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# Datasheet for the decision of 11 September 2019

**Case Number:** T 0308/17 - 3.3.04

**Application Number:** 05811874.6

**Publication Number:** 1805320

**IPC:** C07K16/00, C07K1/113, C07K16/28

**Language of the proceedings:** EN

**Title of invention:**
Methods for refolding of recombinant antibodies

**Patent Proprietor:**
Amgen Inc.

**Opponents:**
Hollatz, Christian
Cabinet Lavoix

**Headword:**
Methods for refolding of recombinant antibodies/AMGEN

**Relevant legal provisions:**
EPC Art. 54
RPBA Art. 12(2), 12(4), 13
EPC R. 106

**Keyword:**
Novelty - main request (no) - auxiliary requests I to IX, XI and XII (no)
Admissibility of requests - auxiliary requests X, XIa, XIIa and XIII to XIX (no)
Right to be heard - opportunity to comment (yes)

**Decisions cited:**
G 0002/88, G 0006/88

**Catchword:**

Europäisches Patentamt
European Patent Office
Office européen des brevets

**Beschwerdekammern**

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**Case Number: T 0308/17 - 3.3.04**

# D E C I S I O N
## of Technical Board of Appeal 3.3.04
## of 11 September 2019

| | |
|---|---|
| **Appellant:** (Opponent 1) | Hollatz, Christian<br>Ter Meer Steinmeister & Partner mbB<br>Nvmphenburger Straße 4<br>80335 Munich (DE) |
| **Representative:** | Ter Meer Steinmeister & Partner<br>Patentanwälte mbB<br>Nymphenburger Straße 4<br>80335 München (DE) |
| **Appellant:** (Opponent 2) | Cabinet Lavoix<br>2, place d'Estienne d'Orves<br>75009 Paris (FR) |
| **Representative:** | Lavoix<br>2, place d'Estienne d'Orves<br>75441 Paris Cedex 09 (FR) |
| **Respondent:** (Patent Proprietor) | Amgen Inc.<br>One Amgen Center Drive<br>Thousand Oaks, CA 91320-1799 (US) |
| **Representative:** | Grund, Martin<br>Grund Intellectual Property Group<br>Patentanwalt und Solicitor PartG mbB<br>Postfach 44 05 16<br>80754 München (DE) |
| **Decision under appeal:** | **Interlocutory decision of the Opposition Division of the European Patent Office posted on 12 December 2016 concerning maintenance of the European Patent No. 1805320 in amended form.** |

**Composition of the Board:**

| | |
|---|---|
| **Chairwoman** | R. Morawetz |
| **Members:** | A. Chakravarty |
| | P. de Heij |

## Summary of Facts and Submissions

I. In an interlocutory decision, the opposition division decided that European patent No. 1 805 320, entitled "*Methods for refolding of recombinant antibodies*", met the requirements of the EPC in amended form on the basis of the main request (Article 101(3)(a) EPC).

II. The patent was opposed by opponent 1 and opponent 2, under Article 100(a) EPC on the grounds of lack of novelty (Article 54 EPC) and lack of inventive step (Article 56 EPC) and under Article 100(b) and 100(c) EPC.

III. Appeals were filed against the opposition division's decision by opponent 1 (appellant I) and opponent 2 (appellant II). The patent proprietor is respondent to the appeals.

IV. In their statement of grounds of appeal, appellant I submitted arguments to the effect that the subject-matter of claim 1 of the main request did not meet the requirements of Articles 54, 56, 83 and 123(2) EPC.

V. In their statement of grounds of appeal, appellant II submitted arguments to the effect that the subject-matter of claims 1 and 20 to 22 of the main request did not meet the requirements of Article 123(2) EPC, that the invention of claims 1 to 22 did not meet the requirements of Article 83 EPC, that the subject-matter of claims 1 to 3, 6 to 8, 12, 13, 17 to 22 did not meet the requirements of Article 54 EPC and that the subject-matter of claims 1 to 16 and 18 to 22 did not meet the requirements of Article 56 EPC.

VI. With the reply to the appellants' statements of grounds of appeal, the respondent submitted a main request and auxiliary requests I to XVIII. The main request corresponded to the request considered allowable by the opposition division. Auxiliary requests I to XVIII were filed for the first time in the appeal proceedings.

VII. The board appointed oral proceedings as requested by the parties and subsequently issued a communication pursuant to Article 15(1) RPBA setting out its preliminary appreciation of substantive and legal matters concerning the appeal. In this communication, the parties were informed, *inter alia*, that the board was of the preliminary view "*that the method disclosed in document D1 anticipates the subject-matter of claim 1* [of the main request and that] *this objection would appear to hold for the subject-matter of claim 1 of auxiliary requests I to IX*".

