4) RPBA is concerned. In first instance proceedings the patentee filed and subsequently withdrew requests which comprised dependent claim 2 and 3 which means that the subject-matter of the before-mentioned combinations was already at issue before the opposition division. Therefore, the board takes the view that requests comprising such combinations of claims could have been filed in first instance proceedings. However, by not filing requests comprising the subject-matter of granted claims 2 and/or 3 in first instance proceedings, the patentee avoided deliberately an opposition division's decision on the subject-matter of these granted claims as it did by withdrawing all requests comprising granted claims 2-3 in the oral proceedings before the opposition division.

For the board this is a sufficient reason not to admit auxiliary requests I, II, III and V into appeal proceedings, exercising its discretion in accordance with Article 13(1) RPBA. Apart from that these auxiliary requests of claims were filed at a very late stage of the appeal proceedings and new substantive issues could well arise because of the new combinations of claims. Therefore, the board considers the patentee's behaviour counteracting procedural economy.

19. For the above reasons the board, exercising its discretion under Article 13(1) RPBA, decided not to admit the appellant's auxiliary requests I, II, III and V into the appeal proceedings.

Auxiliary request IV filed during the oral proceedings on 3 December 2009

20. The subject-matter of the claims of auxiliary request IV corresponds essentially to that of claims 1 and 3 to 5 of auxiliary request VI which was filed with the statement of grounds of appeal (cf. Section V *supra*) and is identical to the sole request considered by the opposition division in its decision. The claims according to auxiliary request IV were amended in such a way as to overcome the objections raised by the board under *inter alia* Article 84 EPC 1973 in the communication pursuant to Rule 100(2) EPC and during the oral proceedings. These amendments and the request itself are regarded as a direct reply to the board's objections, i.e. a justifiable reaction to the board's comments made in the first communication and during the oral appeal proceedings. Moreover, the subject-matter of auxiliary request IV does not raise substantive issues other than those already raised with regard to auxiliary request VI. Therefore, the board, exercising its discretion under Article 13(1) RPBA, decided to admit auxiliary request IV into the appeal proceedings.

Articles 123(2),(3) EPC

21. The application as filed states, with reference to a method for producing *in vitro* HCV RdRp activity, that "*... the proteins containing sequences of NS5B can be expressed in either eukaryotic or prokaryotic heterologous systems: the recombinant proteins containing sequences of NS5B, either purified to apparent homogeneity or present in extracts of overproducing organisms, can catalyse the addition of*

ribonucleotides ... either in a template-dependent (RdRp) or template-independent (TNase) fashion" (cf. page 4, lines 1 to 10). The production of recombinant HCV NS5B protein in insect host cells *Spodoptera frugiperda* (Sf9) and in *E. coli* is shown, respectively, in Examples 1 and 8 of the application as filed. Example 6 discloses the purification of the recombinant HCV NS5B protein from Sf9 host cells using several chromatographic steps. Silver- and immuno-staining of SDS-PAGE are used to identify the chromatographic fractions containing the HCV NS5B protein and to assess their degree of purity. The resulting purified (to apparent homogeneity) HCV NS5B protein is tested for HCV RdRp activity.

22. The application as filed discloses the baculovirus vectors pBac5B and pBac25, the former containing a cDNA region encoding the HCV NS5B protein (SEQ ID NO: 1) and the latter a cDNA region coding the HCV-BK polyprotein (SEQ ID NO:2) (cf. page 6, lines 19 to 30). These vectors are used to produce the recombinant baculovirus clones Bac5B and Bac25 (cf. paragraph bridging pages 6 and 7). Infection of Sf9 host cells with Bac25 results in the detection of correctly-processed HCV NS2, NS3, NS4B, NS4A, NS5A and NS5B proteins (cf. paragraph bridging pages 7 and 8). Claims 2 and 3 of the application as filed contemplate the use of a (recombinant) NS2-NS5B precursor for "*... generating, by means of multiple proteolytic events that occur in the overproducing organism, an enzymatically active form of NS5B*", which, in this way, is incorporated in a reaction mixture (enzymatic test) for producing *in vitro* HCV RdRp activity (claims 6 and 7 as filed).

23. In view of the above cited general disclosure and the exemplified subject-matter, the board is convinced that the application as filed contemplates the use of a recombinant HCV NS5B protein purified to apparent homogeneity in a method for producing *in vitro* HCV RdRp activity. The features introduced into claim 1 ("*recombinant HCV NS5B purified to apparent homogeneity*"), and the claims dependent thereon, are not a novel selection of subject-matter. They were originally contemplated in the application as filed. Moreover, they are an admissible limitation of the claims as granted. Thus, the requirements of Articles 123(2),(3) EPC are considered to be fulfilled.

