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Datasheet for the decision of 15 December 2022

Case Number: T 0679/20 - 3.3.08

Application Number: 09701090.4

Publication Number: 2250251

IPC: C12N5/00

Language of the proceedings: EN

Title of invention:
IMPROVED CULTURE MEDIA ADDITIVE AND PROCESS FOR USING IT

Patent Proprietor:
Sartorius Stedim Cellca GmbH

Opponent:
Oetke, Cornelia

Headword:
Culture media additive/SARTORIUS STEDIM CELLCA

Relevant legal provisions:
EPC Art. 123(2)
RPBA 2020 Art. 12(4)

Keyword:
Main request and auxiliary request 1 - added subject-matter (yes);
Auxiliary requests 2 to 5 - admission (yes); added subject-matter (yes);
Auxiliary requests 6 and 7 - admission (no);

Decisions cited:

Catchword:

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Beschwerdekammern

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Case Number: T 0679/20 - 3.3.08

D E C I S I O N
of Technical Board of Appeal 3.3.08
of 15 December 2022

Appellant: (Opponent)	Oetke, Cornelia Wallinger Ricker Schlotter Tostmann Zweibrückenstraße 5-7 80331 München (DE)
Representative:	Oetke, Cornelia Wallinger Ricker Schlotter Tostmann Patent- und Rechtsanwälte mbB Zweibrückenstraße 5-7 80331 München (DE)
Respondent: (Patent Proprietor)	Sartorius Stedim Cellca GmbH Erwin-Rentschler-Str. 21 88471 Laupheim (DE)
Representative:	Wohlfahrt, Jan Gleiss Große Schrell und Partner mbB Patentanwälte Rechtsanwälte Leitzstrasse 45 70469 Stuttgart (DE)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 3 January 2020 concerning maintenance of the European Patent No. 2250251 in amended form**

Composition of the Board:

Chairwoman	T. Sommerfeld
Members:	P. Julià
	D. Rogers

Summary of Facts and Submissions

I. European patent no. 2 250 251 is based on European patent application no. 09 701 090.4, originally filed under the PCT and published as International patent application WO 2009/087087 (hereinafter, "the patent application"). The patent was granted with 10 claims.

II. An opposition was filed on the grounds set forth in Articles 100(a), 100(b) and 100(c) EPC. The opposition division considered that the main request and auxiliary requests 1 and 2 lacked novelty and that auxiliary request 3 met all requirements of the EPC. Accordingly, the opposition division decided that the patent could be maintained in amended form on the basis of auxiliary request 3.

III. The opponent (appellant) lodged an appeal and filed new documentary evidence in the statement setting out their grounds of appeal. In response thereto, the patent proprietor (respondent) filed a main request, auxiliary requests 1 to 7, and new evidence. As an auxiliary measure, both parties requested oral proceedings.

IV. The board summoned the parties to oral proceedings and, in a communication issued in preparation of these proceedings, the parties were informed of the board's provisional opinion on the issues of the case.

V. Both parties replied to this communication announcing their intention to attend the oral proceedings. Whilst the appellant made submissions as to the substance of the appeal, no such submissions were made by the respondent.

VI. Oral proceedings were held on 15 December 2022 with all parties present.

VII. Claims 1 of the main request and auxiliary request 1 are identical and read as follows:

"1. A serum free culture medium containing at least one polyamine at a concentration of from 30 mg/l to 120 mg/l and at least one iron source at a concentration of from 50 mg/l to 900 mg/l, wherein the polyamine is one or more of the compounds or salts thereof or hydrated or dehydrated forms thereof selected from spermidine and spermine and wherein the iron source is one or more of the compounds or salts thereof or hydrated or dehydrated forms thereof selected from: iron(III) phosphate, iron(III) pyrophosphate, iron(III) nitrate, iron(III) citrate, ammonium iron(III) citrate, and iron-dextran."