VIII. In response to the board's communication the respondent filed a written submission and additional auxiliary requests XIa, XIb, XIIa and XIIb.

IX. Claims 1, 6, 7, 12 and 13 of the main request read:

"1. A method of producing an IgG2 antibody or an IgG2 antibody fragment preparation enriched for one of several separate IgG2 forms comprising:

contacting an IgG2 antibody or an IgG2 antibody fragment that has been recombinantly produced by mammalian cells with a reduction/oxidation coupling reagent at a pH of 5 to 11;

wherein said IgG2 antibody or IgG2 antibody fragment elutes as several separate forms on RP-HPLC and said

method decreases the number of forms eluting on RP-HPLC, or alters the relative distribution of said several separate forms on said RP-HPLC; further comprising contacting said IgG2 antibody with a chaotropic agent before, after or concurrently with said contacting with said reduction/oxidation coupling reagent.

6. The method of Claim 1, wherein the reduction/ oxidation coupling reagent comprises cysteine/cystine.

7. The method of Claim 6, wherein the cysteine/cystine comprises from 0.1 mM to 10 mM cysteine.

12. The method of Claim 1, wherein said contacting produces a IgG2 antibody having at least a two-fold increase in its biological activity compared to the same IgG2 antibody that is not contacted.

13. The method of Claim 1, wherein the chaotropic agent is selected from the group consisting of: urea, arginine, SDS and guanidine hydrochloride."

X. Claim 1 of auxiliary requests I to VI is identical to claim 1 of the main request. Claim 1 of auxiliary requests VII to IX differs from claim 1 of the main request in that references to "an IgG to antibody fragment" are deleted and the phrase "at least" is inserted before the phrase "one of several separate IgG2 forms".

XI. Claim 1 of auxiliary request X has been amended to delete "or an IgG2 antibody fragment" throughout and to insert the words "at least" in front of the word "one" in the second line. Furthermore, the half sentence "wherein said recombinant IgG2 antibody is purified, or

wherein said recombinant IgG2 antibody is partially purified prior to said contacting" has been added after the pH range. Finally, the half sentence "and further comprising isolating a fraction of the contacted IgG2 antibody having a desired refolded confirmation" has been added to the end of the claim.

XII. Claim 1 of auxiliary requests XI and XII is the same and reads:

"1. Use of a chaotropic agent in a method for producing an IgG2 antibody preparation enriched for at least one of several separate IgG2 forms comprising:
contacting an IgG2 antibody that has been recombinantly produced by mammalian cells with a reduction/oxidation coupling reagent at a pH of 5 to 11;
wherein said IgG2 antibody elutes as several separate forms on RP-HPLC and said method decreases the number of forms eluting on RP-HPLC, or alters the relative distribution of said several separate forms on said RP-HPLC; further comprising contacting said IgG2 antibody with said chaotropic agent before, after or concurrently with said contacting with said reduction/ oxidation coupling reagent".

XIII. Claim 1 of auxiliary requests XIa and XIIa is the same and reads:

"Use of a chaotropic agent for enriching at least one of several separate IgG2 forms in an IgG2 antibody preparation, comprising:
contacting an IgG2 antibody that has been recombinantly produced by mammalian cells with a reduction/oxidation coupling reagent at a pH of 5 to 11;
further comprising contacting said IgG2 antibody with said chaotropic agent before, after or concurrently

with said contacting with said reduction/oxidation coupling reagent;
wherein said IgG2 antibody elutes as several separate forms on RP-HPLC and said contacting decreases the number of forms eluting on RP-HPLC, or alters the relative distribution of said several separate forms on said RP-HPLC".

Claim 1 of auxiliary requests XIII and XIV is the same as claim 1 of auxiliary request VII except that it further incorporates the subject-matter of claim 12 of the main request.

Claim 1 of auxiliary requests XV and XVI is the same as claim 1 of auxiliary request VII except that it incorporates the additional feature "at a concentration of 0.1 M to 2 M" after the phrase "chaotropic agent".

Claim 1 of auxiliary requests XVII and XVIII is the same as claim 1 of auxiliary request VII except that it has the additional feature "wherein said chaotropic agent comprises 0.5M to 1.5M guanidine hydrochloride" added to the end of the claim.

XIV. The following document is referred to in this decision.

D1: WO 03/002713

XV. Oral proceedings before the board were held on 11 September 2019. During the course of the proceedings, the respondent submitted a written objection according to Rule 106 EPC.

XVI. The wording of this objection was as follows:

"*We are of the view that a fundamental violation of Art 113 EPC has occurred, in the meaning of Article 112a(2)(c) EPC due to the fact* [sic] *the Board of Appeal has not admitted auxiliary requests X, XIII to XVIII into the proceedings*".