Article 84 EPC 1973

24. The term "*recombinant*" qualifies the HCV NS5B protein used in the method of claim 1 as having been produced recombinantly. This is a language commonly used in patent applications/patents. In the absence of any specific characteristics associated to the recombinant HCV NS5B protein, the said qualification introduces no particular limitation and must be broadly interpreted. However, this alone is not a sufficient reason to object any lack of clarity (cf. "Case Law", *supra*, II.B.1.1.4, page 191).

25. The degree of purity of the recombinant HCV NS5B protein is assessed in the patent-in-suit "*by silver- and immuno-staining of SDS-PAGE*" (cf. *inter alia* page 8, lines 19-20, 23-24 and 27). In line therewith, the feature "*apparent homogeneity*" refers to the presence of homogeneous recombinant HCV NS5B protein determined within the detection limits of these methods or of

similar ones (cf. point 3.4.2, page 5, lines 14 to 17 of the decision under appeal). Contrary to the appellant's view (cf. Section XIII *supra*), that feature requires the recombinant HCV NS5B protein to be free from all other proteins and not from HCV proteins only. In this context, it is worth noticing that Example 5 of the patent-in-suit describes a unique behaviour of the HCV NS5B protein which is used to separate that protein from the bulk of cytoplasmic proteins of Sf9 host cells or, in Example 8, from lysates of *E. coli* (cf. paragraphs [0036] and [0043] of the patent-in-suit).

26. The requirements of Article 84 EPC 1973 are thus fulfilled.

Article 54(1) EPC 1973

27. Document D3 refers to the preparation of tissue homogenates and subfractions thereof from fresh native HCV-infected human liver tissue and their use in a RNA polymerase assay with a synthetic RNA primer-template. The activity detected "*is dependent on the presence of all four ribonucleoside triphosphates, as well as both template and primer RNA strands, indicating that the incorporation reflects the elongation activity of an RNA-dependent RNA polymerase*". Document D3 states:"*we have **partially** purified the enzymatic activity using a variety of chromatographic separations*" (in bold by the board).

28. The board considers that, for the purpose of establishing novelty, in the context of method claim 1 a partially purified enzymatic activity cannot anticipate an enzymatic activity of a purified enzyme

("*at apparent homogeneity*") which is an explicit requirement for the HCV NS5B protein which is to be used (cf. *inter alia* T 90/03 of 17 March 2005, Reasons, points 11 to 13). Since this feature alone confers novelty to the claimed method, it is not necessary to further discuss, *inter alia*, whether the HCV RdRp activity detected in document D3 can be directly equated to the HCV NS5B protein or whether the feature "*recombinant*" in claim 1 can differentiate the HCV NS5B protein used in that claim from a non-recombinant HCV NS5B protein such as that used in document D3.

29. The board cannot follow the respondent's argument that the presence in document D3 of a primer-dependent RdRp activity indicates, at least implicitly, that the degree of purification achieved for that RdRp activity is similar to that achieved in the patent-in-suit for the recombinant HCV NS5B protein (cf. Section XIV *supra*). Although in the patent-in-suit the RdRp activity of cellular extracts of Bac25- and Bac5B-infected Sf9 cells is reported to be primer-independent and a primer-dependent RdRp activity is detected only with a purified HCV NS5B protein (and a homopolymeric RNA template) (cf. paragraphs [0029], [0040] and [0041] of the patent-in-suit), there is no detailed information on the specific primer requirements (dependent or independent) of the RdRp activity for partially purified HCV NS5B proteins such as, for instance, those of the several HCV NS5B containing fractions obtained in the purification method of Example 6 (cf. paragraphs [0037] to [0039] of the patent-in-suit). Moreover, the primer-dependency of the RdRp activity appears also to be related, at least to a certain extent, to the properties of the template

used (ability or inability to form hairpins) (cf. paragraph [0041] of the patent-in-suit), for which document D3 is completely silent. Thus, no conclusions can be drawn on the purity of the RdRp activity of document D3 on the sole basis of its primer-dependency.

30. It follows from the above, that document D3 does not anticipate the claimed subject-matter. Therefore, the requirements of Article 54(1) EPC 1973 are fulfilled.

Article 56 EPC 1973

31. The disclosure of document D3, which represents the closest prior art, has already been discussed in relation to novelty (cf. point 27 *supra*). The document refers to the "*development of an assay for HCV RdRp and the isolation of complexes containing replicase activity*" as a useful step "*in the identification of compounds that can interrupt the viral* (HCV) *replicative cycle*". It thereby provides an explicit motivation for the skilled person to develop an *in vitro* assay for HCV RdRp activity.

