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Datasheet for the decision of 11 December 2024

Case Number: T 0925/23 - 3.3.08

Application Number: 16196486.1

Publication Number: 3315610

IPC: C12P19/18, C12N1/21, C12N9/10, C12N9/12

Language of the proceedings: EN

Title of invention:
Process for the production of fucosylated oligosaccharides

Patent Proprietor:
Chr. Hansen HMO GmbH

Opponent:
Glycom A/S

Headword:
Fucosylated oligosaccharides/HANSEN

Relevant legal provisions:
EPC Art. 123(2)
RPBA 2020 Art. 12(6)

Keyword:
Amendments - extension beyond the content of the application as filed (yes)
Late-filed request - should have been submitted in first-instance proceedings (yes) - circumstances of appeal case justify admittance (no)

Decisions cited:
T 0738/20, T 2011/21

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Case Number: T 0925/23 - 3.3.08

D E C I S I O N
of Technical Board of Appeal 3.3.08
of 11 December 2024

Appellant: (Opponent)	Glycom A/S Kogle Allé 4 2970 Hørsholm (DK)
Representative:	Inspicos P/S Agern Allé 24 2970 Hørsholm (DK)
Respondent: (Patent Proprietor)	Chr. Hansen HMO GmbH Maarweg 32 53619 Rheinbreitbach (DE)
Representative:	Witte, Weller & Partner Patentanwälte mbB Postfach 10 54 62 70047 Stuttgart (DE)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 13 March 2023 concerning maintenance of the European Patent No. 3315610 in amended form**

Composition of the Board:

Chairwoman	T. Sommerfeld
Members:	A. Schmitt
	D. Rogers

Summary of Facts and Submissions

I. The appeal lodged by the opponent (appellant) is against the opposition division's interlocutory decision that European patent No. 3 315 610 B1 (the patent) as amended according to auxiliary request 1 and the invention to which it relates meet the requirements of the EPC.

II. The patent, which is entitled "*Process for the production of fucosylated oligosaccharides*", was granted on the basis of European patent application No. 16 196 486.1, which was published as EP 3 315 610 A1 (the application).

III. The opposition proceedings were based on the grounds for opposition under Article 100(a) EPC in relation to novelty (Article 54 EPC) and inventive step (Article 56 EPC), as well as those under Article 100(b) and (c) EPC.

IV. With its reply to the appeal, the patent proprietor (respondent) made auxiliary request 1 as underlying the decision under appeal its main request, and also filed sets of claims according to auxiliary requests 1 to 8. Auxiliary requests 1 to 5 were new to the proceedings. Auxiliary requests 6 to 8 were identical to auxiliary requests 2 to 4 as filed with the reply to the notice of opposition.

Claim 1 of the main request reads as follows:

"1. Method for the production of fucosylated oligosaccharides using a genetically modified

prokaryotic host cell, the method comprising the steps of:

- providing a prokaryotic host cell, which has been genetically modified, such, that at least (i) the fructose-6-phosphate pool in the cell is increased by lowering or abolishing the activity of a fructose-6-phosphate-converting enzyme, which in the unmodified host cell has a regular level, wherein said fructose-6-phosphate converting enzyme is selected from the group consisting of phosphofructokinase, glucose-6-phosphate isomerase, fructose-6-phosphate aldolase, a transketolase, or a transaldolase, and/or by increasing the activity of a fructose-1,6-bisphosphate phosphatase; (ii) at least one gene encoding an enzyme necessary for the *de novo* synthesis of GDP-fucose is overexpressed in the host cell, wherein the at least one gene encoding an enzyme necessary for the *de novo* synthesis of GDP-fucose is a gene encoding a ManA enzyme catalyzing the isomerization of fructose-6-phosphate to mannose-6-phosphate, a phosphomannomutase encoding gene, a mannose-1-phosphate guanosyltransferase encoding gene, a GDP-mannose-4,6-dehydratase encoding gene, or a GDP-L-fucose synthase encoding gene; (iii) an exogenous gene, encoding an alpha-1,2-fucosyltransferase and/or alpha-1,3-fucosyltransferase, is expressed in the host cell;

- cultivating and/or growing said genetically modified host cell in a cultivation medium from a carbon and/or energy source that is selected from at least one of the following: glycerol, succinate, malate, pyruvate, lactate, ethanol, citrate; and

- providing lactose to the cultivation medium;

thereby producing the fucosylated oligosaccharide obtainable from the medium the host cell is cultivated in."