VIII. Claim 1 of auxiliary requests 2 to 5 are identical to claim 1 of the main request, except for the following amendments:

"1. A serum free culture medium containing as cell culture additive at least one polyamine ... [as in claim 1 of the main request]" (auxiliary request 2);

"1. A serum free culture medium containing a cell culture additive containing at least one polyamine and at least one iron source, wherein the serum free culture medium contains the at least one polyamine at a concentration of from 30 mg/l to 120 mg/l and the at least one iron source at a concentration of from 50 mg/l to 900 mg/l, wherein ... [as in claim 1 of the main request]" (auxiliary request 3);

"1. A serum free culture medium containing ~~at least~~ one polyamine at a concentration of from 30 mg/l to 120 mg/l and ~~at least~~ one iron source at a concentration of from 50 mg/l to 900 mg/l, wherein the polyamine is one ~~or more~~ of the compounds or salts thereof or hydrated or dehydrated forms thereof selected from spermidine and spermine and wherein the iron source is one ~~or more~~ of the compounds or salts thereof or ... [as in claim 1 of the main request]" (auxiliary request 4);

"1. [as in claim 1 of the main request] ... selected from: ~~iron (III) phosphate, iron (III) pyrophosphate, iron (III) nitrate,~~ iron (III) citrate~~,~~ and ammonium iron (III) citrate~~, and iron-dextran~~." (auxiliary request 5).

IX. Claim 1 of auxiliary requests 6 and 7 are identical to claim 1 of the main request and auxiliary request 2, respectively, except for the limitation of the polyamine to spermine and of the iron source to those mentioned in auxiliary requests 5, namely iron(III) citrate and ammonium iron(III) citrate.

X. The arguments of the appellant, insofar as relevant to the present decision, may be summarised as follows:

Main request and auxiliary request 1
Article 123(2) EPC (added subject-matter) - Claim 1

The combination of features in claim 1 was not directly and unambiguously derivable from the content of the patent application. Iron sources were disclosed on page 14, line 9 to page 15, line 11 of the patent application. It was stated therein that iron sources contained Fe(II) and/or Fe(III) ions but no preference

was given to any of these ions. Likewise, for the preferred list of iron sources containing Fe(II) and Fe(III) ions disclosed on page 14, lines 15 to 20 and in claim 9 of the patent application. No preference was given in the patent application to any of these Fe(II) and/or Fe(III) ions, the subject-matter of claims 7 and 8 of the patent application, respectively.

The deletion of some compounds disclosed in these passages and in claim 9 of the patent application resulted in a selection of Fe(III) iron containing salts, a specific subgroup of Fe(III) iron sources which, as such, was not disclosed in the patent application. Thus, the subject-matter of claim 1 of the main request and auxiliary request 1 did not result from a mere deletion of compounds from the lists of iron sources disclosed in the patent application but was a specific selection of a subgroup of Fe(III) iron sources which, as such, was not directly derivable from the patent application.

Moreover, there was no pointer in the patent application for the claimed combination of Fe(III) iron sources with a polyamine selected from spermine or spermidine and therefore this particular combination was not directly derivable from the patent application.

Admission of auxiliary requests 2 and 5 into the proceedings

Auxiliary requests 2 to 5 were introduced into the proceedings by the respondent in reply to appellant's grounds of appeal. They were thus an amendment according to Article 12(4) RPBA and could be admitted only at the board's discretion.

The respondent failed to explain why these auxiliary requests could only be filed in reply to the grounds of appeal and not at earlier stages of the proceedings. The objections addressed by the amendments introduced into claim 1 of these requests were already raised at the earliest stage and/or during the opposition proceedings at first instance. Therefore, these auxiliary requests were all late-filed, they could and should have been filed at first instance. Moreover, the amendments introduced into these requests did not overcome the raised objections but, on the contrary, they all raised further objections.

