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Datasheet for the decision of 7 October 2025

Case Number: T 1758/23 - 3.3.08

Application Number: 17199357.9

Publication Number: 3330370

IPC: C12N5/00, C12P21/00, C07K16/00

Language of the proceedings: EN

Title of invention:
Process for cultivation of CHO cells

Patent Proprietor:
Novartis AG

Opponents:
Strawman Limited
Weinzierl, Gerhard
Dehns Ltd
Maiwald GmbH
Boult Wade Tennant LLP
Pohlman, Sandra M.

Headword:
Process for cultivation of CHO cells/NOVARTIS AG

Relevant legal provisions:
EPC Art. 100(c), 123(2)

Keyword:
Main request, auxiliary requests 1 to 5 - added subject-matter (yes)

Decisions cited:
G 0002/10

Europäisches Patentamt
European Patent Office
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Beschwerdekammern

Boards of Appeal

Chambres de recours

Boards of Appeal of the
European Patent Office
Richard-Reitzner-Allee 8
85540 Haar
GERMANY
Tel. +49 (0)89 2399-0

Case Number: T 1758/23 - 3.3.08

D E C I S I O N
of Technical Board of Appeal 3.3.08
of 7 October 2025

Appellant I: (Opponent 1)	Strawman Limited Orchard Lea Horns Lane Combe, Witney Oxfordshire OX29 8NH (GB)
Representative:	Vossius & Partner Patentanwälte Rechtsanwälte mbB Siebertstraße 3 81675 München (DE)
Appellant II: (Opponent 2)	Weinzierl, Gerhard Schiweck Weinzierl Koch Patentanwälte Partnerschaft mbB Ganghoferstraße 68B 80339 München (DE)
Representative:	Schiweck Weinzierl Koch Patentanwälte Partnerschaft mbB Ganghoferstraße 68 B 80339 München (DE)
Appellant III: (Opponent 3)	Dehns Ltd 10 Salisbury Square London EC4Y 8JD (GB)
Representative:	Dehns 10 Old Bailey London EC4M 7NG (GB)
Appellant IV: (Opponent 4)	Maiwald GmbH Elisenhof, Elisenstrasse 3 80335 München (DE)
Representative:	Maiwald GmbH Elisenhof

Elisenstraße 3
80335 München (DE)

Appellant V: (Opponent 5)
Boult Wade Tennant LLP
Salisbury Square House
8, Salisbury Square
London EC4Y 8AP (GB)

Representative:
Boult Wade Tennant LLP
Salisbury Square House
8 Salisbury Square
London EC4Y 8AP (GB)

Appellant VI: (Opponent 6)
Pohlman, Sandra M.
df-mp Dörries Frank-Molnia & Pohlman
Patentanwälte Rechtsanwälte PartG mbB
Fünf Höfe
Theatinerstraße 16
80333 München (DE)

Representative:
Pohlman, Sandra M.
df-mp Patentanwälte Rechtsanwälte PartG mbB
Theatinerstraße 16
80333 München (DE)

Respondent: (Patent Proprietor)
Novartis AG
Lichtstrasse 35
4056 Basel (CH)

Representative:
Breuer, Markus
Sendlinger Straße 29
80331 München (DE)

Decision under appeal: **Decision of the Opposition Division of the European Patent Office posted on 4 August 2023 rejecting the opposition filed against European patent No. 3330370 pursuant to Article 101(2) EPC**

Composition of the Board:

Chairwoman T. Sommerfeld
Members: R. Morawetz
A. Bacchin

Summary of Facts and Submissions

I. The appeals lodged by opponent 1 (appellant I), opponent 2 (appellant II), opponent 3 (appellant III), opponent 4 (appellant IV), opponent 5 (appellant V) and opponent 6 (appellant VI) lie from the opposition division's decision rejecting the oppositions against European patent No. 3 330 370 B1 ("the patent"). The patent was granted on European patent application No. 17 199 357.9 published as EP 3 330 370 A1 ("application as filed"), which was filed as a divisional application in respect of earlier European patent application No. 11 715 933.5.

