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# Datasheet for the decision of 26 October 2023

**Case Number:** T 0293/19 - 3.3.10

**Application Number:** 11715928.5

**Publication Number:** 2560691

**IPC:** A61L2/10, C07K16/06, A61K9/08, A61K39/395, A61P31/00, A61P37/00

**Language of the proceedings:** EN

**Title of invention:**
PROCESS FOR PREPARING AN IMMUNOGLOBULIN COMPOSITION

**Patent Proprietor:**
Biotest AG

**Opponent:**
Strawman Limited

**Headword:**

**Relevant legal provisions:**
EPC Art. 123(2), 54(2), 56, 83

**Keyword:**
Auxiliary request 10 - allowable

**Decisions cited:**
T 0595/90

**Catchword:**

Europäisches Patentamt
European Patent Office
Office européen des brevets

**Beschwerdekammern**

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**Case Number: T 0293/19 - 3.3.10**

# D E C I S I O N
# of Technical Board of Appeal 3.3.10
# of 26 October 2023

| | |
|---|---|
| **Appellant:** (Patent Proprietor) | Biotest AG<br>Landsteinerstr. 5<br>63303 Dreieich (DE) |
| **Representative:** | Page White Farrer<br>Bedford House<br>21a John Street<br>London WC1N 2BF (GB) |
| **Appellant:** (Opponent) | Strawman Limited<br>Orchard Lea<br>Horns Lane<br>Combe, Witney<br>Oxfordshire OX29 8NH (GB) |
| **Representative:** | D Young & Co LLP<br>120 Holborn<br>London EC1N 2DY (GB) |
| **Decision under appeal:** | **Interlocutory decision of the Opposition Division of the European Patent Office posted on 29 November 2018 concerning maintenance of the European Patent No. 2560691 in amended form.** |

**Composition of the Board:**

| | |
|---|---|
| **Chair** | P. Gryczka |
| **Members:** | R. Pérez Carlón |
| | L. Basterreix |

## Summary of Facts and Submissions

I. The patent proprietor and the opponent appealed the opposition division's decision concerning maintenance of European patent No. 2 560 691 in the form of the second auxiliary request.

II. Notice of opposition had been filed on the grounds of added subject-matter, insufficiency of disclosure and lack of novelty and of inventive step (Article 100(a)(b)(c) EPC).

III. The following documents are relevant to the present decision:

D1 Graber + Pfenninger GmbH, Vibrating Mixer, Laboratory type, 2009
D6 US 5,075,425
D15 EP 0 450 412 A1
D18 US 5,190,752
D20 US 2008/0014122 A1
D21 WO 03/037504 A1, partially translated as D21a
D22 WO 02/38191 A2
D23 US 2007/0164233 A1
D24 US 2008/0081004 A1
D26 Note for guidance on virus validation studies: the design, contribution and interpretation of studies validating the inactivation and removal of viruses, CPMP, 1996
D28 M. Radosevich, T. Burnouf, Intravenous immunoglobulin G: trends in production methods, quality control and quality assurance, Vox Sanguinis 2010, vol. 98, pages 12 to 28

IV. The opposition division concluded that claim 11 of the main request and of auxiliary request 1 lacked a basis in the application as originally filed.

The second auxiliary request was admissible. Claim 11 had the required basis and was clear. The claimed invention was sufficiently disclosed for it to be carried out by a skilled person.

The claimed process was novel, as the state of the art did not disclose preparing IgM compositions with a vibrating agitator. This step imparted structural characteristics to the IgM composition obtained, which was thus novel too.

Document D18 was the closest prior art. The problem underlying the claimed invention was to provide a process for the preparation of improved IgM compositions with regard to downstream processing steps. The solution, which was characterised by requiring a vibrating agitator, would not have been obvious in view of the prior art and was thus inventive.

The opposition division did not admit any of the twenty-three documents filed after the nine-month opposition period.

V. With the statement setting out the grounds of appeal, the appellant-patent proprietor filed its main request, a first auxiliary request which was withdrawn at the oral proceedings before the board on 26 October 2023, and the third to fourteenth auxiliary requests. These auxiliary requests corresponded to those pending before the opposition division, and auxiliary request 2 is the request it found allowable. With a letter dated

8 January 2021, the appellant-patent proprietor filed auxiliary requests 2a, 5a, 8a and 12a.

VI. Claim 1 of the main request and of auxiliary requests 2 to 10 and 2a, 5a and 8a reads as follows:

*"A process for the preparation of an IgM containing immunoglobulin composition from a plasma fraction comprising immunoglobulins, the process comprising:*
*(a) providing a plasma fraction as a solution containing the immunoglobulins;*
*(b) mixing octanoic acid with the solution and treating the mixed solution with a vibrating agitator to precipitate contaminating proteins; and*
*(c) separating the precipitated proteins from the solution to yield the IgM containing immunoglobulin composition."*

