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**Datasheet for the decision
of 19 September 2024**

Case Number: T 2189/22 - 3.3.02

Application Number: 14827224.8

Publication Number: 3131912

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A23L5/00, A23L33/00, A23L29/30,
A61K31/702

Language of the proceedings: EN

Title of invention:

PROCESS FOR EFFICIENT PURIFICATION OF NEUTRAL HUMAN MILK
OLIGOSACCHARIDES (HMO) FROM MICROBIAL FERMENTATION

Patent Proprietor:

Chr. Hansen HMO GmbH

Opponents:

Glycom A/S
Nestlé Deutschland AG
FrieslandCampina Nederland B.V.
Danisco US Inc.
Greaves Brewster LLP
BASF SE

Headword:

Relevant legal provisions:

EPC 1973 Art. 56

EPC Art. 89

RPBA 2020 Art. 13(1), 13(2)

Keyword:

Inventive step

Priority

Late-filed auxiliary requests

Decisions cited:

Catchword:



Beschwerdekammern
Boards of Appeal
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Case Number: T 2189/22 - 3.3.02

D E C I S I O N
of Technical Board of Appeal 3.3.02
of 19 September 2024

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Decision under appeal: **Interlocutory decision of the Opposition
Division of the European Patent Office posted on
8 July 2022 concerning maintenance of the
European Patent No. 3131912 in amended form.**

Composition of the Board:

Chairman M. O. Müller
Members: S. Bertrand
L. Bühler

Summary of Facts and Submissions

- I. The appeals by the patent proprietor, opponent 3 and opponent 5 lie from the opposition division's interlocutory decision finding that European patent No. 3 131 912 in amended form in accordance with auxiliary request 1 comprising the set of claims filed on 29 March 2022 met the requirements of the EPC.
- II. Since the patent proprietor, opponent 3 and opponent 5 are both appellants and respondents in these appeal proceedings, they are referred to as "patent proprietor", "opponent 3" and "opponent 5" in the following.
- III. The patent is concerned with the provision of a process for purification of neutral human milk oligosaccharides produced by microbial fermentation. Human milk oligosaccharide(s) is(are) abbreviated as "HMO(s)" in the following.
- IV. The following documents are used in the present decision:
- | | |
|------|----------------------------|
| D2 | EP 2 896 628 A1 |
| D5 | WO 2015/049331 A1 |
| D8 | WO 2014/086373 A1 |
| D23 | CN101691538A |
| D23a | English translation of D23 |
| D48 | CN101691538B |
- V. In the impugned decision, the opposition division's conclusions included that the subject-matter of claim 1

of the main request lacked novelty in view of the disclosure of D5 and that the subject-matter of claim 1 of auxiliary request 1 involved an inventive step starting from D8.

- VI. In its statement of grounds of appeal, the patent proprietor contested the opposition division's decision on the main request. It also submitted claim sets according to auxiliary requests 1 to 11.
- VII. In their statements of grounds of appeal, opponents 3 and 5 raised objections against the claims of the auxiliary request held allowable by the opposition division.
- VIII. In its reply to opponents 3's and 5's grounds of appeal, the patent proprietor rebutted the objections raised by the opponents.
- IX. In their replies to the patent proprietor's grounds of appeal, opponents 3 and 5 provided further submissions against novelty and inventive step of the subject-matter of claim 1 of the main request and sufficiency of disclosure of the invention underlying that subject-matter. They provided submissions on auxiliary requests 1 to 11.
- X. In further letters, the patent proprietor addressed objections raised by the opponents, and opponent 5 contested the patent proprietor's submissions made in its reply to the grounds of appeal.
- XI. The board summoned the parties to oral proceedings as per their requests and issued a communication under Article 15(1) RPBA.
- XII. Oral proceedings before the board were held by videoconference on 19 September 2024 in the presence of

the patent proprietor and opponents 3 and 5 and in the absence of opponents 4 and 6. During the oral proceedings, the patent proprietor filed a new auxiliary request.

XIII. The parties' requests relevant to the decision were as follows.

The patent proprietor requested:

- that the appealed decision be set aside and that the patent be maintained in amended form on the basis of the claims of the main request filed with the statement of grounds of appeal
- or, alternatively, on the basis of the claim sets of one of:
 - auxiliary request 5
 - the new auxiliary request filed during oral proceedings
 - auxiliary requests 1 to 4 and 6 to 11, auxiliary requests 1 to 11 having been filed with the statement of grounds of appeal.