XVII. During the course of the oral proceedings, the respondent withdrew auxiliary requests XIb and XIIb and submitted auxiliary request XIX.

Claim 1 of auxiliary request XIX is the same as claim 1 of auxiliary request XI except that it includes the additional feature "wherein said contacting produces a [sic] IgG2 antibody having at least a two-fold increase in its biological activity compared to the same IgG2 antibody that is not contacted".

XVIII. At the end of the proceedings the Chair announced the decision of the board.

XIX. The arguments of appellant II regarding admissibility of auxiliary requests I to XVIII are summarised as follows:

*Admissibility of auxiliary requests I to XVIII - Article 12(2), 12(4) and Article 13(1) RPBA*

Auxiliary requests I to XVIII were filed for the first time in the appeal proceedings. They should not be admitted into the proceedings due to a lack of substantiation. The respondent had not explained why the auxiliary requests overcame the objections raised in the statement of grounds of appeal if the main request was held unallowable. In decision T 1732/10, the competent board held that "*unsubstantiated requests normally become effective only at the date on which*

*they are substantiated. Their filing in and of itself plays therefore no role [...] if, as in the present case, the requests are not self-explanatory*" (see reasons 1.5)

Appeal proceedings were wholly separate and independent from the proceedings at first instance, their function being to give a judicial decision upon the correctness of the earlier decision taken by the opposition division. This was reflected in Article 12 RPBA.

Article 13 RPBA concerned amendments to a party's case after it had filed its grounds of appeal. Together, Articles 12 and 13 RPBA aimed at concentrating the parties' submissions at an early stage of the proceedings, to ensure that a case is as complete as possible when it is processed (Case Law of the Boards of Appeal, 8th edition 2016, IV.E.4.1.2).

The boards had frequently held that a statement of grounds, referring generally to submissions made at first instance cannot be considered sufficient for the purposes of Article 108, 3rd sentence, EPC. By analogy and for reasons of equity, reference to submissions made at first instance in the reply to the statement of grounds of appeal should generally not be considered as a proper substantiation of the respondent's requests.

Appellant II argued at the oral proceedings that it was not clear which objection(s) the changes made in claim 1 of auxiliary request X were supposed to overcome and that the respondent could not in appeal proceedings rely on an alleged substantiation given in the first instance proceedings.

XX. The appellants' arguments are further summarised as follows:

*Admissibility of auxiliary requests XIa and XIIa - Article 13(1) RPBA*

These requests were filed in response to the board's communication pursuant to Article 15(1) RPBA. They represented an amendment to the respondent's case and should be treated according to Article 13(1) RPBA. There was no persuasive reason for the late filing of these requests, since the objections made against the claims of auxiliary requests XI and XII had been present in the statements of grounds of appeal. Furthermore the claims of these requests give rise to new objections, for instance according to Article 123(2) EPC and thus their admission would not be procedurally economic.

*Admissibility of auxiliary request XIX - Article 13(1) RPBA*

This request was filed at the last possible moment during the appeal proceedings, i.e. during the oral proceedings before the board. It was therefore late filed and not to be admitted for that reason alone. Moreover, the subject-matter of the dependent claim 12 of the main request on which it was based had been objected to for lack of novelty (see statement of grounds of appeal of appellant II, page 16, third and fourth paragraphs). Thus, its subject-matter was not *prima facie* allowable, since it was not immediately apparent how it overcame the objection raised against auxiliary request XI.

*Main request*
*Novelty - Article 54 EPC*

The method of claim 1 was anticipated by document D1 which disclosed that:

i) an IgG2 antibody (αOPGL-IgG2) was produced by mammalian cells (Cell Line 125Q) and
ii) the IgG2 is secreted in the culture medium and thereby is contacted with a redox coupling reagent (cysteine/cystine) at pH 7 and simultaneously with a chaotropic agent (arginine). The cysteine and cystine concentration was about 0.20 mM each, with a cysteine:cystine ratio of about 1:1. This could be taken from Example 3 of document D1, where the composition of the culture medium used (VM-SoyBatch medium) was disclosed in Table 3.

Example 3 of document D1 disclosed the production of αOPGL-1 antibody in Cell Line 125Q, a clone derived from CHO cells that express the antibody from two plasmids, one encoding αOPGL-1-k (light chain) and the other encoding αOPGL-1-IgG2 (heavy chain) (page 89, paragraph[0218], first sentence). Accordingly, the αOPGL-1 antibody was an IgG2 antibody recombinantly produced in mammalian cells. Said antibody thus necessarily eluted as several separate forms on RP-HPLC. It was noted that the disclosure of the disputed patent itself in paragraphs [0073] to [0075] confirmed that heterogeneity was a general property of IgG2 antibody populations.

