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**Datasheet for the decision of 19 September 2023**

**Case Number:** T 0552/22 - 3.3.08

**Application Number:** 09776698.4

**Publication Number:** 2440661

**IPC:** C12N1/00, C12N15/63, C12P19/00, C12P19/18, C12N9/10, C12N15/70

**Language of the proceedings:** EN

**Title of invention:**
HMO synthesis

**Patent Proprietor:**
Chr. Hansen HMO GmbH

**Opponent:**
Grünecker Patent- und Rechtsanwälte Part GmbB

**Headword:**
HMO synthesis

**Relevant legal provisions:**
EPC Art. 100(b)
RPBA 2020 Art. 12(3), 12(5)

**Keyword:**
Grounds for opposition - insufficiency of disclosure (yes)
Discretion not to admit submission - submission admitted (no)

**Decisions cited:**
G 0002/21, T 0435/91, T 0743/97, T 1913/19

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**Beschwerdekammern**

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**Case Number: T 0552/22 - 3.3.08**

# D E C I S I O N
# of Technical Board of Appeal 3.3.08
# of 19 September 2023

| | |
|---|---|
| **Appellant:** (Opponent) | Grünecker Patent- und Rechtsanwälte<br>PartG mbB<br>Leopoldstrasse 4<br>80802 München (DE) |
| **Representative:** | Grammel, Markus<br>Rudolph Hansen, Marianne<br>Biselli, Elena<br>Grünecker Patent- und Rechtsanwälte<br>PartG mbB<br>Leopoldstraße 4<br>80802 München (DE) |
| **Respondent:** (Patent Proprietor) | Chr. Hansen HMO GmbH<br>Maarweg 32<br>53619 Rheinbreitbach (DE) |
| **Representative:** | Laufer, Gabriele<br>Hübel, Andreas<br>Witte, Weller & Partner Patentanwälte mbB<br>Postfach 10 54 62<br>70047 Stuttgart (DE) |
| **Decision under appeal:** | **Decision of the Opposition Division of the European Patent Office posted on 20 December 2021 rejecting the opposition filed against European patent No. 2440661 pursuant to Article 101(2) EPC.** |

**Composition of the Board:**

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| **Chair** | D. Pilat |
| **Members:** | R. Morawetz |
| | R. Winkelhofer |

## Summary of Facts and Submissions

I. European patent No. 2 440 661 ("the patent") is based on European patent application No. 09 776 698.4, which was filed as an international patent application published as WO 2010/142305 ("the application"). The patent is entitled "*HMO synthesis*".

Claim 1 as granted reads as follows:

"1. A bacterial cell to be stably cultured in a medium for the production of oligosaccharides, said oligosaccharides being fucosyllactose, the cell being transformed to comprise at least one nucleic acid sequence coding for a fucosyltransferase,
**characterized in that**
the cell in addition is transformed to comprise at least one nucleic acid sequence coding for a protein of the Sugar Efflux Transporter (SET) family, which protein is overexpressed, the overexpression leading to an export of the oligosaccharides."

II. The following documents are referred to in the decision:

D1 J.Y. Liu *et al.*, Molecular Microbiology 31, 1999, 1845-51

D3 J.Y. Liu *et al.*, J. Biol. Chem. 274, 1999, 22977-84

D18 Supplementary experimental results of Patentee, submitted on 24 August 2020

D19 Supplementary Figure 1, submitted on 22 September 2021

D20 Supplementary experimental data, submitted by the opponent on 22 September 2021, 1-11

D21 Supplementary experimental data, submitted by the opponent on 22 September 2021, 1-4

D22 Screenshots from different searches performed in the Uniprot database, submitted with the appeal, 1-4

III. One opposition was filed against the granted patent. The patent was opposed under Article 100(a) EPC on the ground of lack of inventive step (Article 56 EPC) and under Article 100(b).

The opposition division rejected the opposition.