32. Starting from this prior art, the technical problem to be solved is the provision of an assay for HCV RdRp activity. The claimed method, which uses a recombinant HCV NS5B protein purified to apparent homogeneity, solves that technical problem (cf. paragraphs [0009] to [0012] of the patent-in-suit).

33. The appellant does not dispute that, although there is no explicit reference in document D3 to the HCV NS5B protein, there is nevertheless a large body of prior art which identifies the HCV RdRp activity with the HCV

NS5B protein, in particular, with recombinant HCV NS5B protein (cf. *inter alia* documents D8 and D11). Thus, it would be have been obvious for the skilled person to consider the HCV NS5B protein as being responsible for the RdRp activity described in document D3. However, the appellant held that, although it might be derivable from that prior art that the HCV NS5B protein is necessary for obtaining the HCV RdRp activity, it cannot be derived therefrom that this protein is also sufficient for that activity. In this respect, the appellant points to the reference in document D3 to "*complexes containing replicase activity*" which in its view motivates the skilled person to look for complexes containing the HCV NS5B protein rather than for just the HCV NS5B protein. The more so in consideration of document D5 where the molecular weight of a native HCV NS5B-related antigen detected in human liver is reported to be larger than that of a recombinant HCV NS5B protein (cf. paragraph bridging pages 269 and 270 of document D5) (cf. Section XIII *supra*).

34. The board is not convinced by the above arguments as it does not see the reference to "*complexes containing replicase activity*" in D3 as a reason for the skilled person to turn his/her attention away from developing an HCV RdRp assay based on the HCV NS5B protein alone as the document is considered to suggest. This is because: firstly, in view of the preceding paragraph in D3 that indicates that the RdRp activity is dependent on the presence of all four ribonucleoside triphosphates, divalent cations as well as both template and primer RNA strands, the skilled reader would have possibly understood the term "complex" as simply referring to such interactions; and, secondly,

there is no suggestion in document D3, let alone an indication, of the possible nature or (structural) characteristics of such complexes nor a reference to a possible contribution of other unspecified (cellular, viral) factors to the RdRp activity which would have required extensive investigation.

35. Moreover, the board does not see the reference in document D5 to a "*slightly larger*" molecular weight of a native HCV NS5B-related antigen from human liver in comparison to that of a recombinant HCV NS5B protein (cf. point 33 *supra*) as again suggesting a possible association of a native HCV NS5B protein with other (cellular, viral) proteins or factors and as information turning the skilled person's attention away from the straightforward development of the HCV RdRp assay suggested by D3. Document D5 explicitly states that the "*discrepancy may have resulted in different host cells, which were cultured mammalian cells in Grakoui's* (recombinant) *study ... and were human liver cells in this study*" (cf. page 270, left-hand column, lines 2 to 5), meaning that the (slight) difference in the molecular weight may have arisen from the particular expression system used to produce the recombinant HCV NS5B protein. The board fails to see in this disclosure any suggestion that may have led the skilled person to believe that the HCV RdRp activity could not be achieved with purified HCV NS5B protein alone and that other unknown (cellular, viral) factors would have been required to achieve that activity.

36. In the board's judgement, for the skilled person it would have been obvious to take the available recombinant HCV NS5B protein (purified to homogeneity),

such as that of *inter alia* document D8, and to use it in the RdRp assay suggested in document D3. No obstacles are seen in the prior art to the development of such an assay based on those teachings.

37. In fact, related prior art had already shown that purified poliovirus RNA-dependent RNA polymerase is sufficient for an RdRp assay, indeed using both a native and a recombinant RdRp enzyme alone, wherein the latter was obtained from several expression systems, namely bacterial (*E. coli*), insect (Sf9) and mammalian (HeLa) host cells (cf. document D28). Although the presence of different contaminating (cellular) activities might influence some properties of partially purified enzymes, such as primer-dependency and dimer-length of the resulting RNA products (as also reported in the patent-in-suit), all purified RdRp enzymes have the same specific activity and no other (cellular, viral) factors are required to achieve their enzymatic activity.

38. In this respect, the appellant argued (cf. Section XIII *supra*) that poliovirus is a picornavirus and not a member of the *Flaviviridae* family, such as the flaviviruses and the pestiviruses, to which HCV is distantly related (cf. *inter alia* page 1112, right-hand column, last paragraph in document D7). Nevertheless, poliovirus is also a single-stranded RNA virus of positive polarity and its viral RNA polymerase is released from the COOH terminus of a large polyprotein precursor by protease-catalyzed autocatalytic cleavage, as is the case for HCV RdRp. Indeed, some similarities between both RNA viruses, poliovirus and HVC, were already known in the art (cf. *inter alia* page 297,

right-hand column, lines 10 to 6 from the bottom in document D14), in particular, the presence of the conserved specific sequence Gly-Asp-Asp (GDD) recognized in all RdRp (cf. page 300, right-hand column, lines 6 to 14 in document D14 and paragraph bridging pages 1107 and 1110 in document D7). In fact, whereas no significant homology is found between the structural and non-structural proteins of HCV and those of the distantly related flavivirus (JEV) and pestiviruses (BVDV), a detectable homology is nevertheless found in NS3 (encoding a serine protease responsible for the trans-cleavage) and in NS5 (cf. paragraph bridging pages 1112 and 1113 and Table 2 of document D7).