II. The patent was opposed in its entirety 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 (c) EPC.

III. In their statement of grounds of appeal, appellant IV maintained added matter objections to claim 9 as granted.

IV. In their reply to the appeal, the patent proprietor (respondent) submitted sets of claims of a main request (claims as granted) and auxiliary requests 1 to 5.

V. Claims 1, 3 and 9 of the main request read as follows:

"1. A process for the production of a recombinant polypeptide comprising culturing CHO cells in a medium and expressing the recombinant polypeptide, wherein
- the cells are grown at a first temperature for at least 3 days and the temperature is then shifted to a

second temperature which is between about 1 and about 8°C lower than the first temperature and the cells are maintained at said second temperature for a period of at least another 2 days;
- the cells are grown at a first pH value for at least 2 days and the pH is then shifted to a second pH value which is between about 0.05 and about 1 pH units lower than the first pH and the cells are grown at said second pH for at least 1 day, wherein the temperature shift is initiated between 1 to 5 days after the pH shift."

"3. The process according to claim 1 wherein the pH is passively changed between said first and said second pH value."

"9. The process according to any of the claims 1 to 7 wherein the first pH shift is followed by a second pH shift after at least 1 day with the third pH value being about 0.05 pH units to about 1 pH unit higher than the second pH value."

Claim 1 of auxiliary request 1 differs from claim 1 of the main request in that the features of claim 9 of the main request have been incorporated into claim 1.

Claim 1 of auxiliary request 2 differs from claim 1 of the main request in that the features of claim 3 of the main request have been incorporated into claim 1 while claim 7 of auxiliary request 2 corresponds to claim 9 of the main request.

Claim 1 of auxiliary request 3 combines the amendments made in claim 1 of auxiliary requests 1 and 2.

Claim 1 of auxiliary request 4 corresponds to claim 1 of auxiliary request 1 and includes the additional requirement "*wherein the pH is passively changed from said second to said third pH value, and wherein the third pH value is maintained until harvest.*"

Claim 1 of auxiliary request 5 combines the amendments made in claim 1 of auxiliary requests 2 and 4.

VI. The board scheduled oral proceedings in accordance with the parties' requests and, in a communication pursuant to Article 15(1) RPBA, expressed the preliminary opinion that claim 9 of the main request contravened Article 123(2) EPC and that auxiliary requests 1 to 5 contravened Article 123(2) EPC for the same reasons as the main request.

VII. The parties' submissions and arguments, in so far as they are relevant to the present decision, are discussed in the Reasons for the Decision.

VIII. The parties' requests relevant to the present decision are as follows.

The appellants request that the decision under appeal be set aside and the patent be revoked in its entirety.

The respondent requests that the opponents' appeals be dismissed and that the patent be maintained on the basis of the main request (claims as granted), or alternatively, that the patent be maintained in amended form on the basis of the set of claims of one of auxiliary requests 1 to 5.

Reasons for the Decision

Main request

Added subject-matter (Article 100(c) in conjunction with Article 123(2) EPC) - claim 9

1. Reference is made below to the page and line numbering of the A1 publication (section I. above), referred to as the application as filed.

2. The standard for assessing compliance with the requirements of Articles 123(2) EPC is the so-called "gold standard" set out in G 2/10 (OJ EPO 2012, 376, Reasons 4.3). Amendments are only permitted 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 as filed. The subject-matter of an amended claim must be at least implicitly disclosed to the skilled person, using common general knowledge, in the application as filed (ibid., Reasons 4.7). After the amendment, the skilled person may not be presented with new technical information (ibid., Reasons 4.5.1).