IV. The opponent (appellant) appealed the opposition division's decision. With the statement setting out the grounds of appeal they submitted, inter alia, document D22.

V. With the reply to the appeal, the patent proprietor (respondent) maintained the patent as granted as their main request and upheld auxiliary requests 1 to 3, submitted on 21 September 2021 during the opposition proceedings.

VI. The board scheduled oral proceedings, in accordance with the parties' requests, and subsequently issued a communication under Article 15(1) RPBA.

VII. During the oral proceedings before the board, the respondent made pending auxiliary request 2 the new auxiliary request 1 and pending auxiliary requests 3 and 1 the new auxiliary requests 2 and 3, respectively.

Claim 1 of the main request is identical to claim 1 as granted.

Claim 1 of auxiliary request 1 is based on claim 1 of the main request, amended to specify that the sugar efflux transporter is SetA.

Claim 1 of auxiliary request 2 is based on claim 1 of the main request, amended to specify that the fucosyllactose is 3'-fucosyllactose and the sugar efflux transporter is SetA.

Claim 1 of auxiliary request 3 is based on claim 1 of the main request, amended to specify that the fucosyllactose is 3'-fucosyllactose.

VIII. The parties' submissions relevant to the decision are discussed in the reasons for the decision below.

IX. The appellant requests that the decision under appeal be set aside and amended such that the patent be revoked.
The respondent requests that the appeal be dismissed (main request) or the patent be maintained in amended form on the basis of auxiliary requests 1 to 3 as submitted on 21 September 2021 and renumbered during oral proceedings.

## Reasons for the Decision

*Admittance and consideration of documents*

1. Documents D18 to D21 had been filed during opposition proceedings. Their admittance and consideration in the appeal proceedings was disputed among the parties.

2. However, given that these documents play no role in the outcome of the appeal proceedings (see below), this question can be left open.

*Main request (patent as granted) - claim 1*

*Claim construction - the claimed invention*

3. Claim 1 is directed to a bacterial cell to be stably cultured in a medium for the production of fucosyllactose, the cell containing a nucleic acid sequence encoding a fucosyltransferase and a nucleic acid sequence encoding a protein of the SET family, where overexpression of the SET protein leads to the export of the fucosyllactose (see section I. above for the complete wording of the claim).

4. The overexpression of the protein of the SET family leading to an export of fucosyllactose is a technical feature of the claim and must accordingly be achieved by the claimed subject-matter across the ambit of the claim.

5. While the SET family of proteins comprises proteins SetA, SetB and SetC (see paragraph [0034] of the patent), claim 1 is not limited to these three proteins but relates generally to any protein of the SET family

of proteins.

*Disclosure of the invention (Article 100(b) EPC)*

6. The opposition division held that with SetA, the patent provided one way of working the invention; that it was not inherently implausible that fucosyllactose could be a substrate for SetB and SetC as well; and that post-published evidence D18 suggested that the invention could also be practised with SetB and SetC. The opposition division concluded that there was not sufficient doubt, supported by verifiable facts, that the person skilled in the art could work the invention over the whole scope of the claim.

7. Under the jurisprudence of the boards of appeal, the requirements of sufficiency of disclosure are met if a person skilled in the art can carry out the invention as defined in the independent claims over the whole ambit of the claims without undue burden based on the disclosure in the patent application (see Case law of the Boards of Appeal of the European Patent Office 10th edition 2022, "CLBA", II.C.5.4). The disclosure of one way of performing an invention is only sufficient if it allows the invention to be performed over the whole range claimed. This principle applies to any invention, irrespective of how it is defined, be it by way of a functional feature or not. A functional definition is acceptable if all alternatives are available and achieve the desired result. For functional definitions of a technical feature, it has to be established whether or not the patent application discloses a technical concept fit for generalisation which makes the host of variants encompassed by the functional definition available to the skilled person (see CLBA, II.C.5.4 and e.g. T 435/91, OJ EPO 1995,

188, Reasons 2.2.1). Sufficiency of disclosure must be shown to exist at the effective date of the patent (priority date or date of filing), i.e. on the basis of the information in the patent application as a whole and taking into account the common general knowledge then available to the skilled person. A lack in this respect cannot be remedied during the proceedings before the EPO by post-published evidence (see CLBA, II.C.1 and G 1/03, OJ EPO 2004, 413, Reasons 2.5.3).