Opponent 3 requested that the appealed decision be set aside and that the patent be revoked in its entirety.

Opponent 5 requested:

- that the appealed decision be set aside and that the patent be revoked in its entirety, and
- that auxiliary requests 1 to 4, 7 and 9 to 11 not be admitted into the proceedings.

XIV. The patent proprietor's case and the opponents' cases relevant to the present decision are summarised below.

Reasons for the Decision

Main request

1. Inventive step - claim 1 - Article 56 EPC

1.1 Opponent 3 submitted that the priority of the patent was not valid, meaning that D8 could be used as prior art for the assessment of inventive step. Accordingly, it objected to the inventive step of the subject-matter of claim 1 of the main request starting from D8.

1.2 Priority - Article 89 EPC

The patent claims the priority date of 20 January 2014 and has a filing date of 23 December 2014.

D8 is an international patent application with a filing date of 5 December 2013, prior to the priority date of the patent, and was published on 12 June 2014, i.e. between the priority date and the filing date of the patent. The requirements of Rule 165 EPC are fulfilled by D8.

Claim 1 of the main request reads as follows:

"1. Process for purification of neutral human milk oligosaccharides (HMOs) in a batch manner or in a continuous manner from a fermentation broth obtained by microbial fermentation, the fermentation broth comprising a neutral HMO, biomass, medium components and contaminants, wherein the neutral HMO is selected from the group consisting of 2'-fucosyllactose, 3-fucosyllactose, 2',3-difucosyllactose, lacto-N-triose II, lacto-N-tetraose, lacto-N-neotetraose, lacto-N-

fucopentaose I, lacto-N-neofucopentaose, lacto-N-fucopentaose II, lacto-N-fucopentaose III, lacto-N-fucopentaose V, lacto-N-neofucopentaose V, lacto-N-difucohexaose I, lacto-N-difucohexaose II, 6'-galactosyllactose, 3'-galactosyllactose, lacto-N-hexaose and lacto-N-neohexaose and wherein the purity of the neutral HMO in the fermentation broth is < 80 %, characterized in that the fermentation broth is applied to the following purification steps:

- i) Separation of biomass from the fermentation broth,*
 - ii) Cationic ion exchanger treatment for the removal of positively charged material,*
 - iii) Anionic ion exchanger treatment for the removal of negatively charged material,*
 - iv) Nanofiltration step and/or electro dialysis step,*
- wherein a purified solution comprising the neutral HMO at a purity of ≥ 80 % is provided and wherein the purified solution is spray-dried."*

Thus, step iv) of the process of claim 1 of the main request includes three alternatives:

- one implying a nanofiltration step
- one implying a nanofiltration step and an electro dialysis step
- one implying an electro dialysis step

The priority document (D2) of the patent does not disclose any step of nanofiltration. It follows that the priority of the patent is not valid for the alternatives of claim 1, which imply a nanofiltration

step or a nanofiltration step and an electro dialysis step.

Pursuant to Articles 54(2) and 89 EPC, D8 can therefore be used for the assessment of the inventive step of claim 1 of the main request, where step iv) is a nanofiltration step or a nanofiltration step and an electro dialysis step. This was not contested by the patent proprietor.

1.3 Disclosure of D8

It was common ground that D8 represents a suitable starting point for the assessment of inventive step of the claimed subject-matter.

D8 (summary of the invention on pages 2 and 3) relates to a process for obtaining an HMO in crystalline form by crystallising the HMO from an alcohol solution.

The last paragraph of page 7 of D8 discloses the separation of a non-acid HMO (a neutral HMO) from a fermentation broth, preferably resulting from fermentation with E-coli. The fermentation broth is centrifuged and subsequently treated with cation and anion exchange resins.

The first paragraph on page 8 of D8 discloses that the resulting solution obtained after treatment with cation and anion exchange resins is then dried by, e.g. spray drying.

In view of the disclosure of D8, the board acknowledges that D8 represents a suitable starting point for the assessment of inventive step of the claimed subject-matter.

It was common ground between the parties that D8 discloses a process for purification of a neutral HMO from a fermentation broth comprising steps i) to iii) as defined in claim 1 of the main request and a step where the solution of HMO is spray dried.

