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**Datasheet for the decision
of 16 January 2014**

Case Number: T 1912/09 - 3.3.02

Application Number: 98935359.4

Publication Number: 967484

IPC: G01N33/569, G01N33/576

Language of the proceedings: EN

Title of invention:
METHODS FOR DETECTING OR ASSAYING VIRUS

Patent Proprietor:
Advanced Life Science Institute, Inc.

Opponent:
Roche Diagnostics GmbH

Headword:
Methods for detection of virus/ADVANCED LIFE SCIENCE

Relevant legal provisions:
EPC Art. 108 sentence 3, 123(2), 56
EPC R. 99(2)
RPBA Art. 12(2), 12(4), 13(1)

Keyword:

Admissibility of appeal - appeal sufficiently substantiated (yes)
Late-filed request - request not examined by the opposition division
Late-filed auxiliary requests - procedural economy
Amendments - added subject-matter (yes)
Inventive step - obvious solution - reasonable expectation of success (yes)

Decisions cited:

T 0015/01, T 0162/97, T 2532/11, T 1023/02, T 1525/10,
T 1993/07

Catchword:



**Beschwerdekammern
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Case Number: T 1912/09 - 3.3.02

D E C I S I O N
of Technical Board of Appeal 3.3.02
of 16 January 2014

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Decision under appeal: **Interlocutory decision of the Opposition
Division of the European Patent Office posted on
17 July 2009 concerning maintenance of the
European Patent No. 967484 in amended form.**

Composition of the Board:

Chairman: U. Oswald
Members: T. Sommerfeld
D. Prietzel-Funk

Summary of Facts and Submissions

- I. European patent No. 967484, based on European patent application No. 98935359.4, which was filed as an international application published as WO 99/06836, was granted with 13 claims.

Independent claim 1 as granted read as follows:

"1. A method for measuring a hepatitis C virus (HCV) or Hepatitis B virus (HBV) or a HCV- or HBV- related virus in a sample by obtaining a sample suitable for detection of virus comprising the step of

(1) treating a virus-containing sample with a treatment solution containing (a) an anionic surfactant and (b) at least one agent selected from the group consisting of an amphoteric surfactant, a nonionic surfactant and a protein denaturant; such that the virus particle is disrupted, the virus antigen is exposed or released; and antibodies against the virus antigen, if present in the sample, are inactivated; and

(2) detecting the virus antigen by immunoassay."

Independent claims 2 and 3 as granted differed from granted claim 1 in that the presence of both an anionic surfactant and an amphoteric surfactant was required; claim 3 further required the presence of a nonionic surfactant and a protein denaturant.

Independent claim 7 as granted read as follows:

"7. A method for measuring a hepatitis C virus (HCV) or Hepatitis B virus (HBV) or a HCV- or HBV- related virus in a sample by obtaining a sample suitable for detection of virus comprising the step of

(1) treating a virus-containing sample with a treatment solution containing (a) a caotropic ion and (b) an acidifying agent; such that the virus particle is disrupted, the virus antigen is exposed or released; and antibodies against the virus antigen, if present in the sample, are inactivated; and
(2) detecting the virus antigen by immunoassay."

Independent claim 8 as granted differed from granted claim 7 in that the treatment solution further contained a nonionic surfactant.

- II. Opposition was filed against the granted patent, the opponent requesting revocation of the patent in its entirety on the grounds of lack of novelty and inventive step (Article 100(a) EPC), lack of sufficiency of disclosure (Article 100(b) EPC) and added subject-matter (Article 100(c) EPC).
- III. The documents cited during the proceedings before the opposition division and the board of appeal include the following:
- D5 US 5124245
 - D6 US 5136027
 - D9 Kashiwakuma, T. et al, J. Immunol. Methods 190 (1996), pp. 79-89
 - D10 Aoyagi, K. et al, J. Clin. Microbiol., Vol.37, No.6 (June 1999), pp. 1802-1808.
- IV. By an interlocutory decision pronounced at oral proceedings on 27 May 2009 and posted on 17 July 2009, the opposition division decided that the patent was to be maintained in amended form on the basis of the fourth auxiliary request filed at the oral proceedings (Articles 101(3) (a) and 106(2) EPC).

The main request and the first auxiliary request were rejected for non-compliance with Article 123(2) EPC; the second and the third auxiliary requests were considered not to comply with Article 56 EPC; the "modified" third auxiliary request was considered to contravene Article 123(2) EPC.

Regarding the fourth auxiliary request, the opposition division considered that the prior art did not suggest that a method using the claimed treatment composition and an incubation temperature of 50°C to 60°C could solve the problem of exposing the virus core antigen and inactivating the antibodies against the virus core antigen present in the sample. Contrary to the opponent's arguments, the technical problem could be considered solved over the whole scope of the claims, as was evidenced by document D10.

- V. Both the patent proprietor (hereinafter Appellant I) and the opponent (hereinafter Appellant II) filed an appeal against said decision.
- VI. With the statement of the grounds of appeal, Appellant I requested that the decision under appeal be set aside and that a patent be maintained according to the (sole) main request which was submitted at the same time. Appellant II requested that the decision be set aside and that the patent be revoked in its entirety. In its reply to the grounds of appeal of Appellant I, Appellant II raised objections under Articles 123(2) EPC, 83 EPC and 56 EPC concerning the then main request of Appellant I. In reaction thereto, Appellant I submitted a new - corrected - main request and auxiliary requests 1, 2 and 3, all filed with letter of 16 June 2010.

VII. The board sent a communication pursuant to Article 15(1) RPBA as an annex to the summons to oral proceedings, expressing its preliminary opinion.

In said communication, the board commented *inter alia* on the admissibility, pursuant to Article 12(4) RPBA, of the main request and of auxiliary request 1, and on the admissibility of document D27, filed by Appellant II with the grounds of appeal, and of document D28, filed by Appellant I in reaction to Appellant II's submissions. Moreover, the board made some comments regarding Article 123(2) EPC, in particular in relation to the features "sandwich" in claim 1 of the main request and "guanidine hydrochloride" in claims 7 and 8 of the main request.