Furthermore, document D1 in Example 3 disclosed that "*The antibody is further purified by cation exchange chromatography using SP Sepharose HP (Amersham Pharmacia) or equivalent. The cation exchange*

*chromatography step removes additional CHO cell proteins, DNA, lower molecular weight proteins, and aggregated forms of αOPGL-1*" (see paragraph [0229]). The removal of aggregated forms meant that the methods as a whole fell within the ambit of the claim.

The opposition division considered that there was no reason not to apply the principles of decision G 2/88 to the case at hand and that the method of claim 1 defined "an enrichment purpose based on a new technical effect obtained by process steps which have not been disclosed in the prior art".

The opposition division however miscategorised the subject-matter of claim 1 as a method achieving an effect, covered by decision G 2/88, whereas it was in fact a method of production of IgG2, as was readily apparent from the wording of the claim.

The case law of the boards of appeal in relation to methods of production (see e.g. T 304/08) consistently held that, for claims directed to a process for producing a product, the purpose (aside from the production) should not be regarded as a functional technical feature in the sense of decisions G 2/88 and G 6/88 but was limiting only to the extent that the method has to be suitable for that use.

The opposition division considered that document D1 did not disclose either the heterogeneity of IgG2 to be purified or that an alteration of the distribution of its forms was brought about by the steps of the treatment disclosed. However, both of these features were made available to the public by document D1.

The opposition division was also wrong to consider that the prior art must "show that the relative distribution of forms is altered by redox/chaotrope treatment" in order to anticipate the claimed subject-matter. The claim language did not support this conclusion because it did not require that the relative distribution of IgG2 forms was a direct result of the redox/chaotrope treatment, as this was merely one of several features of the method of claim 1.

Heterogeneity of IgG2, either recombinantly produced or isolated from serum, such as human serum, was a general property of IgG2s, while the alteration of the distribution of forms resulting from carrying out the method steps was the inevitable result of the contacting of the antibodies with a redox coupling reagent, cysteine/cystine, at pH 7. The concentration of this coupling reagent used in document D1 was about 0.20 mM each of cysteine and cystine with a ratio of about 1 to 1. This corresponded with a range suggested in the patent of about 0.1 mM to about 10 mM, see paragraph [0148] of the patent. In document D1, the secreted IgG2 was at the same time contacted with the chaotropic agent, arginine. The concentration of arginine used was not relevant to achieving an alteration of the distribution of the forms of the IgG2, either in the prior art or in the claimed method of the patent. This was because it was the redox reagent that led to the effect of altering the distribution of forms of IgG2.

In relation to the respondent's arguments that the concentration of cysteine used in document D1 was too low to achieve the effect of reducing the number of diluting forms of IgG2 antibody on RP-HPLC, it was noted that the concentration of 3 to 10 mg/mL present

in the culture broth disclosed in document D1 fell exactly within the range of concentration mentioned in claim 7 of the main request.

XXI. The arguments of the respondent are summarised as follows.

*Admissibility of the auxiliary requests I to XVIII - Article 12(2), 12(4) RPBA and Article 13(1) RPBA*

*Amendments to claims 20 to 22*

No arguments were provided in writing in response to appellant II's objections relating to the lack of substantiation of the auxiliary requests either in the reply to the statement of grounds of appeal or in reply to the board's communication pursuant to Article 15(1) RPBA.

At the oral proceedings it was argued that auxiliary requests I to XVIII had been substantiated in the reply to the appellants' grounds of appeal (see section 3 of the reply). Moreover, essentially the same claim requests had been filed before the opposition division and had been substantiated then, being aimed at overcoming the novelty objections with regard to document D1. No party could now be surprised by the amendments made. It was therefore not justified not to admit any of these claim requests. Indeed, the amendments to the claims of the auxiliary requests were self-explanatory and were done to address the objections of lack of novelty raised in the statements of grounds of appeal of the appellants.

Moreover, any additional changes made were done in response to new objections raised by appellant II for

the first time in the appeal or during the oral proceedings in the first instance. In particular, appellant II raised an objection under Article 100(c) EPC against claims 20 to 22, in section 3.2 of their appeal. These claims had not been objected to for this reason before and the amendments to take this into account were made at the first opportunity. Similarly, the objections under Article 100(b) EPC raised by appellant II against claims 20 to 22 (see section 4 of the statement of grounds of appeal) were raised for the first time during the oral proceedings before the opposition division and because they were unsuccessful, there had been no need at the time to file requests in response.

In relation to auxiliary requests XIII to XVIII, the subject-matter of claim 1 was amended to incorporate subject-matter from claims that were not objected to by the appellants. For instance, claim 1 of auxiliary requests XIII and XIV incorporated the subject-matter of claim 12 of the main request. Claim 1 of auxiliary requests XVII and XVIII incorporated the subject-matter from page 40, line 33 of the application as originally filed.