VII. Claim 11 of the main request relates to an antibody preparation and reads as follows:

*"An antibody preparation comprising immunoglobulins IgG, IgA and IgM, wherein at least 15% of the total immunoglobulins are IgM, wherein the antibody preparation is virus safe with respect to enveloped and non-enveloped virus, has an anticomplementary activity of ≤ CH 50/mg protein, and is stable in liquid form for at least 6 months when stored at 2 to 8°C."*

Claim 11 of auxiliary request 2 reads:

*"An antibody preparation obtainable by the process of claim 8 or claim 9, wherein the antibody preparation is suitable for intravenous administration in humans and comprises immunoglobulins IgG, IgA and IgM, wherein at least 15% of the total immunoglobulins are IgM, wherein*

*the antibody preparation is virus safe with respect to enveloped and non-enveloped virus, has an anticomplementary activity of ≤ CH 50/mg protein, and is stable in liquid form for at least 2 years when stored at 2 to 8°C, and has a proteolytic activity of less than 8U/l."*

Claim 11 of auxiliary request 2a has the features of claim 11 of auxiliary request 2 and requires the antibody preparation to be polyclonal.

In addition to the features of claim 11 of the main request, claim 11 of auxiliary request 4 requires the preparation to be suitable for intravenous administration in humans, to be stable in liquid form for at least two years and to have a proteolytic activity of less than 8U/l.

Claim 11 of auxiliary request 5 has the features of claim 11 of auxiliary request 4 and requires the antibody preparation to be obtainable by the processes of claim 8 or claim 9. Claim 11 of auxiliary request 5a further requires the antibody to be polyclonal.

Claim 11 of auxiliary request 7 has the features of claim 11 of auxiliary request 4 and further requires the preparation not to have been treated during its process of production with beta-propiolactone.

Claim 11 of auxiliary request 8 has the features of claim 11 of auxiliary requests 5 and 7. Claim 11 of auxiliary request 8a requires, in addition, the antibody to be polyclonal.

Auxiliary requests 3, 6 and 9 lack a claim corresponding to claim 11 of the requests mentioned

above.

VIII. Claim 10 of auxiliary request 3 relates to an antibody preparation too and reads as follows:

*"An antibody preparation comprising immunoglobulins obtainable by the process of claim 8 or claim 9, wherein at least 15% of the total immunoglobulins are IgM."*

Claim 10 of auxiliary request 6 requires, in addition

*"wherein the antibody preparation has a proteolytic activity of less than 8U/l, and wherein the process provides a more than 3log$_{10}$ removal of non-enveloped virus."*

Claim 10 of auxiliary request 9 has all the features of claim 10 of auxiliary request 6 and further requires

*"wherein the preparation has not been treated during its process of production with β-propiolactone."*

IX. The appellant-opponent's arguments were as follows.

Claim 11 of the main request and of auxiliary requests 4 and 7 lacked the required basis. Claims 23 and 25 as originally filed contained additional features which were not part of claim 11. With respect to the description, the passage on page 12 linked the required properties to the method of preparation of the composition and required the immunoglobulin to be polyclonal, which were not features of claim 11.

Claim 11 of auxiliary request 2 was drafted in the form of a product-by-process with reference to claims 8 or

9. Page 12 of the application as originally filed disclosed an immunoglobulin obtainable by the process in the passages preceding it. Said process was not the same as the one defined by claims 8 or 9. For this reason, claim 11 of the second auxiliary request lacked the required basis too. The same objection applied to auxiliary requests 5, 5a, 8 and 8a.

The claimed invention was not sufficiently disclosed, as the process steps were not reliably reproducible, the term "vibrating agitator" was too broad and lacked a recognisable meaning in the art, and the claimed process lacked essential steps such as BSA treatment or the specific nanofilters required. The product obtained was not inevitably fully functional and anti-complementary activity was subject to test variability. The patent also lacked a reliable definition of the stability level.

Neither the claimed process nor the claimed immunoglobulin preparations were novel over those disclosed in D15 and D18.

Example 3 of document D18 was the closest prior art. It disclosed a process for making an IgM preparation and the product of that process. If the claimed subject-matter were to be novel, it would be by virtue of the use of a vibrating agitator. No effect could be considered achieved by that difference for want of a comparison with the product of D18, and thus the problem to be solved was merely that of providing an alternative. Since vibrating agitators were known from the prior art, the use of such devices would have been an obvious option for a skilled person. The claimed process and product were thus not inventive.