Auxiliary request 5
Article 123(2) EPC (added subject-matter) - Claim 1

The iron sources mentioned in claim 1 of auxiliary request 5 were disclosed in a list of preferred iron sources on page 14, lines 15 to 20 and in claim 9 of the patent application. Both iron sources were cited as particularly preferred examples of complexed iron with chelators in a list with other iron sources on page 14, lines 22 to 26 of the patent application. But whilst iron(III) citrate was used in Example 7 of the patent application, ammonium iron(III) citrate was neither exemplified nor singled out in any other way in the patent application. The selection of a citrate chelator and a citrate salt represented a selection of a specific subgroup of iron sources which was neither disclosed as such nor directly derivable from the patent application. Nor were the properties of such a subgroup, such as shown on page 2, lines 26 to 29 of document (11) (WO-A1-93/00423), directly derivable from the patent application.

Admission of auxiliary requests 6 and 7 into the proceedings

According to the respondent's submissions in their reply to the grounds of appeal, these auxiliary requests addressed the objections raised under Article 56 EPC. They did not address the objections under Article 123(2) EPC and thus, there was no reason to admit them into the proceedings. The amendments introduced into these requests were not a mere deletion but they still required a selection of combinations of a specific polyamine and Fe(III) compounds as iron sources which, as such, were not directly derivable from the patent application.

XI. The arguments of the respondent, insofar as relevant to the present decision, may be summarised as follows:

Main request and auxiliary request 1
Article 123(2) EPC (added subject-matter) - Claim 1

Both Fe(II) and Fe(III) ions were disclosed as alternative iron sources in the patent application as shown, *inter alia*, by claims 7 and 8 of the patent application. The mere deletion of some compounds from the iron and polyamine sources listed in the patent application, such as in claims 9 and 10, neither singled out any of these compounds nor resulted in a selection of any specific subgroup from the lists of compounds disclosed in the patent application. Indeed, a pointer to the use of Fe(III) ions as iron sources was provided by claim 8 of the patent application. In the examples of the patent application, only spermine and spermidine were used, providing thus a pointer to these specific polyamines. Therefore, there was neither a selection of specific embodiments nor a selection of

features without any pointer in the patent application. The subject-matter of claim 1 of the main request and auxiliary request 1, in particular the polyamine and iron sources listed therein, was directly derivable from the patent application.

Admission of auxiliary requests 2 and 5 into the proceedings

These auxiliary requests were based on auxiliary requests filed at first instance, namely on former auxiliary requests 4, 5 and 6. Therefore, auxiliary requests 2 to 5 were not late-filed but already in the proceedings. The amendments introduced into these requests addressed appellant's objections raised in the grounds of appeal; they were made thus in reaction to the appeal. Since the opposition division upheld the patent on the basis of an auxiliary request 3 that was considered to comply with Article 123(2) EPC, there was no need to introduce these amendments at earlier stages of the proceedings. Auxiliary requests 2 to 5 were thus not late-filed and should be admitted into the proceedings.

Auxiliary request 5
Article 123(2) EPC (added subject-matter) - Claim 1

The iron source in claim 1 was limited to two sources, namely iron(III) citrate used in Example 7 of the patent application and ammonium iron(III) citrate, the latter directly related to the former and, for a skilled person, a plausible, direct broadening of the exemplified iron(III) citrate. In Example 7, spermine was used, an alternative to spermidine used in Example 2 of the patent application. Thus, both polyamines could be used with the exemplified iron(III)

sources, in particular iron(III) citrate and the related ammonium iron(III) citrate. The limitation to an exemplified iron(II) source and a directly related iron source neither represented an undisclosed selection nor singled out an iron source from all iron sources disclosed in the patent application, such as in claim 9 of the patent application. Thus, the iron(III) sources mentioned in claim 1 of auxiliary request 5 were directly derivable from the patent application.

Admission of auxiliary requests 6 and 7 into the proceedings

The reasons for admitting auxiliary requests 2 to 5 into the proceedings applied also to auxiliary requests 6 and 7. The polyamine and iron sources cited in auxiliary requests 6 and 7 were limited to spermine and to those of auxiliary request 5, respectively. No selection was required to arrive at this subject-matter which was only a further limitation of the disclosure already present in the patent application.

XII. The appellant (opponent) requested that the decision under appeal be set aside and the patent be revoked, and that auxiliary requests 2 to 7 not be admitted into the proceedings.