*Admissibility of auxiliary requests XIa and XIIa - Article 13(1) RPBA*

These requests were filed in case the board was inclined to adopt appellant II's position that the subject-matter of claim 1 of auxiliary requests XI and XII was not novel over document D1. In these requests, the purpose of the use was further clarified and now referred to enriching at least one of several IgG2 forms. Since document Dl did not employ chaotropes for

this purpose, it could not prejudice the novelty of the claimed subject-matter.

*Objection pursuant to Rule 106 EPC*

During the course of the oral proceedings in not admitting auxiliary requests X, XIII to XVIII, the board infringed the respondent's right to be heard according to Article 113 EPC. Consequently an objection pursuant to Rule 106 EPC was made.

*Admissibility of auxiliary request XIX - Article 13(1) RPBA*

This request was based on admitted auxiliary request XI and represented a *bona fide* attempt to overcome the objection of lack of novelty against claim 1 of that claim request. Indeed, the amendment represented the addition of subject-matter from dependent claim 12 of the main request that had not been attacked for lack of novelty and was therefore straightforward.

*Main request - claim 1*
*Novelty - Article 54 EPC*

The respondent provided no written arguments on novelty beyond those set out in the decision under appeal. At the oral proceedings the respondent provided the following arguments.

The claimed subject-matter was novel over that disclosed in document D1 for the reasons set out in the decision under appeal. Firstly, document D1 did not directly and unambiguously disclose a method in which an initial IgG2 antibody eluted as several separate forms on RP HPLC nor that the method decreased the

number of forms eluting. In response to the argument that document D1 explicitly disclosed the removal of aggregated forms of IgG2, it was pointed out that the entire disclosure of the patent made it clear that the separate forms referred to were isoforms and not aggregated forms. The claim required that the separate forms eluted separately from RP-HPLC and it was not known if this was true of aggregates.

Secondly, the concentration of cysteine used in Example 4 of the patent was 3 to 10 mg/mL. In document D1 the concentration of cysteine was 70 mg/L. The amount used in the patent was therefore 60 times higher than that used in document D1. The concentration of redox reagent used in D1 was too low to achieve the effect of decreasing the number of forms of diluting IgG2 antibody.

This argument was not a change of case in the sense of Article 13(1) RPBA. The arguments had been raised in the first instance proceedings and were considered by the opposition division in reaching their decision that document D1 did not anticipate the claimed subject-matter (see page 7 of the decision under appeal). It was up to the appellants to show that this decision was wrong.

Even if the arguments concerning the concentration of redox reagent were disregarded, the burden of proof lay with the appellants to show that the disclosure in document D1 was novelty destroying. They had not discharged this burden.

XXII. The appellants requested that the decision under appeal be set aside and that the patent be revoked.

XXIII. The respondent requested that

- the decision of the opposition division be maintained (amounting to a request that the appeals be dismissed);

- alternatively, that the patent be maintained on the basis of the set of claims of one of auxiliary requests I to XI, XIa, XII, XIIa, or XIII to XIX, auxiliary requests I to XVIII filed with the respondent's reply to the grounds of appeal, auxiliary requests XIa and XIIa filed with the respondent's letter dated 10 July 2019 and auxiliary request XIX filed during the oral proceedings before the board.

## Reasons for the Decision

1. The appeals comply with Articles 106 to 108 and Rule 99 EPC and are therefore admissible.

2. All references in this decision to the RPBA are to the 2007 version.

*Main request - claim 1*

*Novelty - Article 54 EPC*

3. The claimed subject-matter is a method of producing an IgG2 antibody/antibody fragment preparation enriched for one of several separate IgG2 forms. The method is defined by two steps. The first step is "contacting an IgG2 antibody or an IgG2 antibody fragment that has been recombinantly produced by mammalian cells with a reduction/oxidation coupling reagent at a pH of 5 to 11" and the second is "contacting said IgG2 antibody with a chaotropic agent before, after or concurrently

with said contacting with said reduction/oxidation coupling reagent".

4. The claim further specifies that the starting IgG2 antibody elutes as several separate forms on RP-HPLC and carrying out the steps of the method leads to a decrease of the number of forms eluting on RP-HPLC, or an alteration in the relative distribution of said forms on said RP-HPLC.

5. In the decision under appeal, the opposition division held that these features (see preceding point) constituted a technical effect of the claimed method and that document D1 did not disclose them ("*Thus, OD finds no reason why the principles of G2/88 should not be taken into account. In summary, the method of claim 1 defines an enrichment purpose based on a new technical effect obtained by process steps which have not been disclosed in the following prior art*" - see page 7 of the decision under appeal).

