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Datasheet for the decision of 17 January 2013

Case Number: T 1157/09 - 3.3.08

Application Number: 97915628.8

Publication Number: 891420

IPC: C12N 5/06, C12N 7/00, A61K 39/145

Language of the proceedings: EN

Title of invention:
Processes for the replication of influenza viruses in cell culture, and the influenza viruses obtainable by the process

Patentee:
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Opponents:
GlaxoSmithKline Biologicals SA
Sanofi Pasteur SA
CRUCELL HOLLAND B.V.
SOLVAY PHARMACEUTICALS B.V.
Akzo Novel NV
Medimmune, Inc.

Headword:
Influenza vaccine/NOVARTIS VACCINES AND DIAGNOSTICS

Relevant legal provisions:
EPC Art. 123(2), 56
RPBA Art. 12(4)

Keyword:
"Main request - requirements of the EPC met"

Decisions cited:
G 0002/10

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Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 1157/09 - 3.3.08

D E C I S I O N
of the Technical Board of Appeal 3.3.08
of 17 January 2013

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Decision under appeal: **Decision of the Opposition Division of the European Patent Office posted 11 March 2009 revoking European patent No. 891420 pursuant to Article 101(3)(b) EPC.**

Composition of the Board:

Chairman: M. Wieser
Members: B. Stolz
C. Heath

Summary of Facts and Submissions

I. The appeal lies against the decision of the opposition division to revoke European patent No. 891420.

II. Six oppositions had been filed on the grounds of Articles 100(a), (b) and (c) EPC.

At oral proceedings, held on 20 January 2009, the opposition division found that

(a) the main request and auxiliary requests I, II and V to IX did not meet the requirements of Article 123(2) EPC,

(b) auxiliary request III lacked an inventive step,

(c) auxiliary request IV lacked novelty, and

(d) auxiliary request X lacked an inventive step.

III. With its grounds of appeal, the patent proprietor (appellant) filed a new main request and new auxiliary requests I to VI.

IV. Opponents (respondents) I to IV, and VI responded to the appellant's statement of grounds of appeal.

V. In a communication pursuant to Article 15(1) of the Rules of Procedure of the Boards of Appeal (RPBA), annexed to a summons to oral proceedings, the board informed of its preliminary, non-binding opinion on some of the issues to be discussed at the upcoming oral proceedings.

VI. The appellant filed further comments, withdrew auxiliary requests II to V, renumbered previous auxiliary request VI as auxiliary request II, and filed

a new auxiliary request III. Respondents II and III also filed further comments.

VII. Respondents II, and IV to VI informed the board that they would not attend the oral proceedings.

VIII. Oral proceedings were held on 17 January 2013. During the proceedings, the appellant filed a new main request comprising claims 1 to 7 and withdrew all previous requests.

IX. Independent claim 1 of the main request reads as follows:

"1. A process for making a vaccine for administration to humans or animals comprising:

(a) replication of influenza viruses in cell culture, in which MDCK 33016 cells (DSM ACC 2219) are cultured in cell culture in suspension in serum-free medium, the cells are infected with influenza viruses and after infection are cultured at a temperature in the range from 30°C to 36°C for virus replication, wherein a protease is added to the cultured cells before or during infection with influenza viruses;

(b) formulation of the replicated influenza viruses to give the vaccine."

Dependent claims 2 to 7 refer to specific embodiments of the process of claim 1.

X. The following documents are cited in this decision:

D1: US Patent No. 4,500,513

D2: Portari Mancini D.A. and Yano A.B., 1993, Rev. Farm. Bioquim. Univ. S. Paulo, vol. 29(2): 89-95

D32: Merten O.W. et al., 1994, Cytotechnology 14: 47-59

D48: Cell culture as a substrate for the production of influenza vaccines: Memorandum from a WHO meeting, Bulletin of the World Health Organization 1995, 73(4): 431-435

D57: Merten O.W. et al., 1996, Adv. Exp. Med. and Biol., 397: 141-151

D76a: English translation of: Nakamura K. and Nishizawa S., 1980, J. of the Japanese Association for Infectious Diseases, vol. 54(6): 306-312

XI. The arguments of the appellant, as far as relevant for the present decision, can be summarized as follows:

Basis for claim 1 could be found in original claims 1 and 11 in conjunction with statements in the description on pages 6 and 7 referring to the growth of MDCK 33016 cells in suspension in serum free medium.

Document D1 represented the closest prior art. Vis-à-vis document D1, the technical problem consisted of providing an improved method of replicating influenza virus in cell culture. The problem was solved by the process of claim 1 comprising the use of the newly

established cell line MDCK 33016. As stated in paragraph 11 of the contested patent, the claimed process provided a particularly simple and efficient method for virus replication. The particular cell line and its use in the claimed process could not be derived from document D1 in conjunction with any of the cited documents.