8. In the case in hand, implementation of the claimed functional requirement of the bacterial cells requires that overexpression of the protein of the SET family leading to an export of fucosyllactose be achievable at the filing date without undue burden over the whole range claimed.

9. The appellant maintained on appeal that the patent, taking into account the common general knowledge of the skilled person, did not provide enough guidance to achieve fucosyllactose export by the overexpression of proteins of the SET family over the whole ambit of the claim without undue burden. Thus, the requirement of sufficiency of disclosure was not met.

10. The current invention lies in the field of fermentative production of human milk oligosaccharides (HMO) (see paragraphs [0001] and [0002] of the patent), in particular the production of fucosyllactose, a trisaccharide composed of L-fucose, D-galactose and D-glucose. 2'-fucosyllactose and 3-fucosyllactose are the most prominent HMOs (see paragraph [0004] of the patent).

11. The patent discloses that the SET family "*first described by Liu and co-workers (Liu et al., 1999a)*

[document D1 in the appeal proceedings] *for E. coli, comprises proteins SetA, SetB and SetC*" (see paragraph [0034]); that "[b]*esides glucose and lactose, the SET exporter proteins display substrate specificity for certain mono- and disaccharides* [...]*(Liu et al., 1999b)*[document D3 in the appeal proceedings]. *Biochemical studies showed, however, that, for example, SetA exhibits a very low to zero transport activity for larger or bulkier molecules such as heptoses or trisaccharides*" (see paragraph [0035]); that "*it could not be expected that exporter proteins of the SET family would be suitable at all for the transport of oligosaccharides*" (see paragraph [0036]); that "*SetA, amongst the biochemically characterized members of the SET family of exporter proteins, features the widest substrate specificity*" (paragraph [0044]); and that "*the inventors have found that, surprisingly, the overexpression of SET exporter proteins leads to a very efficient export of oligosaccharides*" (paragraph [0037]).

12. As for the examples of the patent, Example 1 describes, on a theoretical level, oligosaccharide synthesis and transport inside a gram-negative bacterial cell comprising SetA as a product exporter (see also Figure 1). In Examples 2 to 4, overexpression of SetA in *E. coli* strains expressing α 1,3-fucosyltransferase is shown to lead to export of 3-fucosyllactose from the bacterial cell (see e.g. paragraph [0101]).

13. Overexpression of SetA in *E. coli* leading to export of 3-fucosyllactose is therefore one way of performing the claimed invention that is disclosed in the patent. However, claim 1 is not limited to overexpression of SetA but encompasses overexpression of all SET family members and export of fucosyllactose generally (see

also point 5. above).

14. While the patent mentions SetB and SetC, two further members of the SET family of proteins (see paragraph [0034] and point 11. above), it reports no data on these two proteins or any explanation, reasoning or technical basis that would allow the conclusion that any experimental observation on the substrate specificity of SetA could be transferred to other SET family members, including SetB and SetC.

15. The board therefore agrees with the appellant that if, according to the patent, it already came as a surprise that the SET protein with the broadest substrate specificity - SetA - exports fucosyllactose (see point 11. above), it was not demonstrated to the skilled person that SetB and SetC, having a narrower substrate specificity, also export fucosyllactose. Mentioning SetB and SetC in the patent therefore does not suffice to enable the skilled person to achieve the technical effect claimed over the whole ambit of the claim.