VIII. With letter dated 2 December 2013, Appellant I submitted a new auxiliary request 3, an auxiliary request 4 (corresponding to former auxiliary request 3) and an auxiliary request 5, and provided arguments concerning the issues raised by the board, as well as in relation to inventive step.

IX. With letter dated 11 December 2013, Appellant II also provided arguments concerning the issues raised by the board, as well as concerning Articles 83 and 56 EPC. It also raised an objection concerning the admissibility of Appellant I's appeal.

X. Oral proceedings before the board took place on 16 January 2014.

During the oral proceedings, Appellant I filed auxiliary requests 6 and 7.

Claims 1 and 7 of the **main request** read as follows (amendments in relation to the corresponding claims as granted are shown as: additions underlined, deletions struck through); claim 8 has similar amendments to claim 7:

"1. A method for measuring a hepatitis C virus (HCV) or Hepatitis B virus (HBV) ~~or a HCV or HBV related virus~~ in a sample by obtaining a sample suitable for detection of virus comprising the step of

(1) treating a virus-containing sample at a temperature of 37°C or greater with a treatment solution containing (a) an anionic surfactant and (b) ~~at least one agent selected from the group consisting of~~ an amphoteric surfactant, a nonionic surfactant and or a protein denaturant; such that the virus particle is disrupted, the virus core antigen is exposed or released; and antibodies against the virus core antigen, if present in the sample, are inactivated; and
(2) detecting the virus core antigen by sandwich immunoassay."

"7. A method for measuring a hepatitis C virus (HCV) ~~or Hepatitis B virus (HBV) or a HCV or HBV related virus~~ in a sample by obtaining a sample suitable for detection of virus comprising the step of

(1) treating a virus-containing sample with a treatment solution containing (a) ~~a caotropic ion~~ guanidine hydrochloride and (b) an acidifying agent; such that the virus particle is disrupted, the virus core antigen is exposed or released; and antibodies against the virus core antigen, if present in the sample, are inactivated; and
(2) detecting the virus core antigen by immunoassay."

Claim 1 of **auxiliary request 1** differs from claim 1 of the main request in that the temperature range has been further restricted from "37°C or greater" to "50°C-60°C".

In **auxiliary request 2**, claim 1 has been further amended in relation to auxiliary request 1 by deletion of the term "sandwich".

Auxiliary request 3 differs from auxiliary request 2 in that in claims 7 and 8 the feature "guanidine hydrochloride" has been replaced by "chaotropic ion, wherein the chaotropic ion is a guanidine ion".

Auxiliary request 4 differs from auxiliary request 3 in that claims 1, 7 and 8 have been deleted. This request thus differs from the request considered allowable by the opposition division only by the replacement of the expression "at least one agent" in claim 1 by "an agent".

Auxiliary request 5 contains 5 claims. The amendments to claim 1 are shown in relation to the corresponding claim 2 as granted:

"21. A method for measuring a hepatitis C virus (HCV) ~~or Hepatitis B virus (HBV) or a HCV or HBV related virus~~ in a sample by obtaining a sample suitable for detection of virus comprising the step of
(1) treating a virus-containing sample with a treatment solution containing (a) an anionic surfactant, wherein the anionic surfactant is SDS, (b) an amphoteric surfactant, wherein the amphoteric surfactant is CHAPS, (c) ~~at least one agent selected from the group consisting of a nonionic surfactant,~~ wherein the nonionic surfactant is Triton X100 and a protein

denaturant; such that virus particle is disrupted, the virus core antigen is exposed or released; and antibodies against the virus core antigen, if present in the sample, are inactivated; and
(2) detecting the virus core antigen by immunoassay using an antibody selected from the group consisting of:

a monoclonal antibody produced by a hybridoma cell line HC11-11 (FERM BP-6005), a monoclonal antibody produced by a hybridoma cell line HC11-14 (FERM BP-6006), a monoclonal antibody produced by a hybridoma cell line HC11-10 (FERM BP-6004), a monoclonal antibody produced by a hybridoma cell line HC11-3 (FERM BP-6002) and a monoclonal antibody produced by a hybridoma cell line HC11-7 (FERM BP-6003)."

Auxiliary request 6 also contains 5 claims, which correspond to claims 2 to 6 as granted, claim 1 differing from the corresponding granted claim 2 as shown:

"~~21~~. A method for measuring a hepatitis C virus (HCV) or ~~Hepatitis B virus (HBV) or a HCV or HBV related virus~~ in a sample by obtaining a sample suitable for detection of virus comprising the step of
(1) treating a virus-containing sample at a temperature of 50°C-60°C with a treatment solution containing (a) an anionic surfactant, (b) an amphoteric surfactant (c) ~~at least one~~ an agent selected from the group consisting of a nonionic surfactant and a protein denaturant; such that virus particle is disrupted, the virus core antigen is exposed or released; and antibodies against the virus core antigen, if present in the sample, are inactivated; and
(2) detecting the virus core antigen by immunoassay."

In **auxiliary request 7**, claim 1 of auxiliary request 6 has been deleted and thus claim 1 corresponds to claim 2 of auxiliary request 6, differing from the corresponding granted claim 3 as shown:

"~~32~~. A method for measuring a hepatitis C virus (HCV) ~~or Hepatitis B virus (HBV) or a HCV or HBV related virus~~ in a sample by obtaining a sample suitable for detection of virus comprising the step of (1) treating a virus-containing sample with a treatment solution containing (a) an anionic surfactant, (b) an amphoteric surfactant (c) a nonionic surfactant and (d) a protein denaturant; such that virus particle is disrupted, the virus core antigen is exposed or released; and antibodies against the virus core antigen, if present in the sample, are inactivated; and (2) detecting the virus core antigen by immunoassay."