X. The appellant-patent proprietor's arguments were as follows.

Claim 11 of the main request had a basis in claims 23 and 25 and on page 12 of the description. Any issue which might have arisen from the lack of reference to the process for preparing the IgM composition was absent from claim 11 of auxiliary request 2, drafted in the form of a product-by-process. The appellant-patent proprietor conceded that if the board were to conclude that claim 11 of the main request and of auxiliary request 2 lacked a basis, the issue would not be solved by any of auxiliary requests 2a, 4, 5, 5a, 7, 8 or 8a.

The issues raised by the appellant-opponent on sufficiency related at the most to clarity and did not question the sufficiency of the claimed invention's disclosure.

The prior art was silent on the use of a vibrating agitator and the process of claim 1 of the main request and of auxiliary requests 2 to 10 was thus novel.

The burden of proof that the products obtainable by that process did not differ from those of the prior art lay with the appellant-opponent, and no proof had been provided. The product of claim 10 of auxiliary requests 3, 6 and 9 was thus novel too.

Example 3 of document D18 was the closest prior art. It disclosed a process for obtaining an IgM preparation and the product of that process.

The problem underlying the claimed invention was to provide an improved process and IgM compositions.

In view of Table 1 of the patent, the claimed process allowed more virus to be removed by octanoic acid precipitation than the process of D18, which used a blade agitator. The problem of providing an improved process had thus been credibly solved. The claimed solution, characterised by the type of agitator used, would not have been obvious to a skilled person and was thus inventive.

The claimed IgM product, obtainable by the process of claim 8 or claim 9 of auxiliary request 3, contained less virus and proteins and was closer to its natural conformation. The problem of providing an improved IgM preparation was thus credibly solved. The same arguments applied to claim 10 of auxiliary requests 6 and 9. As the product obtainable by means of a vibrating agitator would not have been obvious to a skilled person seeking an improved product, the claimed solution was inventive.

XI. The board informed the parties in a communication dated 26 August 2020 that it was of the preliminary view that the features of claim 11 of the main request did not have the required basis in the application as originally filed, and that the claimed invention was sufficiently disclosed. The claimed process would appear to be novel and inventive. However, the claimed product would not appear to be either novel or inventive.

XII. The parties' final requests were as follows:

The appellant-opponent requested that the decision under appeal be set aside and the patent be revoked.

The appellant-patent proprietor requested that the decision under appeal be set aside and the patent be maintained with the claims of the main request, or with the claims of one of auxiliary requests 2, 2a, 3-5, 5a, 6-8, 8a, 9-12, 12a, the main request and auxiliary requests 3-12 as filed with the statement of grounds of appeal dated 4 April 2019, auxiliary request 2 as filed before the opposition division on 12 January 2018 and auxiliary requests 2a, 5a, 8a and 12a as filed with a letter dated 8 January 2021.

XIII. At the end of the oral proceedings, the decision was announced.

## Reasons for the Decision

1. The appeals are admissible.

2. Admissibility of documents and experimental reports

2.1 The admissibility of a large number of documents and experimental evidence filed after expiry of the nine-month opposition period was challenged. It includes pieces of evidence filed by both parties. None of these documents were admitted into the proceedings by the opposition division.

2.2 The present decision does not need to address the admissibility of any of these documents.

In the context of the claimed process, the appellant-opponent relied on documents D43, D49 and D50. The board's conclusion on this issue is negative to the appellant-opponent even if the content of these documents is taken into consideration (see point 5.5

below, penultimate paragraph).

The board's conclusion on the claims relating to an IgM preparation accepts the appellant-opponent's arguments without resorting to any of the documents filed by the appellant-opponent.

The admissibility of the documents filed by the appellant-patent proprietor was conditional on the admissibility of those filed by the other party (letter dated 23 August 2019, page 2, second full paragraph). Since none of the documents filed by the appellant-opponent is relevant to the conclusions in this decision which are negative to the appellant-proprietor, it is not necessary to admit any of the documents filed by the latter.

3. Sufficiency of disclosure

3.1 The appellant-opponent argued that the claimed invention was not sufficiently disclosed for it to be carried out by a skilled person for a number of reasons.

3.2 Paragraph [0019] of the patent referred to the sum of protease activity, but the test employed did not measure said sum.

The board fails to see how this should be relevant in the context of sufficiency of disclosure. "Proteases" in the sense of the patent are those which can be detected by the test in paragraph [0019] even if other, non-detectable ones might also be present.

3.3 With reference to document D26, the appellant-opponent also argued that quantifying virus removal was not

necessarily reliable.