XIII. The respondent (patent proprietor) requested, as main request, that the appeal be dismissed, or in the alternative, that the decision under appeal be set aside and that the patent be maintained upon the basis of one of auxiliary requests 1 to 7.

Reasons for the Decision

Main request and auxiliary request 1

1. The main request is identical to the auxiliary request 3 underlying the decision under appeal and upheld by the opposition division and thus, it already forms part of these proceedings. The admission of the main request and auxiliary request 1 into the appeal proceedings was not contested by the appellant.

Article 123(2) EPC (added subject-matter) - Claim 1

2. Claim 1 of these requests is directed to a culture medium characterised by the combination of several features, namely being serum free and containing at least one polyamine and at least one iron source; these sources being further defined by specific concentration ranges and lists of compounds. Whilst the polyamine is defined as "one or more of the compounds or salts thereof or hydrated or dehydrated forms thereof selected from spermidine and spermine", the iron source is defined as "one or more of the compounds or salts thereof or hydrated or dehydrated forms thereof selected from: iron(III) phosphate, iron(III) pyrophosphate, iron(III) nitrate, iron(III) citrate, ammonium iron(III) citrate, and iron-dextran".

3. In order for claim 1 to comply with Article 123(2) EPC, a culture medium with the combination of features cited above must be directly and unambiguously derivable from the patent application (cf. "Case Law of the Boards of Appeal of the EPO", 10th edition 2022, II.E.1.3.1), in particular, the combination of the polyamine and iron sources referred to in this claim. For assessing whether such a combination is directly derivable from

the patent application, the case law concerning a combination of features pertaining to separate lists is highly relevant (cf. "Case Law", *supra*, II.E.1.6).

4. The question arises thus whether the said combination amounts to a particular selection of compounds from the lists of polyamine and iron sources disclosed in the patent application - resulting thereby in a singling out of a particular combination of features not directly derivable from the patent application (cf. "Case Law", *supra*, II.E.1.6.2), or else whether the said combination amounts to a mere deletion of some of the polyamine and iron sources disclosed in the patent application - merely shrinking thereby the lists of these sources but without singling out any combination of features not directly derivable from the patent application (cf. "Case Law", *supra*, II.E.1.6.3).

5. The polyamine and iron sources are disclosed in the patent application at different levels of generalisation.

5.1 The most generic disclosure refers only to "a culture additive containing at least one polyamine ... and at least one iron source ..." without further defining any polyamine or iron source as shown, for instance, in claim 1 of the patent application (see also, *inter alia*, page 1, lines 3 to 6, and page 3, lines 9 to 14 of the patent application).

5.2 A more specific disclosure provides a list of iron sources and polyamines such as in claims 9 and 10 of the patent application. Whilst the list of iron sources in claim 9 reads "... one or more of the compounds or salts ... selected from: iron(III) phosphate, iron(III) pyrophosphate, iron(III) nitrate, iron(II) sulphate,

iron(III) chloride, iron(II) lactate, iron(III) citrate, ammonium iron(III) citrate, iron-dextran and ethylenediaminetetraacetic acid ferric sodium salt", that of polyamines in claim 10 reads "... one or more of the compounds or salts ... selected from: spermidine, spermine, norspermine, norspermidine, homospermine, homospermidine and cadaverine" (see also, *inter alia*, page 14, lines 3 to 6 and lines 15 to 20 of the patent application).

5.3 Several culture media with specific combinations of these polyamine and iron sources are disclosed in Examples 1 to 9 of the patent application, namely spermine and iron(III) phosphate (Examples 1 and 8, see also Figure 1), spermidine and iron(III) pyrophosphate (Example 2; see also page 19, penultimate paragraph), spermine and iron(III) pyrophosphate (Examples 3 and 4), spermine and iron(III) nitrate (Example 5), spermine and iron(III) citrate (Examples 6 and 7), and spermine and iron-dextran (Example 9) (see pages 24 to 30 of the patent application).