XI. Appellant I's submissions, in so far as relevant to the present decision, may be summarised as follows:

Admissibility of Appellant I's appeal

Appellant I argued that the statement of the grounds of appeal did contain reasons as to why the decision of the opposition division should be considered incorrect. Moreover, amended claims had been submitted with the grounds of appeal, in an attempt to redress the decision. Arguments had also been given in the statement of the grounds of appeal concerning claims 7 and 8, which were still defended, and in relation to the cited documents.

Admissibility of the present main request and of auxiliary request 1

The present main request corresponded to the main request filed with the grounds of appeal, differing therefrom only by deletion of the feature "at least one" from claim 2, an amendment which was prompted by an argument of Appellant II.

Claim 1 of the main request was based on the second auxiliary request of the opposition proceedings, differing from said request only in that a limitation regarding the treatment temperature had been inserted in step 1 and the immunoassay in step 2 had been further specified as "sandwich" assay.

All amendments made to the claims were not complex and further limited the scope of the claims. The feature "sandwich" had been added to narrow the core of the invention but was not the only feature justifying an inventive step.

Auxiliary request 2 - Article 123(2) EPC

A basis for the feature "guanidine hydrochloride" in claims 7 and 8 was to be found on page 24 lines 1-4, page 25 lines 30-33 and page 26 line 13. Figure 10, representing a preferred embodiment, as well as the legend thereto at page 10 line 31 also referred to guanidine hydrochloride; even if this disclosure constituted just an example, it did show that this was a preferred embodiment.

Auxiliary request 3 - Article 123(2) EPC

A basis for the feature "a chaotropic ion, wherein the chaotropic ion is a guanidine ion" (claims 7 and 8, step (1)a) was to be found on page 23 line 35 to page 24 line 4, page 25 line 30 to page 26 line 14. As

for auxiliary request 2, it was clear that this feature was a preferred embodiment.

Auxiliary request 4 - Article 123(2) EPC

All features of claim 1 had a basis in the application as filed, and the opponent had had no objections to this claim on grounds of added-matter before the first instance; in fact, it had actually argued that the temperature range was essential. Serum inactivation as mentioned on page 22 implied inactivation of serum antibodies, which was one of the aims of the claimed method.

Auxiliary request 4 - Article 56 EPC

D9 could be considered the closest prior art, since it was directed to the immunodetection of HCV core antigens in serum samples of patients, while D5 and D6 were directed to detection of other viruses. On page 87 right column last paragraph, D9 recognised problems associated with HCV immunodetection, which were: the presence of HCV antibodies in the serum of infected individuals which interfered with immunodetection; the very low quantity of HCV in patients' sera; and the poor accessibility of the HCV core protein for the diagnostic antibody. In order to separate the serum antibodies from the HCV and to concentrate the HCV protein in the sample, D9 included a step of precipitation with polyethyleneglycol (PEG). In contrast thereto, the present claims covered a method in which a virus-containing sample was treated with a specific treatment solution to efficiently release the core antigen while at the same time inactivating serum antibodies that could interfere with detection, the whole pre-treatment being performed in a single step.

Sample pre-treatment was thus considerably simplified (page 4 line 27 to page 5 line 12 of the application as filed). Further steps were not to be read into the claimed method, in accordance with the case law of the boards of appeal and in particular with T 1023/02. D5 was concerned with washing solutions to be employed during the detection step and concerned a different virus, HSV (column 1 lines 1-15); moreover, D5 did not deal with the need to inactivate the serum antibodies present in the sample. Likewise, D6 dealt with a method of renaturing protein and restoring its reactivity (e.g. abstract), mainly in relation to recombinant HIV proteins (examples); D6 plainly provided a method for resolubilising recombinant protein (D6 column 4 second and fourth paragraphs), and the skilled person would not apply the solutions of D6 to an HCV serum sample as the only pre-treatment, since he would expect that serum antibodies would remain functional and interfere with core antigen detection. Even if he did apply them, he would still not arrive at the method of the invention, since D6 taught a two-step method comprising initial SDS treatment followed by the addition of a renaturing surfactant (column 4 lines 12 to 23, claim 1). It was not disclosed in D6 that the two steps could be performed together, and the skilled person would not expect it to work. Examples 4 and 5 of the patent as well as D10 confirmed that the claimed method was a quick test to detect HCV, independently of the detection level being lower than for D9.

Auxiliary request 5 - Admissibility

The request had been submitted in reaction to possible admittance of D27, a document containing experimental

evidence which had been submitted by the opponent only in the appeal proceedings.

Auxiliary request 6 - Admissibility

In this request HBV had been deleted in case this feature was considered not allowable; this objection had been raised only at oral proceedings before the board and therefore this request could not have been submitted earlier.

Auxiliary request 7 - Admissibility

This request was an attempt to overcome possible objections concerning Article 123(2) EPC, e.g. in relation to the temperature feature which had been deleted from this request. It would not prolong the proceedings, because inventive step had already been discussed in relation to claim 2 of auxiliary request 4 as well.

XII. Appellant II's submissions, in so far as relevant to the present decision, may be summarised as follows:

Admissibility of Appellant I's appeal

Appellant I's appeal should be considered as inadmissible, as its statement of grounds of appeal did not contain its complete case, as required by Article 12(2) RPBA. In particular, the grounds of appeal did not indicate why the appealed decision should be set aside. It was also accompanied by a request which was not admissible. The submitted amendments to the claims, said to be intended to overcome the objections of the opposition division, actually constituted an implicit

acceptance of the decision, which meant that the appeal was inadmissible according to decision T 2532/11.

Admissibility of the main request and of auxiliary request 1

In particular, the feature "sandwich immunoassay" had never been discussed in the first-instance proceedings, and it did not appear to address any issue raised for the first time in the decision under appeal or any argument raised by the opponent in its grounds of appeal. Moreover, the patent proprietor had created a completely new case, wherein the claimed method made use of a different temperature and of a different detection assay. In addition, said amendment was not *prima facie* allowable under Article 123(2) EPC.

Auxiliary request 2 - Article 123(2) EPC

In relation to the amendment of claims 7 and 8, the passage indicated by Appellant I on page 23 line 25 to page 24 line 5 referred to a different method. Figure 10 related to a very specific embodiment, namely to that of Example 10 (page 47 lines 7 to 10), while page 26 defined a concentration which was not present in the claim.