The issue of reproducibility of virus validation studies (D26) arises during the evaluation of the product's safety prior to authorisation for clinical use and commercialisation. The issue under sufficiency is, however, whether the claimed virus safe IgM can be prepared, not how reliable the method for measuring its virus level is.

3.4 The appellant-opponent also argued that the term "vibrating agitator" was broad and vague and thus led to an insufficient disclosure. In its letter dated 24 July 2020 it further argued that the agitator could have rendered IgM inactive and that the presence of BSA was of fundamental importance in order to reduce non-specific binding.

The appellant-opponent found no difficulty in retrieving information on vibrating agitators (D1).

If BSA was known to be required, the skilled person would find no difficulty in carrying out the invention by adding it. This argument is thus not convincing either.

3.5 Lastly, the appellant-opponent doubted whether the passage in paragraph [0093] of the patent requiring the binding region of the IgM molecules in the final preparation to be "functionally full active" was credibly corroborated by experimental evidence. However, none of the claims require the IgM in the claimed preparations to be "functionally full active". This argument is thus not convincing either.

3.6 With reference to document D28, the appellant-opponent argued that the anticomplementary activity tests were cumbersome and subject to variability. This should lead to lack of disclosure of the invention.

Whether or not known tests give different values could be the source of a lack of clarity. However, the board sees no reason why the alleged variability of the results could prevent a skilled person from carrying out the claimed invention.

3.7 The appellant-opponent argued that the feature "stable in liquid form for at least 6 months [2 years in some of the requests] when stored at 2 to 8°C" also caused a lack of disclosure, since the patent in suit contained contradictory definitions of the term "stable" [0022] [0057]. It further argued that the second of the definitions required no fragmentation or polymerisation of IgM, which was a pentamer and thus already polymerised. In addition, it could not be determined whether a fragment of IgM was a monomer or a fragment of a monomer.

The board considers that this argument could at most relate to the clarity of the feature "stable", but does not render the disclosure of the patent in suit insufficient. The issue could only have arisen if the required stability could not have been achieved, which is not argued.

3.8 Lastly, the appellant-opponent argued that claim 6 required nanofiltration, but according to the patent only nanofilters of some specific size were suitable.

This in fact shows that the patent contains sufficient information on the type of suitable nanofilters, not

the opposite.

3.9 After receiving the board's communication in preparation for oral proceedings, in which the board expressed its preliminary view that the claimed invention was sufficiently disclosed, the appellant-opponent did not submit further arguments either in writing or at the oral proceedings before the board. The board sees no reason to depart from its preliminary view.

3.10 The claimed invention is thus sufficiently disclosed for it to be carried out by a skilled person.

*Claim 1 of the main request and auxiliary requests 2 to 10, 2a, 5a and 8a: A process for the preparation of an IgM composition*

4. Novelty

4.1 Claim 1 of the main request, auxiliary requests 2 to 10, 2a, 5a and 8a is identical and relates to a process for the preparation of an IgM containing immunoglobulin composition from a plasma fraction.

Claim 1 requires contacting said plasma fraction with octanoic acid (caprylic acid) and treating the mixed solution with a vibrating agitator to precipitate contaminating proteins.

4.2 The appellant-opponent argued that the term "vibrating agitator" was vague and not restricted to a mixer. For that reason, the processes disclosed in documents D6, D15 and D18, which included a separation step by means of a centrifuge, disclosed a process requiring a vibrating agitator.

4.3 Vibrating mixers are known from the prior art (D1). The board cannot see a difference between a vibrating agitator and a vibrating mixer in the context of biotechnological equipment. The feature "vibrating agitator" thus has a meaning for a skilled reader which does not include devices in which some vibration of some kind could be envisaged, for example at the end of a centrifugation, as argued at the oral proceedings before the board.

A skilled person would not consider a vibrating agitator to be embodied by a centrifuge, whose object is not to stir, agitate or mix, let alone by vibration. The process of claim 1 is thus novel.

5. Inventive step

5.1 Closest prior art

The parties agreed with the opposition division's conclusion that D18 was the closest prior art. The board sees no reason to differ.

D18 discloses preparing IgM by treating plasma with octanoic acid (examples 1 and 3) to form a precipitate which is subsequently centrifuged.

D18 does not indicate the means for stirring the mixture of octanoic acid and plasma. The board agrees with the appellant-proprietor that a skilled reader would have considered the examples of D18 to require a blade agitator in view of the amount of product involved (1 kg of Cohn's paste, 5 l buffer), the immiscibility of (aqueous) Cohn's paste and (organic) octanoic acid and the formation of a precipitate in the process.

5.2 Technical problem underlying the invention

The parties had different views on the formulation of the technical problem effectively solved by the claimed invention.