1.4 Distinguishing feature

The patent proprietor submitted that the distinguishing feature of claim 1 of the main request was that, according to the process of claim 1 of the main request, a nanofiltration step or a nanofiltration step and an electro dialysis step were carried out while in the disclosure of D8, a crystallisation step was performed instead. Hence, in the process of claim 1 of the main request, the crystallisation step of D8 was replaced by a nanofiltration step or a nanofiltration step and an electro dialysis step.

The board does not agree.

As submitted by opponents 3 and 5, claim 12 as granted is a claim dependent on, *inter alia*, claim 1 as granted. Claim 12 requires that the purified solution be concentrated and cooled to obtain a crystalline HMO, this implying a crystallisation step. It follows that claim 1 of the main request, which is identical to claim 1 as granted, may include a crystallisation step in addition to the nanofiltration step or the nanofiltration step and the electro dialysis step. Therefore, it cannot be concluded that the distinguishing feature of claim 1 of the main request in view of the disclosure of D8 is the application of a nanofiltration step or a nanofiltration step and an electro dialysis step instead of the crystallisation step of D8.

On the contrary, the distinguishing feature of claim 1 of the main request in view of the disclosure of D8 is only that in addition to the crystallisation step of D8, a nanofiltration step or a nanofiltration step and an electrodialysis step are carried out.

1.5 Objective technical problem

Owing to the avoidance of the crystallisation step of D8, the patent proprietor argued that the technical effect was that the claimed process was more economical and safer and resulted in HMOs having a degree of purity as high as that of the process disclosed in D8. The objective technical problem was therefore "the provision of an improved industrial process for HMO purification".

The board disagrees.

As set out above, the claimed process can include a crystallisation step in addition to a nanofiltration step or a nanofiltration step and an electrodialysis step. It follows that the effect achieved by the absence of crystallisation (a more economical and safer method) cannot be taken into account in the formulation of the objective technical problem.

Furthermore, as submitted by opponents 3 and 5, the patent proprietor did not submit any evidence on the degree of purity achieved by the claimed process in comparison with the process of D8. The alleged degree of purity of the HMO therefore cannot be taken into account either in the formulation of the objective technical problem.

It follows that the objective technical problem is merely the provision of an alternative process for purifying HMOs.

1.6 Obviousness

As submitted by opponents 3 and 5, purification by nanofiltration of oligosaccharides is known to the skilled person, as evidenced by the following documents. D23/D48 relates to the purification of galactooligosaccharides. Paragraph [0028] of D23a (English translation of D23) teaches a nanofiltration step for separating galactooligosaccharides from a reaction mixture. This teaching is also available from D37. D37 relates to a process for the purification of galactooligosaccharides including a nanofiltration step (page 19, first paragraph). It follows that the additional nanofiltration step as required by claim 1 of the main request is merely an arbitrary choice from a host of possible solutions known to the skilled person. It can therefore not contribute to inventive step.

The patent proprietor submitted that the skilled person starting from D8 would not have replaced the crystallisation step disclosed in D8, which was essential, with the far simpler step of nanofiltration (or nanofiltration and electrodialysis) as claimed. There was no teaching motivating the skilled person to modify the process of D8 to arrive at the subject-matter claimed.

The board does not agree. As set out above, claim 1 of the main request covers a process where both crystallisation and nanofiltration are carried out. Hence, to arrive at the claimed subject-matter, it is not necessary to replace the crystallisation step of D8 with nanofiltration as argued by the proprietor. The patent proprietor's submission based on the replacement

of crystallisation with nanofiltration is thus not relevant.

The patent proprietor also submitted that only documents on the purification of HMOs from a fermentation broth would be considered by the skilled person. The skilled person would thus not look at documents such as D23/D48 and D37.

The board disagrees. As argued by opponents 3 and 5, the subject-matter of claim 1 of the main request relates to the technical field of oligosaccharide purification. When looking for alternatives, the skilled person would not have only contemplated applying additional steps used in the technical field of HMOs but would have considered any additional step used in oligosaccharide purification.

- 1.7 In view of the above, the subject-matter of claim 1 of the main request does not involve an inventive step starting from D8.
2. Therefore, the main request is not allowable.