Auxiliary request 3 - Article 123(2) EPC

The passage on page 24 lines 1 to 4 constituted no basis for the amendment of claims 7 and 8 in the context of core antigen. Page 25 lines 30 to 33 required the presence of surfactant, which was not present in claim 7.

Auxiliary request 4 - Article 123(2) EPC

Claim 1 required the presence of three compulsory components, but there was no disclosure in the application as filed for the combination with all other features of the claim.

The temperature range had been selected from a list (page 22 lines 28 to 35), and the mentioned passage taught that the chosen temperature was actually for inactivation of serum, a step which was not present in the claims. Inactivation of serum was not the same as inactivation of serum antibodies. The temperature was only enablingly disclosed in relation to a very specific combination of detergents and conditions. Original claim 10 presented a huge list of viruses to be detected, while the claims were limited to HCV or HBV and core protein: the claimed embodiments resulted from selecting from different lists.

Auxiliary request 4 - Article 56 EPC

D9 also addressed the problem of detecting HCV core antigen, and solved it by using PEG, NaOH (a protein denaturant) and Triton X100 (a non-ionic surfactant). The method of D9 had even more success than the method of the patent application, as it achieved a detection rate of 92% while the method of the patent had a detection rate of 2:3. It was apparent from pages 87 and 88 of D9 that the method therein described was also quick and reliable. The problem could thus be formulated as the provision of an alternative method for detection of HCV core antigen. Both documents D5 and D6 disclosed the use of surfactants in similar technical problems. D6 in particular disclosed the use of SDS and the problems associated with its use; as solution to these problems, it disclosed the use of betaine surfactants and Triton X100. The skilled person

was always prepared to adapt technology by routine experimentation and would thus combine known detergents in order to solve problems. In relation to the alleged need for a precipitation step, it should be noted that the claims also did not exclude the presence of such a step, as they might comprise further steps; the precipitation step would not manifestly counteract steps of claims, contrary to the situation in T 1023/02.

Auxiliary request 5 - admissibility

This request was filed late and it was not clear that it complied with e.g. Article 123(2) EPC. While it was submitted as a reaction to D27, it did not successfully overcome the objections based on D27, as essential features were still missing. Moreover it represented a new case, so that remittal to the first instance would be required. Thus, it should not be admitted into the appeal proceedings.

Auxiliary request 7 - admissibility

Admission of this request - submitted during the oral proceedings - would unnecessarily prolong the oral proceedings. In view of the fact that the temperature feature was still absent from this request, Appellant II would need to introduce D27 also for the discussion of Article 56 EPC.

XIII. The final requests of the parties were as follows.

Appellant I requested that the decision of the opposition division be set aside and that the patent be maintained according to the main request or auxiliary requests 1 or 2 filed with letter of 16 June 2010, or

according to auxiliary requests 3, 4 or 5, filed with letter of 2 December 2013, or on the basis of auxiliary requests 6 or 7, submitted during the oral proceedings.

Appellant II requested that the decision under appeal be set aside and that the patent be revoked in its entirety. It further requested the main request and auxiliary requests 1, 5, 6 and 7 not to be admitted into the proceedings. As an auxiliary measure, it requested that the case be remitted to the department of first instance for further prosecution, and, in this case, that the board order an apportionment of costs.

Reasons for the Decision

1. Admissibility of the appeal

1.1 Regardless of the fact that Appellant II's objection on the admissibility of the appeal was raised only at a late stage of the proceedings, namely after the summons for oral proceedings had been issued, the admissibility of an appeal may, and, if necessary, must at any time be reviewed by the competent board of appeal (T 15/01, OJ 2006, 153, reasons 1).

1.2 Under Article 108 EPC, third sentence, a statement setting out the grounds of appeal shall be filed within four months after the date of notification of the decision in accordance with the Implementing Regulations. Rule 99(2) EPC stipulates that in the statement of the grounds of appeal the appellant shall indicate the reasons for setting aside the decision impugned, or the extent to which it is to be amended, and the facts and evidence on which the appeal is based. As to the content of the statement of the

grounds of appeal, Article 12(2) RPBA requires that it shall contain a party's complete case and set out clearly and concisely the reasons why it is requested that the decision under appeal be reversed, amended or upheld, and should specify expressly all the facts, arguments and evidence relied on. According to Rule 101(1) EPC, if the appeal does not comply with *inter alia* Article 108 EPC or Rule 99(2) EPC, the board of appeal shall reject it as inadmissible.

1.3 The examination of whether the requirements of Article 108 EPC, third sentence, in conjunction with Rule 99(2) EPC are met has to be made on the basis of the contents of both the statement of the grounds of appeal and of the decision under appeal (T 162/97 of 30 June 1999, reasons 1.1.2).

1.3.1 Appellant I's statement of grounds of appeal was undisputedly duly filed within the time limit set by Article 108 EPC. It was accompanied by a new claim request which, according to Appellant I, was based on the second auxiliary request decided upon by the opposition division, differing therefrom in amendments to claims 1, 2, 7 and 8. Under section 2.1 of the grounds of appeal, Appellant I summarised the decision of the opposition division in relation to claims 1, 2 and 7 of the then second auxiliary request, wherein said claims had been considered non-inventive in view of the combination of D9, D5 and D6 (claim 1) or in view of D21 and D22 (claim 7), and as not solving the problem over the whole scope of the claim (claims 1 and 2). These objections were then dealt with separately in the grounds of appeal, respectively in sections 2.2 (entitled "Claim 1 in view of D9, D5 and D6"), 2.3 ("Claims 1 and 2 provide a solution over the whole area claimed") and 2.4 ("Inventive Step of claims 7 and 8").

Sections 2.3 and 2.4 explicitly deal with the objections raised by the opposition division, while in section 2.2 there is indeed no reference to either the contested decision or its reasoning.