The appellant-patent proprietor relied on a number of effects underlying the technical problem. Since the board considered the technical problem of providing a process which made it possible to remove more non-enveloped virus from a plasma fraction during octanoic acid precipitation to be credibly solved in a non-obvious manner (see below), it is not necessary to examine whether any other of the alleged advantages is credibly shown too.

5.3 Solution

The solution to this technical problem is the claimed process, characterised in that the precipitation of contaminant proteins of the plasma fraction with octanoic acid is carried out with a vibrating agitator.

5.4 Success

Example 3 of the patent measures the removal of non-enveloped viruses spiked into a suspended fraction I/III. It compares the result of mixing by means of a vibromixer (claim 1) and by standard stirring (D18). The results, summarised in Table 1 of the patent, show that octanoic acid precipitation in a vibromixer removes one order of magnitude more non-enveloped virus than standard stirring.

The problem as defined in point 5.2 above has thus been

credibly solved by the claimed process.

5.5 It remains to be decided whether the proposed solution to the objective problem defined above would have been obvious to a skilled person in view of the prior art.

It was undisputed that the mixers required by claim 1 are known from the prior art (D1). The appellant-opponent argued that documents D20 to D24 taught the claimed solution.

D20 relates to DNA separation and teaches cell lysis with a laser device which may also include a vibrator [0032]; it is however silent on non-enveloped virus. D21 (see D21a) relates to blood regeneration and refers to viruses, but not to non-enveloped ones. D22 and D23 relate to inactivating micro-organisms by ultraviolet radiation. D24 discloses vibrating agitation in the context of biological aqueous solutions, but not virus removal. Thus none of these documents links virus removal to the kind of stirrer.

The appellant-opponent mentioned in this context documents D43, D49 and D50 at the oral proceedings. The first is a dictionary defining the meaning of "vibrate" and "agitate". D49 relates to removal of equine encephalitis virus by mechanical agitation. It relates neither to the specific type of agitation required by claim 1 nor to non-enveloped viruses. Similarly, D50 discloses the effect of agitation on T7-bacteriophage, which is an enveloped virus too. Thus, regardless of their admissibility, none of these documents teaches the claimed solution.

The state of the art thus does not teach that the use of the specific mixing device required by claim 1 could

lead to less non-enveloped virus during octanoic acid precipitation of plasma.

The claimed solution would not have been obvious to a skilled person and is thus inventive (Article 56 EPC).

5.6 Auxiliary request 10

Auxiliary request 10 has only claim 1 as an independent claim. In view of the board's conclusion on this subject-matter, auxiliary request 10 is allowable.

5.7 The higher-ranked requests are not allowable for the reasons that follow.

*Claims relating to an antibody preparation*

6. Claim 11 of the main request. Amendments

6.1 The board concurs with the reasoning and conclusion of the opposition division that claim 11 of the main request does not have a basis in the application as originally filed.

6.2 Claim 11 relates to an antibody preparation which contains a defined amount of IgM, is virus safe, has an anticomplementary activity below a set threshold and is stable in liquid form under defined conditions.

6.3 The appellant-patent proprietor argued that claim 23 as originally filed, which related to an antibody preparation without reference to its synthesis, provided the required basis. However, claim 23 requires a defined proteolytic activity which is not a feature of claim 11. It also requires a different IgM proportion. Claim 24 requires stability for a period

longer than that required by claim 11. Claim 25 limits the proportion of IgM to at least 15%.

Thus neither claim 23 nor its combination with dependent claims 24 or 25 provides the required basis for the features of claim 11.

6.4 The appellant-patent proprietor also relied on the paragraph bridging pages 12 and 13 of the application. This passage discloses a preparation containing at least 15% of IgM referred to the total amount of immunoglobulins (page 13, line 4). However, the same passage discloses the product as being obtainable by the process "described above" and further discloses the product as being polyclonal (page 12, third and fourth lines from the bottom). By the appellant-patent proprietor's own argument, the preparation process imparts structural features to the claimed product; these features are not required by claim 11.

6.5 Claim 11 of the main request thus contravenes the requirements of Article 123(2) EPC. For this reason alone the main request is not allowable.

7. Claim 11 of auxiliary request 2. Amendments

7.1 This claim is drafted as a product-by-process. The appellant-patent proprietor argued that claim 22 of the application as originally filed, which referred back to claims 17 to 21, provided the required basis for claim 11 of auxiliary request 2. Claim 25 disclosed the feature requiring the preparation to comprise at least 15% IgM.

7.2 However, the proportion of IgM required by claim 11 refers to the total amount of immunoglobulins, whereas

no such reference is disclosed in claim 25 as originally filed. In addition, the features requiring the composition to be virus safe or to have an anticomplementary activity below a defined threshold do not arise from the combination of these claims.