XII. The arguments of the respondents, as far as relevant for the present decision, can be summarized as follows:

The combination of only two out of three features of original claim 11 with the features of original claim 1 represented a previously undisclosed selection.

Starting from document D1 as closest prior art, the claimed invention was obvious in view of e.g. documents D32, D48, D57 and D76 which related to growing cells in serum free medium and to the growth of MDCK cells in suspension.

XIII. The appellant requested that the decision under appeal be set aside and a patent be granted on the basis of the main request.

The respondents requested that the appeal be dismissed.

Reasons for the decision

Article 12(4) RPBA

1. The main request was filed during oral proceedings. It was originally filed as auxiliary request VI with the grounds of appeal and later renumbered as auxiliary request II (cf. paragraph VI above). After deletion of dependent claim 4 which comprised an embodiment no longer falling within the scope of amended claim 1, it became the main request.

2. The appellant and both respondents present at the oral proceedings confirmed that the request (as filed as auxiliary request VI with the grounds of appeal) had been submitted during oral proceedings before the opposition division but was not admitted into the procedure. Although this is not mentioned in the minutes of the oral proceedings, the board sees no reason to challenge this statement.

3. Thus, the question arises whether the request should be admitted in appeal proceedings under the provisions of Article 12(4) RPBA which give the board the power to hold inadmissible requests which were not admitted in the first instance proceedings.

4. The admission of late filed requests in opposition proceedings is at the discretion of the opposition division (Article 114(2) EPC), and the appellant submitted that the opposition division had not exercised its discretion properly.

5. It is established jurisprudence that "[a] board of appeal should only overrule the way in which a department of first instance has exercised its discretion if the board concludes it has done so according to the wrong principles, or without taking into account the right principles, or in an unreasonable way" (Case law of the Boards of Appeal, 6th edition, VII.E.6.6).

6. In the present case however, neither the minutes of the oral proceedings before the opposition division nor the decision under appeal make any mention of such a request, and the board finds itself in a situation where, due to the absence of any evidence why the opposition division did not admit the respective request, it is not in a position to assess the basis on which the opposition division had exercised its discretion.

Under these circumstances, the board, exercising its discretion under Article 12(4) RPBA, decided to admit the main request.

Rule 80 EPC

7. Respondents I and II considered the main request inadmissible. They were of the opinion that the introduction of the feature "for administration to humans or animals" in claim 1 was not occasioned by a ground of opposition.

8. This argument cannot succeed because the feature was not inserted in isolation but as part of a longer amendment. The complete amendment concerns "A process

for making a vaccine for administration to humans or animals". This amendment was clearly occasioned by the novelty objections against the claims as granted.

Article 123(2) EPC

9. The respondents objected to the combination of features in part (a) of claim 1. They argued that the combination of only two of the three points in time specified in original claim 11 with the features of original claim 1 violated the provisions of Article 123(2) EPC.

10. Claim 11 as originally filed read:

"11. The process as claimed in one of claims 1 to 10, in which a protease is added to the cultured cells before, during or after infection with influenza viruses."

In the respondent's view, claim 11 stated in essence that the point in time of adding the protease did not matter, and the combination of only two out of three possible points in time of adding the protease with the features of claim 1 represented a selection which was not derivable from the application as filed and which resulted in the addition of technical information.

11. In point 1.2.1 of its decision, the opposition division stated that "The presence of an alleged technical effect resulting from such a selection has no relevance when assessing Art. 123(2) EPC".

The board does not agree with this statement.

Any amendment to the parts of a European patent application or of a European patent is subject to the mandatory prohibition on extension laid down in Article 123(2) EPC and can therefore, irrespective of the context of the amendment made, only be made within the limits of what a skilled person would derive directly and unambiguously, using common general knowledge, and seen objectively and relative to the date of filing, from the whole of the application documents as filed (cf. point 4.3, 1st paragraph, of decision G 2/10 of 30 August 2011). The test for an amendment to a claim, also for an amendment by limitation, is that after the amendment the skilled person may not be presented with new technical information (cf. point 4.5.1 of decision G 2/10).

Whether an amendment of the type in question meets the requirements of Article 123(2) EPC depends therefore on the facts of the case and includes an assessment whether the amendment results in new technical effects.

12. Regarding claim 1 of the main request, no argument has been put forward by any of the parties that the selection of two out of the three points in time for adding the protease provided any technical teaching going beyond the application as filed. Since claim 11 as filed directly referred to claim 1 and disclosed three individual points in time for adding the protease, no technical information is added by limiting present claim 1 to two out of the three points in time for adding the protease.