1.3.2 While not specifically stated, it is however evident that section 2.2 of the grounds of appeal addresses the decision of the opposition division in relation to claim 1 of the then second auxiliary request, whereby the opposition division decided that the claimed subject-matter was not inventive over D9 in combination with either D5 or D6. According to said decision, D9, the closest prior art, already disclosed a method for detection of HCV in serum, by using a different sample treatment to that of the patent, and "[t]he person skilled in the art would have tried the combination of solutions disclosed in D5 or D6 to solubilize viral antigens also in the detection of HCV core antigen as target structure with expectation of success, as the solutions provided in D5 and D6 solubilize viral antigens like structural proteins" (page 7 of the decision, section 4.3).

1.3.3 Section 2.2 of the grounds of appeal contains Appellant I's arguments why new claim 1 should be considered inventive over D9, D5 and D6. Appellant I starts from D5 or D6 as closest prior art, and concludes that "the skilled person in the art would not have attempted to combine the sandwich immunoassay of Hepatitis C virus disclosed in D9 and the solution disclosed in D5 or D6" (section 2.2.5) because, as explained in section 2.2.2, it would be expected that "since anionic surfactants such as SDS have a very strong protein denaturing effect, the function of an immobilized antibody in a sandwich immunoassay is also decreased by the anionic surfactants" and for that

reason "anionic surfactants are not generally used in sandwich immunoassays". In sections 2.2.6 and 2.2.7, Appellant I further provides arguments for the existence of a surprising effect.

- 1.3.4 It is a fact that there is not a single reference to the decision of the opposition division in section 2.2 of the grounds of appeal, but it is also apparent from this argumentation that Appellant I relies on a further limitation of the claim (by introducing the feature "sandwich immunoassay") to overcome the objection of the opposition division. This argumentation, together with the corresponding amendment, is thus considered a *bona fide* attempt to redress the decision. Whether said amendment and corresponding new line of argumentation are admissible at this stage of the proceedings is a different question, to be dealt with when considering the admissibility of the claim request (see below).

- 1.4 Appellant II argued that the facts of the present case were very similar to those of decision T 2532/11 of 14 October 2013, wherein it was decided that the appeal was inadmissible because it was insufficiently substantiated. In said decision, board 3.3.05 came to the conclusion that, since the appellant had confirmed that the reasons for filing modified requests were based on the assumption that the decision of the opposition division was right in its findings, the aim of the said appeal was thus "to gain an opportunity to get the patent maintained in amended form through new claims making the revoked patent compliant with the reasons given by the opposition division, or through the introduction of new features thus forming different embodiments of the alleged invention which were never discussed before regarding their compliance with the requirements of the EPC" (reasons 2.7.1).

1.5 The board notes however that, contrary to the situation in T 2532/11, in the present case there is no implicit acceptance of the appealed decision. Not only is part of the reasoning of said decision directly contested (sections 2.3 and 2.4 of the grounds of appeal), but also section 2.2 attempts to provide more reasons why the subject-matter of claim 1 was not obvious, contrary to the findings of the opposition division. The introduced feature does not lead to the claiming of a different embodiment but to a restriction of the general embodiment previously claimed to a more specific one. There is thus a direct link between the decision under appeal and the statement of the grounds of appeal, and the grounds of appeal do indeed contest the decision, thus fulfilling the two conditions for admissibility of the appeal which in contrast were considered not to be met in decision T 2532/11 (reasons 2.6.2 and 2.7).

1.6 The board thus comes to the conclusion that the statement of the grounds of appeal fulfils the requirements of Article 108 EPC, third sentence, Rule 99(2) EPC and Article 12(2) RPBA in that it deals with the objections of the opposition division which are still relevant for the claims pursued. Appellant I's appeal is thus considered admissible.

1.7 Appellant II's appeal, whose admissibility has not been contested, is also considered admissible.

2. Main request - Admissibility

2.1 The set of claims according to the main request submitted with letter of 16 June 2010 was to replace the set of claims according to the main request which

had been filed with the statement of the grounds of appeal. It differs from the previous main request in its "marked-up copy" version solely by an amendment in claim 2, which was made in reaction to Appellant II's grounds of appeal. Although the "marked-up copy" version of the main request filed with the grounds of appeal was not identical to the "clean copy" version submitted at the same time, it is apparent from the grounds of appeal that the set of claims which Appellant I intended to submit as main request was indeed that corresponding to the "marked-up copy" version. Hence, despite the fact that it was filed later, the board considers that the new main request is not an amendment to the party's case after it filed the grounds of appeal. The admissibility of this request is thus to be examined under the provisions of Article 12 RPBA rather than of Article 13 RPBA.

2.2 Pursuant to Article 12(4) RPBA, it is at the discretion of the boards of appeal to admit requests which could have been presented in the proceedings before the examining or opposition division. When exercising their discretion, the boards take into account the circumstances of the particular case and the arguments put forward by the parties.

2.3 The present main request includes amendments which have not been examined by the opposition division and is thus *de facto* a new request. In particular this request contains the new features "at a temperature of 37°C or greater" in step 1 of claim 1 and "sandwich immunoassay" in step 2 of claim 1. These amendments were not present in any of the claim requests considered by the opposition division. As argued by Appellant II, such a claim request could have been submitted already during the opposition

proceedings, as it simply addresses issues already raised during the written and oral proceedings before the opposition division and not issues raised for the first time in the decision under appeal or arguments raised by Appellant II in its grounds of appeal. Appellant I did not deny that this claim request could have been filed earlier but argued that it would have been useless because the opposition division would have considered that it still lacked inventive step. However, by deciding not to submit such a request already in first instance, Appellant I has indeed hindered the opposition division from giving a decision on this subject-matter. To admit this claim request into the proceedings would thus mean that the board would have either to decide on it for the first time or remit the case to the first instance, as explicitly requested in that eventuality by Appellant II.