Claim 1 of auxiliary request 1 differs from claim 1 of the main request in that the feature "a ManA enzyme catalyzing the isomerization of fructose-6-phosphate to mannose-6-phosphate" in item (ii) of the claim has been deleted.

V. The board summoned the parties to oral proceedings in accordance with their requests. In a communication under Article 15(1) RPBA, it expressed its preliminary opinion that, *inter alia*, claim 1 of the main request did not meet the requirements of Article 123(2) EPC. Moreover, it was not inclined to admit any of auxiliary requests 1 to 8 into the appeal proceedings.

VI. Oral proceedings were held as scheduled. During the oral proceedings, the respondent withdrew auxiliary requests 2 to 8.

VII. The appellant's arguments, in so far as they are relevant to the decision, are summarised as follows.

Main request
Amendments (Article 123(2) EPC)

The application did not disclose that the gene for the enzyme mannose 6-phosphate isomerase (ManA) was one of the genes to be overexpressed in item (ii) of the claim. Paragraph [0054] taught that ManA was the starting enzyme in the *de novo* synthesis of GDP-L-fucose, and that phosphofructokinase A (PfkA) competed with ManA for the substrate, but it did not disclose that ManA should be overexpressed in a genetically

modified host cell to be used in the claimed method. The same language as that used in paragraph [0054] was also used in Example 5 of the application (paragraph [0115]), in which the deletion of the pfkA gene was discussed, but not the overexpression of ManA, and this was not taught in any of the other examples either.

The same was true of Figure 1, which showed ManA as a member in the pathway for the *de novo* synthesis of GDP-L-fucose, but not that ManA was overexpressed in the illustrative host cell depicted in this figure. This was also clear from paragraph [0097] of the application, which disclosed that the exogenous enzymes necessary for the *de novo* synthesis of GDP-L-fucose which were overexpressed in the host cell shown in Figure 1 were phosphomannomutase (ManB), mannose-1-phosphate guanosyltransferase (ManC), GDP-mannose-4,6-dehydratase (Gmd), and GDP-L-fucose synthase (WcaG). ManA, however, was not mentioned. The application therefore did not disclose that a gene encoding a ManA enzyme was to be overexpressed in a host cell used in the claimed method.

Auxiliary request 1
Admittance (Article 12 RPBA)

Auxiliary request 1 should not be admitted into the appeal proceedings as it addressed objections that had been raised in the notice of opposition, and therefore it should have been filed in the opposition proceedings. The respondent did not present any justification, nor were any special reasons apparent, as to why this request was only filed on appeal. The respondent did not explain why decisions T 2011/21 and T 738/20 allegedly supported its argument that

auxiliary request 1 should be admitted. These decisions were not relevant to the case at hand as decisions on admittance were always case-specific.

VIII. The respondent's arguments, in so far as they are relevant to the decision, are summarised as follows.

Main request
Amendments (Article 123(2) EPC)

Feature (ii) of claim 1 of the application defined that at least one gene encoding an enzyme necessary for the *de novo* synthesis of GDP-fucose was overexpressed in the host cell, without any limitation with respect to this gene. The same teaching was present in paragraphs [0010], [0015], [0056] and [0059] of the application.

Paragraph [0054] and Figure 1 of the application taught that ManA was the starting enzyme in the pathway for the *de novo* synthesis of GDP-L-fucose. Paragraph [0054] also linked ManA to the inactivation of PfkA, and paragraph [0056] taught that at least one of the genes necessary for the *de novo* synthesis of GDP-L-fucose was to be overexpressed in the host cell. This directly linked ManA with feature (ii) of the claim.

This fact was further supported by the teaching in paragraphs [0095] and [0096], indicating that Figure 1, which identified ManA as one of the genes to be overexpressed, showed an exemplary illustration of a genetically modified host cell to be used in the method of the invention and was an embodiment of the invention.