16. As for the scientific publications cited in the patent (see paragraphs [0034] and [0035] and point 11. above), document D1 concerns the identification of the SET family based on amino acid sequence similarity. It discloses that two *E. coli* members of this family, YabM (SetA) and YeiO (SetB), have lactose efflux activity but that another *E. coli* member of this family, YicK (SetC), was unable to transport lactose (page 1847, left-hand column, last paragraph). The high degree of sequence similarity was, however, considered by the authors of document D1 to suggest that YicK (SetC) may also function as a sugar efflux pump "whose substrates remain to be identified" (page 1848, left-hand column,

second paragraph, last sentence).

17. Document D3 concerns the functional and biochemical characterisation of SET proteins and discloses that "SetA has broader substrate specificity than SetB. SetA also transports glucosides and galactosides with alkyl or aryl substituents" (see page 22983, right-hand column, first paragraph); that "although vesicles or cells with the *setC* expression constructs were unable to transport glucose, galactose or lactose, the high degree of protein sequence identity of SetC to SetB (70%) suggests that the function is also conserved" (ibid.) and that "additional transport studies with other sugars are warranted to identify substrates for SetC" (ibid.).

18. Hence, document D3 does not relate to members of the SET family generally but to SetA, SetB and SetC, and it discloses that there might be a similar function between SetB and SetC. With respect to the sugars transported by these proteins of the SET family, the skilled person derives from document D3 that SetA, SetB and SetC have different substrate specificities, with SetA having the broadest, while the substrates of SetC remain unknown.

19. Accordingly, neither document D1 nor document D3 provide a technical basis for the conclusion that any experimental observation on the substrate specificity of SetA can be transferred to SetB and SetC, let alone to any other member of the SET family of proteins.

20. The board therefore agrees with the appellant that it cannot be derived from document D3 that any finding for SetA can be extended to SetB and SetC, contrary to what

was held in the decision under appeal.

21. The board furthermore agrees with the appellant that, based on documents D1 and D3, which teach that the SET family is functionally varied, it is also not to be expected that any activity for SetA can simply be transferred to SetB or SetC or any other SET family member.

22. No conclusion on conservation of any substrate specificity, let alone specificity for fucosyllactose between SetA, SetB and SetC, can be derived from document D3. Accordingly, the skilled person would not derive from document D3 that "the members of the SET family can be employed interchangeably", contrary to the respondent's argument (see reply, section II.4).

23. In view of the above considerations, the board agrees with the appellant that also when taking into account the prior art cited in the patent, the technical teaching of the patent on SET family members which upon overexpression lead to export of fucosyllactose is limited to SetA and the export of 3-fucosyllactose (see paragraphs [0034] to [0037] and [0044] and the examples of the patent). Which other proteins of the SET family - if any - will result in fucosyllactose export upon overexpression cannot be inferred from the patent.

24. With respect to the respondent's reliance on the decision under appeal, G 2/21 holds that "the term 'plausibility' [...] does not amount to a distinctive legal concept or a specific patent law requirement under the EPC, in particular under Article 56 and 83 EPC" (Reasons 92). Moreover, G 2/21 explicitly rules on plausibility only in the context of Article 56, distinguishing it from the context of Article 83 (see

headnote and Reasons 11, 73, 74 and 77). Therefore, nothing can be gained by the respondent by referring to plausibility in the given context.

25. Moreover, contrary to the respondent's assertion (see reply, section II.3), the opposition division did not find that "the patent specification already contains experimental evidence showing the plausibility of the claimed technical effect". Instead, the opposition division held that the possibility "that fucosyllactose could be a substrate for all three of SetA, B, and C" was not "inherently implausible" (see decision under appeal, Reasons 20.2.1). However, something not inherently implausible is not necessarily sufficiently disclosed. Furthermore, the opposition division did not explain why it was not "inherently implausible that fucosyllactose could be a substrate for all three of SetA, B, and C", let alone explain that or why it would be shown, based on the teaching in the patent and the common general knowledge available to the skilled person, that if fucosyllactose is a substrate for SetA, it is also a substrate for other members of the SET family of proteins, including SetB and SetC. Indeed, as regards the teaching in the patent, the opposition division merely noted that it "contains an example which teaches the skilled person to overexpress SetA so that fucosyllactose is exported" (see decision under appeal, Reasons 20.2.5), while post-published evidence D18 was considered to be "showing for the first time an effect of SetB and SetC" (see decision under appeal, Reasons 17.2).