- 2.4 With the present request, Appellant I has created a new case in relation to the case before the first instance, wherein the claimed method now is characterised by the use of a different temperature range and of a specific type of immunoassay. The presently claimed method requires a temperature of 37°C or greater, in contrast to no temperature limitation as in all requests refused by the opposition division or to a restriction to a temperature between 50°C and 60°C as in the request found allowable by the opposition division; and it defines the immunoassay to be used for detection as a "sandwich immunoassay". A different line of argumentation is then followed in relation to inventive step, as Appellant I now heavily relies on the new feature "sandwich immunoassay". Finally, the board considers this amendment as *prima facie* not allowable under Article 123(2) EPC, because no basis for the feature "sandwich immunoassay" is found in the

application as filed in the context of present claim 1, as argued by Appellant II and further discussed by the board in the communication accompanying the summons to oral proceedings.

2.5 The board thus decides to make use of its discretionary power under Article 12(4) RPBA not to admit the main request into the proceedings.

3. Auxiliary request 1 - Admissibility

3.1 Auxiliary request 1 was not filed with the statement of the grounds of appeal or as a reply to Appellant II's grounds of appeal, as foreseen in Article 12(2) RPBA. Instead this request was filed as an apparent reaction to Appellant II's reply to Appellant I's grounds of appeal. Its admission into the proceedings is thus governed by Article 13(1) RPBA, which gives the board the discretionary power to admit or refuse any amendment to a party's case after it has filed its grounds of appeal or reply.

3.2 In this request, claim 1 still contains the new feature "sandwich immunoassay", while the temperature range has been changed to "50°C to 60°C".

3.3 At least in view of the presence of the feature "sandwich immunoassay", the same considerations regarding admissibility as set out above in relation to the main request apply also to this request.

3.4 Accordingly, the board decides to make use of its discretionary power under Article 13(1) RPBA not to admit auxiliary request 1 into the proceedings.

4. Auxiliary request 2

- 4.1 This request no longer comprises the term "sandwich", and Appellant II had no objections concerning its admissibility. The board thus decides to admit this request into the proceedings (Article 13(1) RPBA).
- 4.2 Article 123(2) EPC
- 4.2.1 Appellant II had a number of objections under Article 123(2) EPC against claim 1. It also considered the feature "guanidine hydrochloride" in claims 7 and 8 to amount to unallowable added subject-matter.
- 4.2.2 According to Appellant I, the basis for the feature "guanidine hydrochloride" in claims 7 and 8 was to be found at page 23 line 25 to page 24 line 5, page 25 line 30 to page 26 line 13, as well as in Figure 10 and the legend thereto on page 10 line 31.
- 4.2.3 The board however considers that the above-mentioned passages do not constitute an appropriate basis for said amendment in the context of claims 7 and 8. The passage on pages 23 and 24 discloses "guanidine chloride" (synonymous with "guanidine hydrochloride") as an example of salts that "have a property of making refractory proteins watersoluble" and goes on to disclose that "ions produced from salts (chaotropic agents) having such a property are called 'chaotropic ions'". This is not a disclosure of the use of guanidine (hydro)chloride in the method of claims 7 and 8. Apart from the fact that the whole passage contains no reference to the method of the invention, it is also noted that it is included in a section entitled "Removal of interference by hemoglobin" (heading on page 22) and specifically refers, on page 22 last line to page 23 line 5, to the use of serum samples (and not

to virus-containing samples in general): thus, this passage is not in the context of the claimed method. Figure 10 and its legend on page 10 line 31 disclose the use of guanidine hydrochloride in the pre-treatment of virus-containing serum samples. While this might be a preferred embodiment of the invention, as argued by Appellant I, it is still in the context of a specific example, namely that of Example 10 (page 47 lines 1 to 10), wherein serum samples and given concentrations of the different solution components are used. It is thus no adequate basis for the amendment in the general context of claims 7 and 8.

The same is true in relation to the passage of page 26 line 13, wherein the concentrations for guanidine hydrochloride are defined.

4.2.4 Accordingly, at least claims 7 and 8 of auxiliary request 2 comprise amendments which constitute an unallowable extension of subject-matter. In view of these findings, it is not necessary at this point to examine also the amendments to claim 1 of this request.

4.2.5 The board thus comes to the conclusion that auxiliary request 2 is not allowable for lack of compliance with Article 123(2) EPC.

5. Auxiliary request 3

5.1 Admissibility

5.1.1 According to Appellant I, claim 1 of this request is based on claim 1 of the fourth auxiliary request found allowable by the opposition division, only differing therefrom by replacement of "at least one agent" in step 1(c) by "an agent". This amendment was made in

reaction to Appellant II's objection under Article 123(2) EPC raised in its grounds of appeal.

5.1.2 Although this request was filed only after oral proceedings had been arranged, the board considers that it is indeed a *bona fide* attempt to overcome outstanding objections. Hence, and in view of the fact that Appellant II had no objections regarding its admissibility, the board decides to admit this request into the proceedings (Article 13(1) RPBA).

5.2 Article 123(2) EPC

5.2.1 In claims 7 and 8, the term "guanidine hydrochloride" in the previous claim requests was replaced by the expression "chaotropic ion, wherein the chaotropic ion is a guanidine ion". As a basis for this amendment, Appellant I indicated page 23 to page 24, page 25 lines 30 to 33 and page 26 line 14 of the application as filed.

5.2.2 The board agrees with Appellant II's view that the indicated passages do not constitute an adequate basis for the above amendment. As noted above in relation to auxiliary request 2, the passage on pages 23 and 24 discloses "guanidine ions" as an example of chaotropic ions, and it is within a section entitled "Removal of interference by hemoglobin" wherein specific reference is made to serum samples rather than to virus-containing samples in general. This is not a disclosure of the use of guanidine ions in the method of claims 7 and 8. Nor is the passage of page 25 lines 30 to 33 in the context of the method as claimed. In relation to page 26 line 14, it is noted that this passage refers to a specific embodiment, further defined by specific parameters, such as the concentration of guanidine

hydrochloride to be used, the presence - in a given concentration - of Triton X100 and Tween 20, and a given temperature.