In the description, the passage bridging pages 12 and 13 discloses the proportion of IgM to be 15% with respect to the total immunoglobulin amount. However, it also discloses the product to be obtainable by the process "described above".

Claim 11 requires the claimed product to be obtainable by a number of step combinations arising from claim 8 or claim 9. All the combinations require steps (a) to (c) of claim 1, the incubating step at a defined pH of claim 4 and the treatment with UVC irradiation of claim 7. This specific combination of steps is however not disclosed in the paragraphs "described above" preceding the cited passage on page 12. Neither are most of the other combinations of features arising from the back references of claim 8 and claim 9.

7.3 For these reasons, the application as originally filed does not disclose a product having the properties required by claim 11 and being obtainable by a process with the features of claims 8 or 9.

8. Auxiliary requests 2a, 4, 5, 5a, 7, 8, 8a: Amendments

It was undisputed that the conclusion on added subject-matter in the preceding points applied analogously to claim 11 of auxiliary requests 2a, 4, 5, 5a, 7, 8 and 8a. None of these requests is thus allowable.

9. Auxiliary request 3 - inventive step

9.1 Claim 10 of auxiliary request 3 relates to an antibody preparation obtainable by the process of claim 8 or claim 9 having a proportion of IgM of at least 15% with respect to the total immunoglobulins.

9.2 The appellant-opponent argued at the oral proceedings that the claimed preparation was neither novel nor inventive.

9.3 The board arrived at the conclusion that the claimed IgM preparation, even if novel, is not inventive for the reasons below.

9.4 Closest prior art

The parties agreed with the opposition division's conclusion that example 3 of D18 was the closest prior art. The board sees no reason to differ.

D18 discloses the obtention of IgM from plasma to yield compositions having at least 15% IgM such as that of example 3. This was not disputed.

9.5 Technical problem underlying the invention

The appellant-patent proprietor formulated the problem underlying the claimed invention as being to provide an improved IgM product better for human administration.

The improvement resided in having less proteolytic activity and virus load, and in being more stable and closer to its native structure.

9.6 Solution

The claimed solution is the product of claim 10 obtainable by the process of claim 8 or claim 9, which is characterised by the structural features imparted to it by the process of claim 8 or claim 9.

9.7 Success

9.7.1 The appellant-patent proprietor argued that the burden of proof on this point resided with the appellant-opponent.

It was arguably for the appellant-opponent to show that the product of example 3 of D18 was not distinguishable from that of claim 10 in the context of novelty.

However, on the issue of inventive step the appellant-patent proprietor has the burden of proving the advantages on which it relies.

9.7.2 The appellant-patent proprietor relied on various properties of the product obtained by the method of claim 8 or claim 9 to show that the technical problem was credibly solved.

9.7.3 Amount of non-enveloped virus

Example 3 of the patent compares non-enveloped virus removal during octanoic acid precipitation using a vibrating agitator and using a blade stirrer. The former is superior (Table 3).

The process leading to the product of example 3 of D18 however requires a number of additional steps: once the product was precipitated it was centrifuged, and the

supernatant dialysed against tromomethamine at a specific pH. The solution was retained on an Accell column, washed, eluted, treated with beta-propiolactone and PEG 400. The supernatant was buffered in a Sephadex column, ultrafiltered and filtered sterile. Every one of these steps arguably modifies or improves the product, including removing undesired components such as non-enveloped virus.

The available evidence does not compare this final product with that obtainable by the process of claim 8 or claim 9. An effect in this respect is thus not considered credibly achieved.

9.7.4 Proteolytic activity

D18 does not disclose the proteolytic activity of the products obtained. It is known from the prior art that proteolytic activity should be low (D6, column 1, lines 31 to 45).

For want of a direct comparison which might show the claimed product to have less proteolytic activity than that of D18, this effect cannot be considered credibly achieved.

9.7.5 Stability

According to column 6, lines 38-40, the product of D18 is stable: it behaves like the commercially available Pentaglobin with respect to shelf life. No direct comparison of product stability is provided between the claimed product and that of D18, and no improvement over the shelf stable product of D18 can thus be acknowledged either.

9.7.6 Resemblance to native structure

The appellant-patent proprietor argued that the lack of treatment with beta-propiolactone led to an IgM product closer to its natural conformation.

However, claim 10 does not exclude such treatment. Any advantage which could be associated with avoiding this step is thus not achieved over the whole scope of the claimed subject-matter. On the issue of beta-propiolactone treatment see also points 11.5 and 11.6 below.