6. The Enlarged Board set out in decision G 2/88 (OJ EPO 1990, 93, Reasons, point 2.2) that there are basically two different types of claim, namely those to a physical entity (e.g. product, apparatus) and those to a physical activity (e.g. method, process, use) - see also Case Law of the Boards of Appeal of the European Patent Office, 9th edition, 2019, II.A.1.2.

7. The case law of the Boards of Appeal has consistently differentiated between methods or processes for producing a product characterised by process steps wherein the purpose of carrying out said process steps is indicated in the claims and those for the use of a substance for achieving an effect. The second non-medical use claims considered in decisions G 2/88 and

G 6/88 of the Enlarged Board of Appeal were directed to the use of a substance for achieving an effect but not to methods/processes/uses for the production of a product. For the former type of claim, attaining of a "*newly discovered technical effect*" should be considered as a functional technical feature of the claim, whereas for the latter type of claim it should not (see Case Law of the Boards of Appeal of the European Patent Office, 9th edition 2019, I.C.8.1.1 and 8.1.3).

8. According to the case law mentioned above, a disclosure in the state of the art of a method for producing a product having the same process steps as the claimed process would anticipate the claimed subject-matter even if that disclosure did not explicitly mention the effect of carrying out said process steps, since the effect would necessarily be achieved by following the steps of the method.

9. Document D1 discloses, in paragraphs [0208] and [0218], a method for producing the IgG2 antibody αOPGL-1. The antibody is produced by expression in Chinese hamster ovary cell line in a culture medium (VM-Soy Batch Medium). This culture medium is further described in Table 3 in paragraph [224], from which it can be seen that it contains both L-cysteine and L-cystine at concentrations of 35.12 mg/L and 62.58 mg/L, respectively (about 0.20 mM each). The culture medium also contains L-arginine at a concentration of 295 mg/L. Furthermore, it is disclosed in paragraph [0222] that the pH of the culture medium in which the antibody is produced is 7.0.

10. Turning to the claims of the main request, claim 1 refers to reduction/oxidation coupling reagent in

general and to a chaotropic agent in general. However, it can be seen from dependent claim 6 that the reduction/oxidation coupling reagent may be cysteine/ cystine and from dependent claim 13 that the chaotropic agent may be arginine. Thus, the method disclosed in document D1 matches the claim in respect of these features.

11. Document D1 does not explicitly disclose either that IgG2 antibodies are secreted in several separate forms or that the effect of contacting the secreted antibodies with the reduction/oxidation coupling reagent and the chaotropic agent is the one specified in the claim. However, with respect to the former, the board has seen no reason to doubt the statement made in paragraph [0075] of the patent that "*there is significant conformational heterogeneity in recombinant IgG2 antibodies expressed in mammalian cells*" is correct. Thus, the board is persuaded that heterogeneity is a property shared by recombinant IgG2 antibodies produced by mammalian cells in general and that the antibodies disclosed in document D1 can be taken to be inherently heterogeneous.

12. With respect to the decrease of the number of forms/ the alteration of the relative distribution of several separate forms of the IgG2 antibody on RP-HPLC (see point 4.), the board must conclude that this is an inherent effect, achieved when performing the steps of the (claimed) method. The concentration of the redox reagent used in document D1 falls within the range specified in dependent claim 7 of the main request and thus also within the ambit of claim 1 of the main request (which does not specify a concentration of the redox reagent). The fact that in the method set out in Example 4 of the patent, the concentration of the redox

reagent is significantly higher than that used in document D1 does not alter this conclusion.

13. As already noted above (point 8.), it is not relevant in the assessment of novelty whether the authors of document D1 recognised that this effect was taking place in the method that they disclosed.

14. Thus, document D1 discloses a method of producing an IgG2 antibody falling within the ambit of claim 1, the subject-matter of which therefore lacks novelty.

*Auxiliary requests I to IX - claim 1*

*Novelty - Article 54 EPC*

15. Although admittance of these sets of claims was contested by appellant II, there is no need to give reasons for the admittance and substantive assessment of these requests by the board, since, for the reasons given below, these requests could not be allowed.

16. The embodiment of claim 1 of the main request relating to a method of producing an IgG2 antibody is also an embodiment of claim 1 of auxiliary requests I to IX. The subject-matter of claim 1 of these requests lacks novelty over the disclosure in document D1 for the same reasons as set out above for the subject-matter of claim 1 of the main request.

*Auxiliary request X*

*Admissibility - Articles 12(2), 12(4) and 13 RPBA*

17. Article 12(2) RPBA stipulates that "*The statement of grounds of appeal and the reply shall contain a party's*

*complete case. They shall 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*".

18. The case law of the Boards of Appeal has consistently held that this requirement is not met if claim requests are not substantiated, except if the amendments made are self-explanatory. It has also held that requests that are not self-explanatory are to be considered as submitted only on the date of their substantiation (see the Case Law of the Boards of Appeal of the European Patent Office, 9th edition, 2019, V.A.4.12.5).