3. It is also well established in the case law of the boards of appeal that the content of an application must not be considered to be a reservoir from which features pertaining to separate embodiments of the application or to separate lists of features can be combined in order to artificially create a particular embodiment. In the absence of any pointer to that particular combination, this combined selection of features does not, for the person skilled in the art, emerge clearly and unambiguously from the content of

the application as filed (see Case Law of the Boards of Appeal of the European Patent Office, 11th edition 2025 ("Case Law"), II.E.1.6.1 a) and I.E.1.6.2 a)). A pointer to the combined selection of features may be an example or embodiment in the description. The fact that the features in question were mentioned as "preferred" in the description may also serve as a pointer. Conversely, the mere fact that something was not excluded in the application as originally filed does not constitute a pointer.

4. Claim 9 of the main request, read in conjunction with claim 1 of the main request, defines a process for the production of a recombinant polypeptide comprising a first pH shift, a temperature shift which is initiated between 1 and 5 days after the first pH shift, and a second pH shift at least 1 day after the first pH shift (see section V. above for the full wording of claims 1 and 9 of the main request).

5. It is common ground that claim 1 of the main request is based on claim 1 as filed to which the feature "*wherein the temperature shift is initiated between 1 to 5 days after the pH shift*" was added before grant and that dependent claim 9 of the main request corresponds literally to claim 9 as filed.

6. Neither claim 1 as filed nor claim 9 as filed define the relative timing of temperature shift and pH shift(s). Claim 9 as filed, read in conjunction with claim 1 as filed, therefore discloses a process which, in addition to the pH and temperature shifts defined in claim 1 as filed, comprises a second pH shift, but wherein the relative timing of the temperature shift with respect to the two pH shifts is not specified.

7. While claim 9 of the main request has not been amended with respect to claim 9 as filed, the amendment in claim 1 (point 5. above) has the consequence that claim 9 of the main request relates to a different process compared to claim 9 as filed.

8. The sole issue addressed in this decision is whether the claimed combination of the relative timing of temperature shift and second pH shift in the process according to claim 9 has a basis in the application as filed.

9. The opposition division held that "*the only selection which has been made compared to original claims 1 and 9 was to limit the relative timing of the temperature and pH shift in claim 1 based on par. 52. This corresponds to one single selection from one single list of three options for performing the temperature shift, prior to, simultaneously with or after the pH shift. Consequently, also any putative overlap of temperature and second pH shift was already disclosed in the original application, i.e. in claims 1 and 9 and par. 52.*" (decision under appeal, Reasons 5.3.1)

10. The feature which has been added to claim 1, i.e. "*wherein the temperature shift is initiated between 1 to 5 days after the pH shift*" derives from a specific embodiment in paragraph [0052] of the application as filed. This embodiment is one of several equally preferred embodiments disclosed in paragraph [0052] of the application. Even if it were accepted that the addition of the timing feature to independent claim 1 "*corresponds to one single selection from one single list*", it does not necessarily follow - contrary to the opposition division's view - that the combination of features in dependent claim 9 resulting from the

amendment to claim 1, is therefore also directly and unambiguously derivable from the application as filed. Put simply, the process according to claims 1 and 9 as filed is not the same as the process according to amended claim 1 plus claim 9. That amended claim 1 has a basis is not therefore sufficient to allow the conclusion to be drawn that amended claim 1 plus claim 9 has a basis.

11. For the purpose of the analysis below, the board accepts the respondent's position that the disclosure in paragraph [0052] of the application as filed relates to the pH and temperature shifts as defined in claim 1 as filed, i.e. that in paragraph [0052] of the application as filed the relative timing of the temperature shift is indicated with respect to the first pH shift.

12. Paragraph [0052] of the application as filed is silent about a second pH shift and any relative timing of the temperature shift and a second pH shift. Claims 1 and 9 as filed are also silent about any relative timing between temperature and pH shift(s). Any overlap between temperature shift and second pH shift is therefore not already disclosed in paragraph [0052] and claims 1 and 9 of the application as filed.

13. The opposition division's reasoning cannot therefore hold. The board moreover agrees with appellant IV that, in order to arrive at the subject matter of claim 9 of the main request, further features would have to be selected from the application as filed in addition to the selection identified by the opposition division.