26. The respondent's submission that the "[p]roprietor has, in the opposed patent as such [...] made plausible that the invention can be worked by one skilled in the art over the whole scope of the claims" (see reply, section

II.10, emphasis in the original) is a mere assertion devoid of any substantiation and, as stated above, "plausibility" would not be enough in the given context (see again G 2/21). SetA is the sole protein of the SET family disclosed in the patent to lead to an export of fucosyllactose (3-fucosyllactose) upon overexpression.

27. To meet the requirement that the disclosure of the invention be sufficiently clear and complete for it to be carried out by the person skilled in the art, the patent would have to credibly disclose either that all SET family proteins lead to an export of fucosyllactose upon overexpression or provide the skilled person at least with sufficient guidance on how to select the SET family proteins that do lead to an export of fucosyllactose upon overexpression without undue experimentation (see also point 7. above).

28. The respondent has not submitted that the skilled person could rely on common general knowledge, and neither is this apparent. It did, however, submit that the patent also mentioned SetB and SetC and that testing SetB and SetC did not constitute an undue burden for the skilled person.

29. This argument fails for two reasons. First, since claim 1 extends to all SET family members, even if testing two SET family members did not constitute an undue burden, it does not suffice. Second, and more importantly, it is apparent from the above considerations (see points 11. to 23.) that the patent provides no technical rationale on the basis of which the skilled person could predict which proteins of the SET family lead to fucosyllactose export upon overexpression. The skilled person wanting to perform the claimed invention therefore has to test the SET

family members - including SetB and SetC - to determine whether their overexpression leads to export of fucosyllactose. Furthermore, based on the teaching in the patent, the skilled person has no guarantee that any of the tested proteins will work.

30. Under the jurisprudence of the boards of appeal, experimentation and testing is reasonable when the patent or common general knowledge provides the person skilled in the art with sufficient information that leads necessarily and directly to success after evaluating initial failures. However, if the skilled person can only determine by experimenting whether they have selected a parameter (in the current case, the protein of the SET family) in such a way that a satisfactory result will be achieved (in the current case, export of fucosyllactose) without the confidence that this result can be achieved at all, this amounts to an invitation to perform a research programme without any guarantee of success. This amounts to an undue burden for the skilled person, even if it involves routine experimentation (see also CLBA, sections II.C.6.7 and II.C.7.4).

31. The jurisprudence relied on by the respondent is not applicable to the facts of the case. In T 743/97 (Reasons 9), the claim under consideration was a broad group of t-PA variants which were functionally and structurally characterised. The opponents-respondents had expressed no doubt as to the possibility of making these t-PA variants, and the board did not have any doubt either (T 743/97, Reasons 10). It held that in these circumstances, there were no doubts about the possibility of preparing and testing the claimed variants with undue burden or application of inventive skill (T 743/97, Reasons 11). By contrast, in the case

at hand, it has been established (see above) that testing would create an undue burden on the skilled person trying to perform the claimed invention.

32. Therefore, the respondent's additional line of argument cannot succeed, and the appellant is right that the claimed invention cannot be practised over the entire scope of the claim without undue burden of experimentation.

33. Finally, sufficiency of disclosure must be given at the effective date of the patent (see point 7. above), and post-published evidence is manifestly unsuitable for guiding the skilled person in carrying out the claimed invention on the effective date. Lack of disclosure on the suitability of SET family members for fucosyllactose export upon overexpression could not therefore be remedied by post-published evidence such as D18 (see CLBA, II.C.1 and G 1/03, OJ EPO 2004, 413, Reasons 2.5.3).