Auxiliary request 5

3. Inventive step - claim 1 - Article 56 EPC
- 3.1 Claim 1 of auxiliary request 5 is identical to claim 1 of the main request.
- 3.2 The board thus concludes that the reasons given for inventive step of the subject-matter of claim 1 of the main request apply *mutatis mutandis* to the subject-matter of claim 1 of auxiliary request 5. This conclusion was not disputed by the patent proprietor.
4. Auxiliary request 5 is thus not allowable.

New auxiliary request

5. Admittance of the new auxiliary request
- 5.1 During the oral proceedings before the board, the patent proprietor filed a new request.
- 5.2 Opponents 3 and 5 objected to the admittance of this new request into the appeal proceedings.
- 5.3 Claim 1 of the new auxiliary request differs from claim 1 of the main request in that, for step iv), the two alternatives implying a nanofiltration step have been deleted. Step iv) in claim 1 of the new auxiliary request is limited to an electro dialysis step.
- 5.4 Under Article 13(2) RPBA, any amendment to a party's appeal case made after notification of a communication under Article 15(1) RPBA must, as a rule, not be taken into account unless there are exceptional circumstances justified with cogent reasons by the party concerned.
- 5.5 The patent proprietor submitted that the limitation made in claim 1 of the new auxiliary request restored priority for the subject-matter claimed and thus overcame the inventive-step objection starting from D8, which was no longer prior art. The limitation made in claim 1 of the new auxiliary request restricted the subject-matter to one of the three alternatives covered by claim 1 of the main request discussed before the opposition division and on appeal. The limitation did not trigger a new discussion on inventive step starting from D23/D48 since the patent proprietor's position had always been that these documents related to different chemical entities and were not suitable as a starting point for the assessment of inventive step.

5.6 The board understands the proprietor's argument to be that the new auxiliary request did not constitute an amendment of the proprietor's appeal case. The board disagrees with the patent proprietor. As submitted by opponents 3 and 5, since document D8 is no longer prior art suitable for the assessment of the inventive step of the subject-matter of claim 1 of the new auxiliary request, inventive step over the other documents, including D23/D48 cited by the opponents for lack of inventive step, becomes an issue. As discussed during the oral proceedings, as regards D23/D48, in view of the amendment carried out in step iv) of claim 1, it would need to be discussed for the first time whether this step, i.e. the remaining alternative of electro dialysis, is an additional distinguishing feature.

The limitation to electro dialysis in step iv) of claim 1 of the new auxiliary request thus represents an amendment of the patent proprietor's appeal case. It needs thus to be examined whether there were exceptional circumstances within the meaning of Article 13(2) RPBA that justify admittance of this amendment.

According to the proprietor, the submission of the new auxiliary request was a reaction to the board's conclusion on inventive step of the main request made during the oral proceedings.

However, as submitted by opponents 3 and 5, there are no exceptional circumstances. The objection based on lack of inventive step in view of D8 has been on file during the entire opposition proceedings, and the opposition division's decision on inventive step starting from document D8 was contested by opponent 3 on appeal. The board has merely accepted opponent 3's arguments presented on appeal. An outcome in appeal

different from that before the opposition division cannot be considered to amount to exceptional circumstances.

5.7 For these reasons, the board decided not to admit the new auxiliary request into the appeal proceedings.

Auxiliary requests 1 to 4, 6 to 9 and 11

6. Inventive step - claim 1 - Article 56 EPC

6.1 Claim 1 of auxiliary requests 1 to 4, 6 to 9 and 11 was amended as follows.

- Auxiliary request 1: claim 1 of auxiliary request 1 is a combination of claims 1 and 2 of the main request. The fermentation broth is obtained by microbial fermentation using a recombinant bacteria or yeast, more preferably a recombinant bacteria or yeast grown in a chemically defined medium, where the biomass separated in step i) is optionally recycled to the microbial fermentation.
- Auxiliary request 2: claim 1 of auxiliary request 2 further specifies, in view of claim 1 of the main request, that the yield of the neutral HMO is defined as > 70%.
- Auxiliary request 3: claim 1 of auxiliary request 3 further specifies that the fermentation broth separated from the biomass is passed over the cationic ion exchanger or is diafiltered and/or concentrated, preferably with a nanofiltration membrane.
- Auxiliary request 4: claim 1 of auxiliary request 4 is based on claim 1 of the main request and specifies that the fermentation broth separated from the biomass is passed over the cationic ion

exchanger (in proton form) or is diafiltered and/or concentrated, preferably with a nanofiltration membrane.