9.8 Reformulation of the technical problem

In view of the above, the problem as formulated by the appellant-patent proprietor cannot be considered solved in all aspects and needs reformulation.

The problem underlying the claimed invention is considered to be to provide an alternative IgM product. The IgM preparation of claim 10 obtainable by the process of claim 8 or claim 9 credibly solves that problem, as the examination of inventive step presupposes the claimed product to be different from that of the prior art.

9.9 It thus remains to be decided whether the proposed solution to the objective problem defined above would have been obvious to a skilled person in view of the prior art.

9.9.1 In point 5. above the board arrived at the conclusion that the claimed process for preparing IgM was inventive. A product is however not automatically novel or inventive by virtue of being obtainable by a novel

and inventive process: it needs to be novel and inventive on its own merit.

In the present case, the advantages of the specific octanoic acid treatment of claim 1 are not inevitably present in every product obtainable by a process including that step. The problem solved by the claimed IgM preparation is thus merely that of providing an alternative, in contrast to the conclusion in the context of the claimed process.

9.9.2 A skilled person would have considered any IgM product with different structural characteristics as a suitable alternative, such as a product having the structural characteristics imparted to it by the method of claim 8 or claim 9. The claimed solution would thus have been obvious to a skilled person and is not inventive (Article 56 EPC).

9.10 As the product of claim 10 is not inventive, auxiliary request 3 is not allowable.

10. Auxiliary request 6, inventive step

10.1 Claim 10 of auxiliary request 6 relates to an IgM preparation obtainable by the process of claim 8 or claim 9, in which at least 15% with respect to the total immunoglobulins is IgM, having a proteolytic activity of less than 8U/l and wherein the process provides a more than $3\log_{10}$ removal of non-enveloped viruses.

10.2 Closest prior art

It was undisputed that example 3 of D18 was the closest prior art. The product of example 3 contains 73% IgM

(column 4, line 32) and its preparation induces a $7\log_{10}$ removal of non-enveloped virus Φ X 174 (Table 4). Its proteolytic activity is not disclosed.

10.3 Technical problem underlying the invention

As with respect to the third auxiliary request, the appellant-patent proprietor formulated the problem underlying the claimed invention as being to provide an improved IgM product.

The improvement resided in having less proteolytic activity and virus load, being more stable and having IgM closer to its native structure.

10.4 Solution

The claimed solution is the product of claim 10, which is characterised by the structural features imparted to it by the process of claims 8 or 9, and by having a proteolytic activity below a set value.

10.5 Success

10.5.1 For the reasons given in the context of claim 10 of auxiliary request 3, in view of the available evidence the alleged effects of providing an IgM preparation having less virus, being more stable or being closer to its natural configuration have not been credibly achieved.

10.5.2 Example 3 of D18 does not disclose the product's proteolytic activity in terms of the definition required by claim 10 (see paragraph [0055] of the patent) and the question also arises whether an effect in that regard has in fact been achieved.

In favour of the appellant-patent proprietor, the following examination assumes that the IgM preparation of claim 10 has less proteolytic activity than the IgM composition of example 3 of D18.

The problem of providing an improved IgM preparation is thus considered credibly solved by a preparation having a proteolytic activity below the threshold set by claim 10.

10.6 It thus remains to be decided whether the proposed solution to the objective problem defined above would have been obvious to a skilled person in view of the prior art.

10.6.1 It is known from the prior art that the proteolytic activity of an immunoglobulin preparation should be as low as possible (D6, column 1, lines 32-33). This has not been contested by the appellant-patent proprietor.

10.6.2 There is no effect linked to the threshold set by claim 1, over and above what is known in the prior art, namely that the lower, the better. The prior art teaches using Sephadex columns to reduce it (D6, column 1, lines 44 and 45). A low proteolytic activity would thus have been an obvious option for a skilled person seeking an improved IgM preparation. The claimed solution is thus not inventive (Article 56 EPC) and auxiliary request 6 not allowable.

10.6.3 The appellant-patent proprietor argued that the situation in the present case was comparable to that underlying decision T 595/90. There was no process in the prior art which could lead to a product having the required proteolytic activity. Even if said property

were to be envisaged as an obvious aim, there was no process at the disposal of the skilled person which could provide said product, which was inventive for this reason alone.

The board in T 595/90 concluded that a product which could be considered as an obvious improvement was nevertheless inventive if there was no method at the disposal of a skilled person which might have led to its obtention.

It is disputable whether other processes known from the prior art could lead to the preparation of a product having a proteolytic activity below the threshold set by claim 1. In favour of the appellant-patent proprietor, the board will nevertheless assume it not to be the case.