6. The specific iron sources and polyamines cited in claim 1 of the main request and auxiliary request 1 are not those listed in claims 9 and 10 of the patent application. Nor is the list of iron sources cited in said claim 1 identical to any of the lists of iron sources disclosed in the patent application. Thus, neither claims 9 and 10 of the patent application nor any of the lists of iron sources disclosed in the patent application can be seen as a basis for the specific combinations of polyamine and iron sources cited in claim 1.

6.1 Whilst the polyamines cited in claim 1 are those used in the examples of the patent application (spermine in

Examples 1 and 3 to 9, spermidine in Example 2; see also page 5, lines 19 and 20 of the patent application), this is not the case for the iron sources because ammonium iron(III) citrate is cited in claim 1 but not used in any of the examples of the patent application.

6.2 Thus, neither the generic and intermediate disclosures in the claims and description of the patent application nor the more specific disclosures described in the examples of the patent application provide a basis for the specific combinations, and in particular the list of iron sources, cited in claim 1 of the main request and auxiliary request 1.

7. It may be argued, as the respondent does, that the polyamines and iron sources listed in claim 1 result from a mere deletion of the polyamines and iron sources listed in claims 9 and 10 of the patent application. The board, however, cannot agree with the respondent.

7.1 In the list of iron sources cited in claim 1, all iron(II) sources that were always present in all the specific lists of iron sources disclosed in the patent application have been deleted, such as the iron(II) sulphate and iron(II) lactate listed in claim 9 and on page 14, lines 15 to 20 of the patent application. Thus, the list of iron sources in claim 1 of the main request and auxiliary request 1 amounts to a selection of specific iron sources with Fe(III) ions. However, this list is neither limited to the specific Fe(III) iron sources disclosed in the examples of the patent application - ammonium iron(III) citrate is cited in claim 1 but not exemplified, nor to the Fe(III) iron sources listed in claim 9 of the patent application -

iron(III) chloride is cited in claim 9 but not in claim 1 of the main request and auxiliary request 1.

7.2 Moreover, whilst, as argued by the appellant, iron sources with either Fe(II) ions or Fe(III) ions are disclosed as equal alternatives in the patent application, the opposition division referred to iron sources with Fe(III) ions as a feature contributing to the inventive step (see page 11, point 4.7.3.3.6 of the decision under appeal). Reference has also been made in the context of Article 56 EPC and in appeal proceedings to the advantageous properties of Fe(III) iron sources over those with Fe(II) ions (see page 10, point d), of respondent's response to the grounds of appeal).

7.3 In the light thereof, the board considers the specific combinations of polyamine and iron sources cited in claim 1 of the main request and auxiliary request 1, in particular the list of Fe(III) iron sources, not to arise from a mere deletion of those disclosed in the patent application but to be a (purposive) selection that is neither directly nor unambiguously derivable from the content of the patent application.

8. Thus, the main request and auxiliary request 1 do not comply with Article 123(2) EPC.

Auxiliary requests 2 to 5
Admission into the appeal proceedings

9. The admission of these auxiliary requests into the appeal proceedings is contested by the appellant.

10. These auxiliary requests are based on former auxiliary requests 4, 5 and 6 filed at first instance (see page 1, point 5 of the decision under appeal). None of

these requests were examined by the opposition division because auxiliary request 3 underlying the decision under appeal was considered to overcome all objections raised in the proceedings at first instance and to meet all requirements of the EPC (see page 12, points 4.8 and 5 of the decision under appeal). According to the respondent, these auxiliary requests and the amendments introduced therein were filed and made in direct response to, and in order to deal with, the objections raised by the appellant in the grounds of appeal.

11. In view thereof and in order for the board to consider and examine these auxiliary requests and the amendments introduced therein, the board, in exercise of its discretion (Article 12(4) RPBA), decides to admit auxiliary requests 2 to 5 into the appeal proceedings.