- Auxiliary request 6: based on claim 1 of the main request, claim 1 of auxiliary request 6 incorporates the limitation that the fermentation broth is obtained by microbial fermentation using a recombinant bacteria or yeast only when step iv) is a nanofiltration step or a nanofiltration step and an electro dialysis step.
- Auxiliary request 7: claim 1 of auxiliary request 7 is based on claim 1 of the main request, and when step iv) is a nanofiltration step or a nanofiltration step and an electro dialysis step, it additionally comprises a disclaimer excluding the disclosure combining embodiments disclosed on pages 9 and 12 of D5.
- Auxiliary request 8: claim 1 of auxiliary request 8 is identical to claim 1 of auxiliary request 1.
- Auxiliary request 9: claim 1 of auxiliary request 9 is identical to claim 1 of auxiliary request 2.
- Auxiliary request 11: claim 1 of auxiliary request 11 is identical to claim 1 of auxiliary request 4.

6.2 During the oral proceedings, the chairman stated that in the absence of any argument for any effect resulting from the features that had been added to claim 1 of auxiliary requests 1, 2, 4, 6 to 9 and 11, the objective technical problem could only be formulated as the provision of an alternative process for purifying HMOs, and the additional features were thus merely an arbitrary choice from a host of possible solutions known to the skilled person. The subject-matter of

claim 1 of these auxiliary requests thus appeared not to be inventive starting from D8.

In the absence of any submission in reply to this observation, the board concludes that the reasons given for the subject-matter of claim 1 of the main request apply *mutatis mutandis* to the subject-matter of claim 1 of each of auxiliary requests 1 to 4, 6 to 9 and 11.

7. Auxiliary requests 1 to 4, 6 to 9 and 11 are for this reason not allowable.
8. Since it was found that auxiliary requests 1 to 4, 7, 9 and 11 were not allowable, a decision on their admittance was not required.

Auxiliary request 10

9. Inventive step - Claim 1 - Article 56 EPC
 - 9.1 Compared to claim 1 of the main request, claim 1 of auxiliary request 10 further specifies that the fermentation broth separated from the biomass is passed over the cationic ion exchanger or is diafiltered and/or concentrated, preferably with a nanofiltration membrane.
 - 9.2 The parties agreed that D8 represented the closest prior art for the subject-matter of claim 1 of auxiliary request 10.
 - 9.3 The patent proprietor submitted that claim 1 of auxiliary request 10 required that the product obtained after the separation of the fermentation broth from the biomass, i.e. after step i) of the claims, be diafiltered. Therefore, the diafiltration step of the fermentation broth after separation of the biomass represented a further distinguishing feature over D8 in

addition to the nanofiltration step discussed for the main request.

- 9.4 The board does not find the patent proprietor's submission convincing.

The feature "*wherein the fermentation broth separated from the biomass: is passed over the cationic ion exchanger; or is diafiltered and/or concentrated, preferably with a nanofiltration membrane*" in claim 1 of auxiliary request 10 provides two alternatives after the separation of the biomass (step i) in the claim). The first alternative is that the fermentation broth separated from the biomass is passed over the cationic ion exchanger. The second alternative is that the fermentation broth separated from the biomass is diafiltered and/or concentrated.

While it is accepted that the second alternative encompasses a diafiltration step of the fermentation broth separated from the biomass representing a further distinguishing feature in view of D8, the first alternative corresponds to step ii) of the claim ("*Cationic ion exchanger treatment for the removal of positively charged material*"), as submitted by opponents 3 and 5, and does not represent an additional feature in view of the disclosure of D8. As discussed during the oral proceedings, there is thus no further distinguishing feature over D8 in addition to that identified for the subject-matter of claim 1 of the main request.

- 9.5 The board thus concludes that the reasons given for lack of inventive step of the subject-matter of claim 1 of the main request apply *mutatis mutandis* to the subject-matter of claim 1 of auxiliary request 10.

10. Consequently, auxiliary request 10 is not allowable.
11. Since it was found that auxiliary request 10 was not allowable, a decision on its admittance was not required.
12. None of the patent proprietor's claim requests is both admissible and allowable.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.
2. The patent is revoked.

The Registrar:

The Chairman:



U. Bultmann

M. O. Müller

Decision electronically authenticated