Auxiliary request 1
Admittance (Article 12 RPBA)

The deletion of a gene encoding a ManA enzyme from the list in feature (ii) of claim 1 addressed the added-matter issues discussed with respect to claim 1 of the main request and was neither complex nor prejudicial to procedural economy since it neither raised new issues nor changed the respondent's case. It was not a surprising amendment as the same amendment had been present in auxiliary request 3 as filed with the reply to the notice of opposition. The requirements of Article 12(4) RPBA, which are to be taken into consideration by a board when exercising its discretion to admit an amendment, were met.

A combination of the amendments present in the current auxiliary request 1 could not have been filed earlier as the opposition division had discussed the objections raised by the opponent under Article 123(2) EPC at the same time, and had not considered a combination of the amendments that were present separately in former auxiliary requests 1 and 3 to be necessary. Once the opposition division had provided its opinion on the issue of added matter, it was no longer possible for an auxiliary request to be filed that addressed both objections.

Decisions T 2011/21 and T 738/20 showed that boards had previously admitted auxiliary requests on appeal and remitted the cases to the opposition division. The same was appropriate in the present case.

IX. The parties' requests, where relevant to the decision, were as follows.

The appellant requested that the decision under appeal be set aside, that the patent be revoked and that auxiliary request 1 not be admitted into or considered in the appeal proceedings.

The respondent requested that the appeal be dismissed (main request), or, in the alternative, that the patent be maintained on the basis of the set of claims of the new auxiliary request 1.

Reasons for the Decision

Main request
Amendments (Article 123(2) EPC) - claim 1

1. Claim 1 of the main request concerns a method for the production of fucosylated oligosaccharides using a prokaryotic host cell that is genetically modified as indicated in items (i), (ii) and (iii) (see section IV. above for the full wording of the claim).

2. Item (ii) of claim 1 of the application stipulates that "*at least one gene encoding an enzyme necessary for the de novo synthesis of GDP-fucose is overexpressed in the host cell*". The same disclosure is present in paragraphs [0010], [0015] and [0056] of the application. This feature was amended in claim 1 of the main request by the further specification that the gene is one of five different genes, namely "*a gene encoding a ManA enzyme catalyzing the isomerization of fructose-6-phosphate to mannose-6-phosphate, a phosphomannomutase encoding gene, a mannose-1-phosphate*

guanosyltransferase encoding gene, a GDP-mannose-4,6-dehydratase encoding gene, or a GDP-L-fucose synthase encoding gene".

3. A gene encoding the enzyme ManA is not, however, disclosed in the application as one of the genes to be overexpressed in a genetically modified host cell. Indeed, each of the passages of the application that further defines the genes encoding the enzymes necessary for the *de novo* synthesis of GDP-fucose that are to be overexpressed in the genetically modified host cell lists the four other genes recited in the claim, but not a gene encoding ManA.

4. For example, claim 5 of the application, which is dependent on claim 1, discloses that "*the genes encoding enzymes necessary for the de novo synthesis of GDP-fucose are a phosphomannomutase encoding gene, preferably manB, a mannose-1-phosphate guanosyltransferase encoding gene, preferably manC, a GDP-mannose-4,6-dehydratase encoding gene, preferably gmd, and a GDP-L-fucose synthase encoding gene, preferably wcaG*".

5. Paragraph [0060] of the application teaches that "[i]*n an embodiment of the present invention, the exogenous genes encoding the enzymes necessary for the de novo synthesis of GDP-fucose are a gene coding for a phosphomannomutase, preferably manB, a gene coding for a mannose-1-phosphate guanosyltransferase, preferably manC, a gene coding for a GDP-mannose-4,6-dehydratase, preferably gmd, and a gene coding for a GDP-L-fucose synthase, preferably wcaG*".

6. Moreover, the genes encoding the enzymes for the *de novo* synthesis of GDP-L-fucose that were integrated

into the host cell genome were also *manB*, *manC*, *gmd* and *wcaG*, but not *manA*, in the examples of the application (paragraphs [0108] and [0120]).