34. The respondent's assertions that not taking post-published evidence D18 into account was a violation of their right to be heard are not persuasive.

35. The right to be heard does not entail the right to have post-published evidence considered for sufficiency of disclosure. It entails a right to present views that the patent application, taking into account the common general knowledge then available to the skilled person, disclosed the claimed invention in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art.

36. Finally, in the case at hand, there is no relevant guidance in the patent application and the common

general knowledge on SET family proteins which lead to export of fucosyllactose upon overexpression in bacterial cells, except SetA. The patent application and the prior art do not demonstrate that any teaching shown in the patent on SetA can be extended to other SET family proteins, including SetB and SetC. The appellant was therefore under no obligation to provide further experimental evidence to support the insufficiency objection.

37. The board concludes from the above considerations that the claimed invention is not disclosed in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art over the ambit of the claim, without undue burden, using common general knowledge, at the effective date of the patent.

38. The ground for opposition under Article 100(b) EPC therefore prejudices the maintenance of the patent as granted.

*Auxiliary requests 1 to 3*

*Admittance and consideration (Article 12(3) and (5) RPBA)*

39. Auxiliary requests 1 to 3 submitted on 21 September 2021 were re-submitted in reply to the appeal and were renumbered during oral proceedings. The appellant requested that auxiliary requests 1 to 3 not be admitted on the grounds that they had not been substantiated in appeal.

40. Article 12(3) RPBA stipulates that claim requests submitted in reply to the appeal must be justified by reasons as to the extent to which the amendments made overcome the objections raised in the appeal. Pursuant

to Article 12(5) RPBA, the board has discretion not to consider claim requests filed with the reply that do not meet the requirements of Article 12(3) RPBA.

41. In the appeal, the appellant raised objections of sufficiency of disclosure and inventive step.

42. In their reply to the appeal, the respondent provided no reasons why the amendments in auxiliary requests 1 to 3 were made and how they were intended to overcome the objections raised by the appellant. Instead, the respondent referred to their submission of 21 September 2021, filed during opposition proceedings. In that submission, the amendments made in claim 1 of auxiliary requests 1 to 3 submitted on 21 September 2021 and their basis is indicated. However, no reasons are provided on why the amendments are made or which objections they are meant to address. Instead, reference is made to an earlier submission of 27 March 2019 (the reply to the notice of opposition), and it is stated that the arguments made there for the main request (patent as granted) apply to auxiliary requests 1 to 3.

43. First, a generic reference to submissions filed in opposition is not sufficient for providing substantiation in appeal. It can also not be expected that the board or the appellant piece together the respondent's arguments for auxiliary requests 1 to 3 from three different submissions.

44. Second, regarding the respondent's argument that the amendments made in auxiliary request 2 were self-explanatory in that they addressed the appellant's sufficiency of disclosure objection, the board notes that the appellant also raised objections as to lack of

inventive step and that the respondent did not provide any explanation as to how the amendments made in auxiliary request 2 address these objections. Even if including both SetA and 3'-fucosyllactose were considered to address sufficiency of disclosure, it would not be self-explanatory why an inventive step should be acknowledged for the claimed subject-matter given that the appellant also addressed SetA overexpression and 3'-fucosyllactose export in their inventive-step objection against the main request.

45. The respondent's submissions on auxiliary requests 1 to 3 therefore do not meet the requirements of Article 12(3) RPBA.

46. Since Article 13 RPBA mainly serves to allow account to be taken of changes of fact or the subject-matter of the appeal proceedings, within narrow limits, and does not extend to the subsequent substantiation of claim requests, substantiation of auxiliary requests 1 to 3 could not be provided at the oral proceedings (see T 1913/19, Reasons 16).

47. Auxiliary requests 1 to 3 could thus not be admitted and considered in 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 Chair:

L. Malécot-Grob D. Pilat

Decision electronically authenticated