Whether a novel and inventive process inevitably leads to obtaining a novel and inventive product depends on the facts of the case. The simplest example is that of an inventive process for preparing a known product: the product of the process is not patentable since it lacks novelty. Therefore, whereas a patentable product confers patentability on its process of preparation, the patentability of a process does not necessarily confer patentability on the product obtained by this process.

The standard for examination of inventive step by the Boards of Appeal is the problem-solution approach. At no point it includes the question of whether a product could or could not be obtained by a process known from the prior art for it to be inventive.

A product which can be envisaged as an obvious

improvement by a skilled person is not necessarily inventive for the reason alone that it cannot be prepared by the methods available at the filing date. The conclusion on this point would necessarily depend on the facts of the case and the claim's wording.

In the present case, a low proteolytic activity is known to be advantageous. An IgM having such property is thus an obvious solution to the problem of providing an improvement. Even if at the filing date no process could have led to that product (i.e. the product is novel), the invention resides in developing such process (claim 1), not in the product, at least not in the terms of the distinguishing features chosen by the appellant-patent proprietor.

This argument is thus not convincing.

11. Auxiliary request 9 - inventive step

11.1 Claim 10 of auxiliary request 9 relates to an IgM preparation having the features of claim 10 of auxiliary request 6. It requires it, in addition, to be obtainable by a method not including treating with beta-propiolactone.

11.2 Closest prior art

It was not disputed that example 3 of D18 is the closest prior art. It lacks the structural characteristics imparted to the product by the process of claim 8 or claim 9 and the required proteolytic activity. In addition, the IgM preparation of example 3 of D18 has been obtained with the aid of beta-propiolactone.

11.3 Problem underlying the claimed invention

The appellant-patent proprietor formulated the problem underlying the claimed invention as being to provide an improved IgM product.

It relied in this respect on the product having less proteolytic activity and virus load, and being more stable and closer to its native structure.

11.4 Solution

The claimed solution is the product of claim 10, which is characterised by the structural features imparted to it by the process of claim 8 or claim 9 and by having been prepared in the absence of beta-propiolactone. The product is also characterised by having a defined proteolytic activity.

11.5 Success

11.5.1 For the reasons provided in the context of the third and sixth auxiliary requests, neither the stability nor the virus load is considered to have been credibly improved with respect to the product of D18.

11.5.2 For the reasons given with respect to the sixth auxiliary request, the claimed IgM product is considered to have a reduced proteolytic activity.

11.5.3 Beta-propiolactone is a reactive molecule. The use of that molecule in the process is likely to modify IgM by reacting with residues on the immunoglobulin surface. The claimed IgM preparation is thus more similar to native IgM than an IgM product treated with beta-

propiolactone such as that of D18.

11.5.4 The problem of providing improved IgM preparations is thus considered solved by the features of claim 10 in view of the non-modified nature of the IgM and its enhanced proteolytic activity.

11.6 It remains to be decided whether the proposed solution to the objective problem defined above would have been obvious to a skilled person in view of the prior art.

11.6.1 The method of preparation as in claims 8 and 9 does not impart structural features to the IgM leading to an improved product for the reasons provided in the context of the third auxiliary request.

11.6.2 For the reasons provided in the context of the sixth auxiliary request, a skilled person would have regarded an IgM preparation with a proteolytic activity below the threshold set by claim 10 as an obvious improvement.

11.6.3 Treatment with beta-propiolactone is known to modify the outer surface of proteins in general and of immunoglobulins in particular by the appellant-patent proprietor's own argument. A skilled person would thus have envisaged a product not treated with beta-propiolactone as an obvious improvement. A different issue is how to arrive at such a product, in other words how to put forward a process for producing an IgM composition which does not require a beta-propiolactone treatment. This is however a matter to be considered under examination of inventive step of the process (see claim 1), not of the product obtained by that process.

11.7 The claimed solution would thus have been obvious to a skilled person seeking an improvement and is thus not inventive (Article 56 EPC), with the consequence that auxiliary request 9 is not allowable.

11.8 Auxiliary request 10 contains only claims directed to a process having claim 1 as the sole independent claim. This auxiliary request is thus allowable for the reasons in points 3. to 5. above.

12. The board decided to exercise its discretion and remit the case to the opposition division for the description to be adapted (Article 111(1) EPC), if required.

**Order**

**For these reasons it is decided that:**

The decision under appeal is set aside.

The case is remitted to the opposition division with the order to maintain the patent on the basis of claims 1-9 of auxiliary request 10, filed with the statement of grounds of appeal dated 4 April 2019, and a description to be adapted.

The Registrar: The Chair:

C. Rodríguez Rodríguez P. Gryczka

Decision electronically authenticated