39. In this context, it is worth pointing out that the presence in the NS5B region of the HCV genome of a sequence encoding the conserved Gly-Asp-Asp (GDD) motif is accepted in all the cited prior art as a direct and clear indication that the HSV NS5B region encodes a putative HCV NS5B protein with the HCV RdRp activity. Even though, as rightly argued by the appellant (cf. point XIII *supra*), this prior art is mostly concerned with the structure, organization and processing of a recombinant HCV genome and it does not actually provide any experimental evidence to support that assumption, i.e. showing the HCV RdRp activity of a HCV NS5B protein, the board fails to see any piece of prior art or evidence speaking against the correctness of that assumption and as casting serious doubts and uncertainty on the use of a recombinant HCV NS5B protein in the RdRp assay suggested in document D3. The availability of recombinant HCV NS5B proteins has not been disputed and is supported by the disclosures in the prior art of suitable expression constructs

producing recombinant HCV NS5B proteins (cf. *inter alia* page 8148, left-hand column, last full paragraph, and Figure 1, page 8153, left-hand column, last paragraph to page 8154, left-hand column, first paragraph, and page 8155, left-hand column, last paragraph in document D8 and page 1386, last line in Table 1 of document D11).

40. In conclusion, no inventive contribution is seen in the claimed method and, therefore, the requirements of Article 56 EPC 1973 are not considered to be fulfilled. Thus auxiliary request IV is not allowable.

Auxiliary request VI filed with the statement of grounds of appeal

41. Auxiliary request VI is identical with the auxiliary request filed with the statement of grounds of appeal and thus with the sole request forming the basis for the decision under appeal (Section X *supra*). In view of this, the board, exercising its discretion under Article 12(4) RPBA, decided to admit this request into the appeal proceedings.

Article 56 EPC 1973

42. The board considers that the above reasoning outlined in respect of the auxiliary request IV applies *mutatis mutandis* to the subject-matter of auxiliary request VI, since in this request the HCV NS5B protein is defined in terms of the feature "*wherein said NS5B is expressed in either an eukaryotic or prokaryotic heterologous system*" (cf. Sections IV and V *supra*) which can be equated to the feature "*recombinant*" of auxiliary request IV.

43. Thus, for the reasons given above, the subject-matter of auxiliary request VI is considered not to fulfil the requirements of Article 56 EPC 1973. Hence, auxiliary request VI is also not allowable.

Auxiliary requests VII and VIII for remittal of the case to the first instance

44. According Article 111(1), second sentence EPC 1973, the board may either exercise any power within the competence of the department which was responsible for the decision appealed or remit the case to that department for further prosecution.

45. The appellant requested remittal to the opposition division should its main request, auxiliary requests I, II, III and V not be admitted into the appeal proceedings (auxiliary request VII)(cf. Section XV *supra*).

46. Indeed the board decided not to admit the main request and the auxiliary requests I, II, III and V into the appeal proceedings for the reasons as set out above (cf. points 1 to 19). However, it would contravene the function of appeal proceedings (cf. point 14 above) and the provisions of Articles 12(4) and 13(1) RPBA if the present case were remitted to the first instance for further prosecution simply because the board had not admitted the above-mentioned requests into the appeal proceedings. Thus, the appellant's auxiliary request VII is not allowable.

47. The appellant further requested to remit the case to the opposition division for further prosecution on the basis of auxiliary request IV (auxiliary request VIII) (Section XV *supra*).

48. However, the board admitted auxiliary request IV into the appeal proceedings (cf. point 20 *supra*) and decided within the opposition division's competence that auxiliary request IV is not allowable because the claimed subject-matter does not involve an inventive step (cf. points 31 to 40 *supra*). If the board remitted the present case to the first instance, the opposition division would be bound by the *ratio decidendi* of the board pursuant to Article 111(2), first sentence EPC 1973. It follows that the board's finding that the subject-matter of claim 1 of auxiliary request IV does not involve an inventive step would be binding on the opposition division in case of a remittal. Hence, the board has no reason for remitting the case to the opposition division for further prosecution on the basis of auxiliary request IV.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

V. Commare L. Galligani