5.2.3 For these reasons, the board concludes that auxiliary request 3 does not fulfil the requirements of Article 123(2) EPC.

6. Auxiliary request 4

6.1 Admissibility

6.1.1 This request corresponds to the fourth auxiliary request before the opposition division, which was found allowable, and differs therefrom only by replacement of "at least one agent" in step 1(c) of claim 1 by "an agent".

6.1.2 As discussed above in relation to auxiliary request 3, this amendment is considered a *bona fide* attempt to overcome objections under Article 123(2) EPC raised by Appellant II in its statement of the grounds of appeal. The board thus decides to admit auxiliary request 4 into the proceedings (Article 13(1) RPBA).

6.2 Article 123(2) EPC

6.2.1 Claim 1 of auxiliary request 4 is based on originally filed claims 2, 10 and 12, with further features taken from different passages in the description. In relation to Appellant II's objections, the board notes the following:

6.2.2 While the passage on page 22, disclosing the temperature range, does indeed refer to serum inactivation, this is not interpreted as a statement

that the temperature range is obligatorily to be used for serum inactivation; instead this passage merely states that the temperature which is most effective in the method of the invention is identical to the temperature which is commonly used for inactivation of serum. Although the selection of this particular temperature range implies a selection among three different ranges disclosed on page 22 (4°C to 100°C, >37°C, and 50°C to 60°C), the claimed range of 50°C to 60°C is indicated as being the most preferred ("more effective"). The argument that this temperature range is only enablingly disclosed in relation to a very specific combination of detergents and conditions cannot be followed either, since the disclosure on page 22 is a general disclosure. The fact that the examples also use this temperature range in combination with other specific conditions just confirms that this is the preferred temperature range; it does not however change the fact that this feature is also disclosed in a general context.

6.2.3 Limitation to HCV or HBV is indeed a selection from the list of viruses to be detected according to original claim 10. However it is apparent from the whole disclosure of the application as filed that HCV and HBV are the preferred target of the methods of the invention. Most of the text of the application refers to HCV, which is also the subject of almost all examples, while HBV is referred to on e.g. page 9 lines 10 to 20, a passage which specifically describes the "treating method of the present invention" as providing "detection or determination of a virus", the virus being further defined as "HCV or HBV". The board also accepts that the reference on this passage to "disrupting a virus particle" and thereby "fully exposing the virus antigen" is an implicit disclosure

of the core antigen. Although this passage does not disclose the composition of the solution as claimed, it does refer to the "treating method of the present invention", which allows this passage to be combined with the originally claimed subject-matter. Detection of HBV core antigen is specifically disclosed in Example 14, and the statement at the end of this example (page 54 lines 3 to 10) can be interpreted as a general statement about the suitability of the methods of the invention for detection of HBV.

6.2.4 The board thus comes to the conclusion that the claims of auxiliary request 4 fulfil the requirements of Article 123(2) EPC.

6.3 Article 56 EPC

6.3.1 According to the patent, the problem that the present invention purports to solve is to provide methods for detecting viruses, in particular HCV and HBV, which are as sensitive as PCR-based methods, but do not have the shortcomings associated with those methods. The methods of the invention are based on immunodetection of viral core antigen and are designed to overcome the disadvantages associated with the prior-art methods for core antigen detection (patent, paragraphs [0009] and [0010]). To overcome said disadvantages of the prior art, the method of detection according to the patent comprises a sample treatment step which causes the virus to be disrupted and to expose the core antigen, and at the same time inactivates serum antibodies which would interfere with the detection method (patent, paragraph [0015]).

6.3.2 D9 discloses methods of HCV detection, which are also based on immunodetection of the core antigen. D9 thus

appears to be the most suitable starting point for the discussion of inventive step, which is in line with the view of the opposition division and of Appellant I. D9 teaches detection of hepatitis C virus specific core protein in serum of patients by means of a fluorescence enzyme immunoassay (FEIA). A method for treatment of the serum samples is disclosed on page 82 right column of D9 and comprises: incubation with polyethylene glycol (PEG) followed by centrifugation; the precipitates are then suspended in NaCl and sodium citrate, followed by treatment with NaOH, and then neutralised with a solution of NaH_2PO_4 and Triton X-100 (nonionic surfactant, as disclosed in e.g. paragraph [0045] of the patent). D9 further teaches (page 87, right column last two lines to page 88, left column line 9) that the PEG precipitation and the alkali treatment served to inactivate anti-HCV core antibodies, while the detergent treatment (with Triton X-100) effectively released the HCV core protein.

6.3.3 The difference to present claim 1 is thus that another method for pre-treatment of the serum samples is used for the same purpose, namely for inactivation of serum HCV-core antibodies and exposure of HCV antigen. According to Appellant I, the claimed method is improved in relation to the method of the closest prior art (see below), and thus the technical problem can be formulated as the provision of an improved method for detection of HCV core antigen.

6.3.4 The proposed solution is a method according to claim 1, wherein a virus-containing sample is treated at a temperature of 50°C to 60°C with a treatment solution containing an anionic surfactant, an amphoteric surfactant and either a nonionic surfactant or a protein denaturant. The claimed method is thus

simplified in relation to that of D9, as it only requires a one-step treatment, in contrast to the prior art methods - such as that of D9 - using polyethylene glycol treatment (patent, paragraph [0011]). In so far as a method simplification can be considered an improvement, the board is satisfied that the technical problem is plausibly solved. It thus has to be examined whether the claimed solution would be obvious for the skilled person.

6.3.5 Document D6 also relates to immunoassay methods, in particular enzyme immunoassay methods as in D9, to detect antigens from pathogenic organisms in body fluids (D6, column 1 first and second paragraphs). While HIV-recombinant antigens are used, D6 nevertheless teaches that the method may also be employed for other proteins, including other antigens, haptens and antibodies (column 3 lines 50 to 56). The skilled person would thus consider D6 when searching for ways to modify the method of D9. D6 discloses the use of SDS (anionic surfactant: paragraph [0060] of the patent) as being one of the conventional ways to solubilise proteins, and further discusses the problems associated with its use (column 1 line 59 to column 2 line 1). As a solution to these problems, it teaches the use of betaine surfactants (which are amphoteric surfactants, as disclosed in paragraph [0081] of the patent) and the non-ionic surfactant Triton X100 (column 2 line 40, column 4 line 12). The combination of documents D9 and D6 thus discloses all features of claim 1, except for the temperature range and the simultaneous use, in one step, of the different surfactants.