19. Furthermore, it is established case law that parties to an appeal cannot rely on submissions made before the first instance, since the appeal procedure is not a continuation of the opposition procedure, but a distinct procedure in which any facts, evidence or arguments considered relevant must, if need be, be resubmitted (see G 10/91, OJ 1993, 420; G 9/92 and G 4/93, both in OJ 1994, 875)" (*Id.* at V.A.1.1). Neither this case law nor its applicability to the case at hand was disputed by the respondent.

20. Since the respondent's reply to the statements of grounds of appeal contains no explanation relating to the auxiliary requests, beyond the statement that "all of these requests address the newly raised objections against claims 20 to 22", the board can only hold that the amendment made to claim 1 in auxiliary request X was not substantiated therein. In view of the above mentioned case law (see point 19.), it is not relevant whether or not the claim requests were substantiated in the proceedings before the opposition division. It

remains to be decided whether or not the amendments made to claim 1 are self-explanatory as suggested by the respondent (see section XXI. above).

21. The board notes that no case has been made in writing why amended claim 1 is allowable. Contrary to the respondent's position, it was not self-explanatory which objections were addressed by each of the numerous amendments of claim 1 of the request (see section XI), i.e. whether it was lack of novelty or inventive step or any other objection raised in the statements of grounds of appeal against claim 1 of the main request (see sections IV and V) nor why the amendments would overcome any of these objections.

22. The submissions of the respondent (i.e. the amended claim request itself) do not suffice to place neither the board nor the other parties in a position to understand the rationale behind the request. Thus the requirements of Article 12(2) RPBA which stipulates that parties to appeal proceedings should present their complete case [...] and should specify expressly all arguments relied on are not met.

23. Article 12(4) RPBA provides that, without prejudice to the power of the board to hold inadmissible facts, evidence or requests which could have been presented in the first-instance proceedings, everything presented by the parties pursuant to Article 12(1) RPBA, i.e. in *inter partes* proceedings, the notice(s) of appeal, the statement(s) of grounds of appeal and any timely filed written reply of the other party or parties, shall be taken into account by the board if and to the extent it relates to the case under appeal and meets the requirements in Article 12(2) RPBA.

24. The board, in line with the established case law (*Id.* at V.A.4.12.5), concludes that it has discretion over whether or not to hold inadmissible claim requests which fail to meet the requirements in Article 12(2) RPBA.

25. Furthermore, substantiation of the auxiliary request for the first time at the oral proceedings constitutes an amendment of the case previously presented, admissibility of which needs to be assessed applying Articles 13(1) and 13(3) RPBA. Admitting such a late substantiated request would have necessarily extended the scope of discussion as determined by the grounds of appeal and the respondent's reply to newly presented facts, evidence and arguments, not just concerning novelty, but also inventive step, for which neither the other parties or the board could have been properly prepared. The admission of the auxiliary request therefore would have necessitated adjournment of the oral proceedings (Article 13(3) RPBA) as the case was likely to develop in unforeseen directions. The admission of the request would thus go against the need for procedural economy.

26. In view of the above considerations, the board decided not to admit auxiliary request X into the proceedings.

*Auxiliary requests XI and XII*

*Admissibility - Articles 12(2), 12(4) and 13 RPBA*

27. Although admittance of these set of claims was contested by appellant II, there is no need to give reasons for the admittance and substantive assessment of these requests by the board, since, for the reasons given below, these requests could not be allowed.

*Claim 1*

*Novelty - Article 54 EPC*

28. The claim differs from claim 1 of the main request primarily in that it is directed to the use of a chaotropic agent in a method for producing an IgG2 antibody, where that method is essentially the method of claim 1 of the main request.

29. The board understands that the respondent's intention in formulating the claim as a 'use' claim, was to ensure that the subject-matter included the effect of decreasing the number of IgG2 forms eluting on RP-HPLC and altering the relative distribution of several separate forms of IgG2 on RP-HPLC, as technical features of the claim. It was the respondent's view that the criteria relating to the novelty of second non-medical uses set out in decisions G 2/88 and G 6/88 applied to such a claim.

30. As already noted in point 6. above, it is long established case law that it is irrelevant whether the claim refers to a 'method' or a 'use', as both these words describe a physical activity. In order to determine what the subject-matter claimed is, it is necessary to consider the particular wording of the claim. The board is of the view that given the wording of the claim as a whole, the claimed subject-matter can only be regarded as a process for the production of an IgG2 antibody. The claimed 'use' must be interpreted as the 'use' in the method (physical activity) defined by the "contacting" steps set out in the claim. In other words, in the context of the claim, the 'use' is in fact the same as the "contacting". Indeed, it is the

board's view that the subject-matter of the claim is identical to that of claim 1 of auxiliary request VII.