13. Thus, the features of part (a) of claim 1, i.e. replicating the virus in cell culture at a temperature from 30 to 36 degrees C and adding a protease to the cultured cells before or during infection with influenza virus, are based on original claim 11 via its reference to original claim 1. Furthermore, according to the general part of the description as originally filed (page 6, lines 12 to 16), the use of cells growing in suspension, in particular in serum free medium is a preferred embodiment allowing particularly simple and efficient virus replication. The patent application as filed also discloses an MDCK derived cell line, MDCK 33016, adapted to growth in suspension in serum free medium, which is "particularly preferably used in the process according to the invention" (cf. page 5, lines 31 to 38).

14. Dependent claims 2 to 7 are based on originally filed claims 2 and 3, and 12 to 15, and the general parts of the description, respectively (page 4, lines 33 to 36; page 7, lines 14 to 17; page 7, lines 27 to 28).

15. The board is therefore satisfied that the requirements of Article 123(2) EPC are met.

Articles 123(3), 84, 83 and 54 EPC

16. The respondents did not raise any objections under the provisions of Articles 123(3), 83, 84 and 54, respectively, and the board has no reason to raise any of its own motion.

Article 56 EPC

17. Document D1 represents the closest prior art. It discloses the production of influenza vaccines by culturing influenza virus at temperatures from 34 to 35 degrees C in Cutter Lab Dog Kidney (CLDK) cells and the addition of a protease to the cell culture after infection of the cells with virus. CLDK cells are similar to Madin Darby Canine Kidney (MDCK) cells (cf. column 3, line 10). In the general part of the description growth in suspension culture in a medium to which fetal calf serum may be added is suggested (cf. column 5, Method C). The examples disclose virus production in adherently growing CLDK cells which were pre grown in serum containing medium.

18. In light of this disclosure, the technical problem underlying the present invention can be seen in the provision of an improved process for making an influenza virus vaccine.

19. For the solution of this problem, the patent proposes the method of claim 1, comprising the replication of influenza virus in cell line MDCK 33016 in suspension in serum free medium at a temperature between 30 to 36 degrees C.

20. As shown in Examples 3 and 4, influenza virus can be efficiently replicated in cell line MDCK 33016, and the carry over of unwanted proteins is reduced due to the absence of serum components. The board is therefore satisfied that the above mentioned problem is solved.

21. It remains to be established if the claimed solution, i.e. the use of the cell line MDCK 33016, involved an inventive step.

22. The respondents cited several documents which, in their view, when staring from document D1 as closest prior art, rendered the claimed solution obvious.

23. Document D76a disclosed the growth of MDCK cells in suspension culture with the aim of providing a means for isolating influenza viruses from patient samples. For growth, the MDCK cells were however cultured in suspension in the presence of foetal bovine serum, and for virus replication the cells were cultured in a medium comprising bovine serum albumin (cf. section "Methods", part 3, and Tables I and II).

Document D57 disclosed the preparation of influenza virus in MDCK cells grown in serum free medium in suspension cultures. The MDCK cells were however adherently grown on suspended micro carriers (cf. page 143, "Reactor cultures"), while the claimed method relies on a cell line growing in serum free medium in suspension without micro carriers.

Document D48, a memorandum from a WHO meeting, disclosed several ways of growing influenza viruses inter alia in MDCK cells in serum free medium (cf. page 433, and page 434, last paragraph). The cells were however not grown in suspension.

Document D32 disclosed a serum free medium suitable for the production of biologicals. Several cell lines were tested for growth in Spinner and bioreactor cultures

(cf. "Materials and Methods"). MDCK cells were however not among the tested cell lines.

Document D2 disclosed the replication of influenza virus in MDCK cells at 35 degrees C in the presence of trypsin. The authors grew the cells however as adherent monolayers in the presence of fetal bovine serum (cf. page 90, left column, "Materials e Métodos").

24. Since document D1 neither alone nor in combination with any of the documents cited in these proceedings disclosed, suggested or rendered otherwise obvious a cell line having the characteristics of the deposited cell line MDCK 33016, which grows in serum free medium in suspension at a temperature from 30 to 36 degrees C, the board is satisfied that the claimed solution involves an inventive step.

Adaptation of the description

25. At oral proceedings before the board, the description has been amended to bring it into conformity with the scope of the claims.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the first instance with the order to maintain the patent based on claims 1 to 7 of the main request and pages 2 - 8 of the description, all filed at oral proceedings.

The Registrar: The Chairman:

A. Wolinski M. Wieser