6.3.6 While the temperature range is not disclosed in either D9 or D6, the board considers that this would be an

obvious modification which per se cannot justify an inventive step. Indeed, the patent itself states in paragraph [0067] that "the temperature used for the treatment of samples may be any temperature *commonly* used in the laboratory" and "the treatment at a temperature of 50-60°C which is *commonly* used for the inactivation of the serum is more effective" (emphasis added by the board). The fact that this temperature range is commonly used for serum inactivation would in itself prompt the skilled person to try it. A possible enhancement of the detergent treatment effect - for which there is no evidence in the patent - would most likely be expected or at the most come as a bonus effect. Indeed, this is also confirmed by Appellant I in its grounds of appeal (section 2.3.2).

6.3.7 In relation to the second difference, Appellant I argued that D6 teaches a multi-step method, and that the skilled person would not consider combining all detergents of D6 in one single solution to have a one-step pre-treatment, because it would not expect it to work. The board notes however that there is no prior art teaching away from mixing detergents. On the contrary, mixtures of detergents are very often used in protein solubilisation, as is quite apparent from e.g D5, which discloses a "wash composition" for extraction of antigens in a biological specimen, wherein the antigen is to be preferably detected by immunoassay (column 4 lines 46 to 47); the wash "extraction composition" according to D5 comprises, among other components, nonionic surfactants (column 3 lines 30 to 59) as well as anionic surfactants (column 4 lines 3 to 21).

6.3.8 Appellant I further argued that the skilled person would not apply solutions of D6 as the only pre-

treatment of serum samples to be used for detection of HCV core antigen, because it would expect that serum antibodies would remain functional and interfere with the detection method. The board however notes that treatment with SDS, as disclosed in D6, would be expected to have exactly this effect, namely inactivation of antibodies. The patent itself confirms that it was known in the art that most proteins are denatured by heat treatment in the presence of SDS and thus that the addition of a treatment agent comprising an anionic surfactant such as SDS causes disruption of viruses as well as the denaturing of antibodies against the virus antigen (patent, paragraph [0058]); in this context, reference is made to D9 in paragraph [0059] of the patent, to confirm that it would be "readily understood by a person skilled in the art that the addition of a denaturant comprising SDS to a sample causes efficient release of antigens". Like D6, the patent then comments on the problems associated with the use of SDS, and states that "the denaturing effect following SDS treatment need[s] to be weakened by some means or other" (paragraph [0060]); these means consist of the "addition of a treatment agent containing a surfactant other than an anionic surfactant" (paragraph [0064] of the patent. In any case, it is noted that D6 teaches the use of the detergents as claimed in the pre-treatment of samples for use in immunoassay detection methods, and thus the skilled person would just have to follow this teaching: if this pre-treatment then unexpectedly resulted in inactivation of interfering serum antibodies, this would come as a bonus effect.

6.3.9 In addition, it is noted that although indeed the examples of the patent and the description in general do not foresee a PEG precipitation step in the pre-

treatment of the virus-containing samples according to the invention, the fact is that the open language of the present claims does not exclude the presence of further method steps: this broadest interpretation has to be taken into account when analysing inventive step, and thus it is not appropriate to rely on the absence of a given method step for inventivity, if embodiments where such a step may be present are also within the limits of the claim. Such a broad interpretation of the claim would not be illogical or devoid of technical sense, and thus the rationale of decision T 1023/02 of 19 May 2006 (reasons 7) does not apply to the present case.

6.3.10 Finally, even if the claim were construed as directed to a one-step pre-treatment method and it were assumed that the skilled person would indeed expect it to be less sensitive, the board still considers that the skilled person would be motivated to try it when attempting to get a quick, simplified method. Indeed it is apparent from the data of the patent in comparison to that of D9 that the simplification of the method as claimed is at the cost of sensitivity, as can be concluded from the comparison of a sensitivity of 92.1% disclosed for the method of D9 (page 86 right column last 4 lines) and a sensitivity of 2:3 for the method according to the patent (Figures 3, 4, 5 and 12).

6.3.11 For these reasons, the board comes to the conclusion that claim 1 of auxiliary request 4 does not fulfil the requirements of Article 56 EPC.

7. Auxiliary request 5 - Admissibility

7.1 According to Appellant I, auxiliary request 5 was submitted as ab precautionary measure, in case the

board admitted Appellant II's document D27 into the proceedings.

7.2 The board considers that, in view of the fact that document D27 has *de facto* not been admitted into the proceedings, the reason given by Appellant I for submitting this request is deprived of factual basis. Therefore, the board decides not to admit auxiliary request 5 into the proceedings (Article 13(1) RPBA).

8. Auxiliary requests 6 and 7 - Admissibility

8.1 As has been repeatedly stated in the case law, 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 (T 1525/10 of 20 September 2011, reasons 2.3). Moreover amended claims submitted at the latest possible stage of appeal proceedings, namely at the oral proceedings, should be admitted only if clearly allowable in the sense that it can be quickly ascertained that they overcome all outstanding issues without raising new ones (T 1993/07 of 13 October 2011, reasons 4.4.3).

8.2 Auxiliary requests 6 and 7, which were both submitted during oral proceedings before the board, do not *prima facie* overcome the objections on file regarding lack of inventive step, while auxiliary request 7 at the same time prompts other objections from Appellant II, both under Article 56 EPC and Article 83 EPC. Accordingly, the board decides not to admit either of auxiliary requests 6 and 7 into the proceedings (Article 13(1) RPBA).

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.
2. The patent is revoked.

The Registrar:

The Chairman:



N. Maslin

U. Oswald

Decision electronically authenticated