31. In view of the above, the claimed subject-matter lacks novelty over the disclosure in document D1 for the reasons given for claim 1 of the main request.

*Admissibility of auxiliary requests XIa and XIIa - Article 13(1) RPBA*

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

33. The requests were filed with the respondent's letter dated 10 July 2019, in response to the board's communication setting out its preliminary appreciation of substantive and legal matters concerning the appeal. The respondent argued that in these requests, claim 1 had been amended such that the purpose of the use was further clarified and now referred to enriching at least one of several IgG2 forms. Since document Dl did not employ chaotropes for this purpose, it could not prejudice the novelty of the claimed subject-matter.

34. In the board's view, several factors weigh against admitting these requests into the proceedings. Firstly, the requests were, according to the respondent, filed to overcome an objection of lack of novelty with respect to document D1. However, this objection was already raised in the statements of grounds of appeal

of the appellants and no persuasive explanation for the late filing was provided.

35. Secondly, despite the change from "use of a chaotropic agent in a method for producing an IgG2 antibody" to "use of a chaotropic agent for enriching at least one of several separate IgG2 forms", the board is of the view that the subject-matter remains a method for producing an IgG2 antibody preparation (see point 30., above). Thus, the claimed subject-matter is not clearly allowable and its admission to the proceedings would conversely not serve the interests of procedural economy.

36. Therefore the board decided not to admit auxiliary requests XIa and XIIa into the proceedings.

*Admissibility of auxiliary requests XIII to XVIII - Admissibility - Articles 12(2), 12(4) and 13 RPBA*

37. The board refers to the comments set out in points 17. and 18. relating to Article 12(2) RPBA. The amendments made to claim 1 of these requests are not self-explanatory because it is not immediately apparent whether the amendments were done to address problems of lack of novelty or of lack of inventive step, bearing in mind that appellant II objected to claim 1 of the main request both for reasons of lack of novelty and lack of an inventive step. Moreover, it is also not apparent how the amendments overcome the objections raised, since e.g. the subject-matter of claim 12 of the main request - which was incorporated into claim 1 of auxiliary requests XIII and XIV - was also objected to by appellant II as lacking novelty. Thus, the considerations set out in points 17. to 26. for auxiliary request X apply equally to these auxiliary

requests, and they were therefore not admitted into the proceedings.

*Objection pursuant to Rule 106 EPC*

38. The objection concerns the non-admittance of auxiliary requests X, XIII to XVIII into the proceedings.

39. The board could not conclude that the non-admittance of the auxiliary requests in question constituted a fundamental procedural violation, in particular of the right to be heard pursuant to Article 113(1) EPC.

40. The respondent submitted auxiliary requests X and XIII to XVIII together with the reply to the appellants' statements of grounds of appeal. However, none of the amendments made to claim 1 of the auxiliary requests were substantiated during the written proceedings and the amendments made therein are not considered self-explanatory, as explained above.

41. The respondent was given extensive opportunity during the oral proceedings to comment on why the auxiliary requests should be admitted (see minutes of the oral proceedings), however their submissions did not persuade the board for the reasons set out above. That the respondent was not heard on the allowability of these auxiliary requests is the result of these requests not being admissible.

42. Thus, the board concluded that the respondent's right to be heard had been respected and that the objection according to Rule 106 EPC was unfounded and had to be dismissed.

*Admissibility of auxiliary request XIX - Article 13(1) RPBA*

43. The criteria applied by the boards when exercising their discretion according to Article 13(1) RPBA are summarised in point 32., above. The reasons that the board exercised its discretion not to admit auxiliary request XIX are as follows:

i) The late stage of the proceedings. This request was filed at the very last possible moment during the appeal proceedings, although the objections it seeks to address, *inter alia* lack of the novelty (of claim 1 of the main request and of auxiliary request XI) over the disclosure in document D1 had been raised in the statements of grounds of appeal of the appellants,

ii) The amendments made do not result in a clearly allowable request. The proposed amendments introduce the subject-matter of dependent claim 12 of the main request into claim 1 of auxiliary request XI. However it is not immediately apparent that this amendment leads to an allowable claim because claim 12 of the main request had been objected to as lacking novelty over the disclosure of document D1 (see section V and statement of grounds of appeal of appellant II, third and fourth paragraph on page 16). Thus, admitting the request at this stage of the proceedings, would not have been in keeping with the principle of procedural economy.

44. Thus, the board decided not to admit auxiliary request XIX into the proceedings.

45. In view of the above considerations, no claim request is allowable.

**Order**

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

The decision under appeal is set aside.

The patent is revoked.

The Registrar: The Chair:

I. Aperribay R. Morawetz

Decision electronically authenticated