14. Although the respondent conceded that paragraph [0052] of the application as filed does not contain any

teaching concerning the relative timing of the temperature shift of claim 1 and the second pH shift according to claim 9, it submitted that this would mean that paragraph [0052] did not contain any teaching "excluding" the possibility that the temperature shift as defined in claim 1 overlaps with the second pH shift as defined in claim 9.

15. However, the board notes that a pointer to the claimed combination of features is needed (point 3. above). The fact that something is not excluded does not constitute a pointer. Therefore, even if it were accepted that paragraph [0052] of the application as filed does not exclude the possibility of a temperature shift as defined in claim 1 overlapping with a second pH shift as defined in claim 9, this would not provide sufficient basis for the claimed combination of features in claim 9 of the main request within the meaning of Article 123(2) EPC.

16. The respondent's argument, namely that paragraphs [0057], [0058], [0061] and [0062] of the application as filed also did not exclude the possibility of the temperature shift and the second pH shift occurring at the same time if the temperature shift is initiated 1 to 5 days after the pH shift to a second pH value, fails for the same reasons.

17. In a further line of argument, the respondent submitted that paragraph [0058] of the application as filed supported the possibility that the second pH shift and the temperature shift "may occur" at the same time. This argument was not found persuasive for the following reasons.

18. The board notes that "*may occur*" is not sufficient to provide a pointer (point 3. above).

19. Furthermore, paragraph [0058] of the application as filed actually reads "[i]*n a further aspect of the invention the second pH shift may also occur actively or passively to reach said third pH value. In the first embodiment this can be done by actively changing the pH set point as already outlined for the first pH shift (see above). The timing of the second pH shift can be defined in days after the first pH shift and/or again made dependant on metabolic parameters, such as e.g. lactate concentration. Such a shift may typically occur between 1 and 10 days after the first shift in pH.*" (emphasis added by the board).

20. Therefore, firstly, paragraph [0058] of the application as filed discloses that defining the timing of the second pH shift in terms of days after the first pH shift is just one option among several. Therefore, relying on one option instead of the others requires a selection to be made.

21. Secondly, and more importantly, the occurrence of a second pH shift between 1 and 10 days after the first shift in pH is disclosed in the context of a pH shift that is made dependent on metabolic parameters. Therefore, this disclosure is irrelevant to the claimed subject-matter. Thirdly, paragraph [0058] of the application as filed contains no information about the timing of a temperature shift in relation to the second pH shift and is completely silent as to whether it is intended for the second pH shift to overlap with the temperature shift.

22. As regards the respondent's argument that the period indicated in paragraph [0058] of the application as filed for the second pH shift overlaps with the period defined in claim 1 of the main request for initiation of the temperature shift, the board notes that any pointer to the claimed combination of features must be provided in the application as filed (point 2. above). Therefore, the respondent cannot rely on the feature "*wherein the temperature shift is initiated between 1 to 5 days after the pH shift*" in claim 1 of the main request to provide a pointer to the combination of the claimed features, because this feature is not present in claim 1 as filed, but derives from an embodiment which does not comprise a second pH shift (paragraph [0052] of the application as filed).

23. During the oral proceedings before the board, the respondent provided a further line of argument as follows. Only one selection was required to arrive at the subject-matter of claim 9 of the main request, namely to limit claim 1 as filed based on a selection from the various options disclosed in paragraph [0052] of the application as filed. In the paragraphs following paragraph [0052], the application as filed disclosed further possible aspects of the process of the invention including, in paragraph [0057], the possibility of a further pH shift. The definition of the pH shift in paragraph [0057] was identical to that in claim 9 as filed. Example 2 fell within the process as defined in claim 9 and therefore provided a pointer to the claimed combination of features. The relative timing of temperature shift and second pH shift covered in the process of claim 9 of the main request was therefore disclosed in the application as filed.

24. The board disagrees. Paragraph [0057] reads "[i]*n a further aspect of the invention the first pH shift is followed by a second shift. The second pH shift occurs at least 1 day after the first one and the third pH value that is reached is at least 0.05 pH units higher than the second pH.*" (emphasis added by the board).