Auxiliary requests 2 to 4
Article 123(2) EPC (added subject-matter) - Claim 1

12. Claim 1 of of auxiliary requests 2 and 3 is directed to a serum free culture medium containing a cell culture additive characterised by the presence of at least one polyamine and at least one iron source, which are further defined by specific concentration ranges and lists of particular compounds as in claim 1 of the main request. In auxiliary request 4, the claimed serum free culture medium is defined as in claim 1 of the main request except for the culture medium containing only one polyamine and one iron source, each selected from the polyamines and iron sources listed in claim 1 of the main request. None of the amendments introduced into claim 1 of auxiliary requests 2 to 4 relates to, or is concerned with, the specific iron sources listed in said claim.

13. Thus, since the list of iron sources in the serum free culture medium of claim 1 of auxiliary requests 2 to 4 is identical to the list of iron sources in claim 1 of the main request, the objection raised above under Article 123(2) EPC against the main request applies also to auxiliary requests 2 to 4.

14. Therefore, auxiliary requests 2 to 4 do not comply with Article 123(2) EPC.

Auxiliary request 5
Article 123(2) EPC (added subject-matter) - Claim 1

15. Claim 1 of auxiliary request 5 reads as claim 1 of the main request except for the limitation of the iron sources to iron(III) citrate and ammonium iron(III) citrate. Thus, the iron sources listed in claim 1 of this auxiliary request contain only Fe(III) ions, there is no iron source with Fe(II) ions.

15.1 Whilst Example 7 of the patent application discloses a cell culture medium with a combination of spermine and iron(III) citrate - as polyamine and iron source, respectively (see page 27, line 21 to page 28, line 15 of the patent application), there is no example in the patent application disclosing a cell culture medium with a combination of any polyamine whatsoever with ammonium iron(III) citrate. Moreover, although both, iron(III) citrate and ammonium iron(III) citrate, are cited in a list of particularly preferred examples of complexed iron with chelators, this list is not limited to these specific iron sources but further contains three other iron sources, namely iron(II) lactate hydrate, iron-dextran and ethylenediaminetetraacetic (EDTA) acid ferric sodium salt (see page 14, lines 22 to 26 of the patent application).

15.2 There is neither an indication nor a pointer in the patent application to a (serum free) cell culture medium containing a specific subgroup of iron sources limited solely to iron(III) citrate and ammonium iron(III) citrate, let alone in combination with spermine and spermidine as sole polyamine sources.

15.3 The appellant has also drawn the board's attention to the disclosure in document D11 stating that "[t]o avoid iron precipitation and potential toxic effects of the iron on the cultured cells, the citrate chelator should be mixed with the iron salt so as to generate an equilibrium prior to the addition to the culture medium" (see page 2, lines 26 to 29 of document (11), WO-A1-93/00423). The board understands appellant's argument as indicating that the specific subgroup of iron sources in claim 1 of auxiliary request 5 may have (advantageous) properties that are not directly derivable from the patent application, i.e. the specific subgroup of iron(III) sources in claim 1 of auxiliary request 5 does not amount to a mere deletion of other iron sources but arises from a (purposive) selection not directly derivable from the patent application.

15.4 In view of these considerations above, the board considers that the limitation in the claimed (serum free) cell culture medium of the polyamines to spermine and spermidine and the iron sources to a specific subgroup of iron sources, namely those based only on citrate and containing only Fe(III) ions, is not directly and unambiguously derivable from the content of the patent application.

16. Therefore, auxiliary request 5 contravenes Article 123(2) EPC.

Auxiliary requests 6 and 7
Admission into the appeal proceedings

17. The admission of these auxiliary requests into the appeal proceedings is contested by the appellant.

18. In view of the parties' arguments pleading against and for the admission of these auxiliary requests into the appeal proceedings and the nature of the amendments introduced into auxiliary requests 6 and 7, which are acknowledged by the parties to be identical to the amendments and combinations thereof introduced into auxiliary requests 1 to 5 and already considered by the board above, there is no further reason for the board to admit these auxiliary requests into the proceedings.

19. Thus, the board, in the exercise of its discretion (Article 12(4) RPBA), does not admit any of auxiliary requests 6 and 7 into the appeal proceedings.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The patent is revoked.

The Registrar: The Chairwoman:

L. Malécot-Grob T. Sommerfeld

Decision electronically authenticated