25. As correctly noted by the appellants, paragraph [0057] of the application as filed is silent about the relative timing of the second pH shift with respect to any temperature shift and also silent as to whether the second pH shift is intended to overlap with the temperature shift. The appellants are also right that paragraph [0057] refers to one of several "further" aspects of the invention (see paragraphs [0053], [0055], [0056] and [0058] of the application as filed) and that the combination of the particular aspect of paragraph [0057] of the application as filed with the timing requirement of one of the timing options disclosed in paragraph [0052] of the application as filed and the process of claim 1 as filed therefore requires more than one selection. In addition, as explained by the board in the oral proceedings, contrary to the respondent's view, paragraph [0057] of the application as filed is not identical to claim 9 as filed because it defines the third pH value as being "*at least 0.05 pH units higher than the second pH*" while claim 9 defines it as "*being about 0.05 pH units to about 1 pH unit higher than the second pH value*".

26. As regards the respondent's reliance on Example 2, the board notes that this describes a process for the production of a recombinant antibody comprising culturing mAb2-producing CHO cells in a 300-L bioreactor. The relevant passage of Example 2 reads "[o]*n day 5, the temperature of the bioreactor is*

shifted from 36.5°C to 33°C. The pH setpoint is 6.90 and the deadband is 0.10. As a result, the culture starts at pH 7.00, the pH drifts down to 6.80 between day 2 and day 4, and then progressively returns to 7.00 due to lactic acid consumption by the cells (Fig. 6). The shift to pH 6.80 enables to reduce the addition of base compared to a scenario with a constant pH 7.00." (application as filed, page 14, lines 3 to 7).

27. The appellants are right that the pH shifts are not spelled out in example 2 and that the application as filed does not provide a pH profile for Example 2. They are also right that it is not possible to derive directly and unambiguously from the indication that "*the pH drifts down to 6.80 between day 2 and day 4, and then progressively returns to 7.00 due to lactic acid consumption by the cells (Fig. 6)*" that the pH is kept constant for "at least one day" and hence that the cells are grown at the second pH for at least 1 day. Accordingly, it cannot be derived directly and unambiguously from the application as filed that in Example 2 the second pH shift occurs "*at least one day*" after the first pH shift.

28. In this context, the board notes that Figure 6 shows the lactate concentration over cultivation time in Example 2. As pointed out by the appellants, it was the respondent's position throughout the proceedings that the pH profile cannot be inferred directly and unambiguously from the lactate profile (e.g. reply, page 30, last paragraph to page 31, last paragraph).

29. The appellants are therefore also right that Example 2 of the application as filed cannot provide the required pointer for the combination of the timing requirement disclosed in paragraph [0052] of the application as

filed, the further pH shift as defined in paragraph [0057] of the application as filed and the process of claim 1 as filed.

30. The board concludes from the above that the application as filed does not provide any pointer to the claimed combination of the relative timing of temperature shift and second pH shift in the process according to claim 9 of the main request. The subject-matter of claim 9 is therefore not directly and unambiguously derivable from the application as filed.

31. The ground for opposition in Article 100(c) in conjunction with Article 123(2) EPC therefore prejudices maintenance of the patent as granted.

Auxiliary requests 1 to 5

32. In auxiliary requests 1, 3, 4 and 5, the subject-matter of claim 9 of the main request has been introduced into claim 1 (see section V. above). In auxiliary request 2, claim 7 corresponds to claim 9 of the main request (ibid.). Hence, each of auxiliary requests 1 to 5 contains a claim comprising the subject-matter of claim 9 of the main request.

33. Auxiliary requests 1 to 5 therefore contravene Article 123(2) EPC for the same reasons as set out above for claim 9 of the main request. This was not disputed by the respondent.

Conclusion

34. None of the requests on file is allowable. Therefore, the decision under appeal must be set aside and the patent revoked.

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:

C. Rodríguez Rodríguez T. Sommerfeld

Decision electronically authenticated