7. In fact, the enzyme ManA is only mentioned in the application in paragraphs [0054] and [0115] and in Figure 1. Paragraph [0054] discloses that the synthesis of GDP-L-fucose "*starts from the ManA catalyzed isomerization of fructose-6-phosphate to mannose-6-phosphate*" and that "*on a gluconeogenic substrate like glycerol, the phosphorylation of fructose-6-phosphate by PfkA* [phosphofructokinase A] *is a highly ATP consuming treadmill reaction and, in addition, it competes with ManA for the substrate*". This latter part of the sentence is also present in paragraph [0115]. These paragraphs thus merely mention ManA as the starting enzyme in the synthesis of GDP-L-fucose and as competing with PfkA for the same substrate; they do not disclose the overexpression of ManA in a host cell.

8. The same is true of Figure 1. This figure shows a "*schematic, exemplary illustration of a genetically modified host cell to be used in the method according to the invention*" (paragraph [0095]), in which ManA is depicted in the pathway for the *de novo* synthesis of GDP-L-fucose, but not, contrary to the assertions of the respondent, as being overexpressed in this host cell.

9. This fact is also evident from paragraph [0097] of the application, which describes the metabolic pathway depicted in Figure 1 and the genetic modifications of the illustrative host cell shown. The genetic modifications of this host cell are listed as overexpression of an exogenous fructose-1,6-bisphosphate phosphatase gene, inactivation of PfkA and

"*overexpression of exogenous enzymes necessary for the de novo synthesis of GDP-fucose, i.e. phosphomannomutase ManB, mannose-1-phosphate guanosyltransferase ManC, GDP-mannose-4,6-dehydratase Gmd, and GDP-L-fucose synthase WcaG*".

10. This description of Figure 1 hence explicitly lists all the exogenous enzymes necessary for the *de novo* synthesis of GDP-L-fucose that are overexpressed in the host cell, and this list does not include ManA, despite ManA being depicted in Figure 1 as an enzyme necessary for the *de novo* synthesis of GDP-L-fucose. Thus, none of the sections of the application that mention ManA disclose that ManA is (to be) overexpressed in a host cell to be used in the method of the invention.

11. The respondent asserted that since the application taught that "at least one" unspecified (endogenous or exogenous) gene encoding an enzyme necessary for the *de novo* synthesis of GDP-L-fucose was to be overexpressed in the host cell (e.g. claim 1 and paragraphs [0010], [0015], [0056] and [0059]), and that the *de novo* synthesis of GDP-L-fucose started from the ManA catalysed reaction (e.g. paragraph [0054] and Figure 1), the skilled person was able to derive from the application that ManA was one of the (unspecified) genes necessary for the *de novo* synthesis of GDP-L-fucose mentioned in feature (ii) of claim 1 that could be overexpressed in the genetically modified host cell.

12. However, the mere disclosure that ManA is an enzyme necessary for the synthesis of GDP-L-fucose does not amount to a direct and unambiguous disclosure that ManA is to be overexpressed in the genetically modified host cell described in the claim. In fact, as assessed above (see points 3. to 10.), ManA is deliberately excluded

from the genes disclosed in the application as examples for item (ii) of claim 1. The skilled person is therefore unable to derive, in a direct and unambiguous manner, from the cited passages of the application that ManA is to be overexpressed in the genetically modified host cell. The skilled person might consider it obvious that ManA could also be overexpressed based on these passages of the application; however, obviousness is not the correct criterion for the assessment of the allowability of an amendment.

13. In view of these considerations, none of the passages of the application cited by the respondent as the basis for the claimed method, whether taken alone or in combination, directly and unambiguously discloses that ManA is overexpressed in a prokaryotic host cell as defined in the claim for use in the claimed method.

14. Consequently, claim 1 of the main request contains subject-matter that extends beyond the content of the application as filed, contrary to the requirements set out in Article 123(2) EPC.

Auxiliary request 1
Admittance (Article 12 RPBA)

15. Auxiliary request 1 was filed for the first time in the proceedings with the reply to the appeal. It therefore constitutes an amendment of the respondent's case that may only be admitted at the discretion of the board (Article 12(4) RPBA in conjunction with Article 12(2) RPBA).

16. It is correct, as pointed out by the respondent, that Article 12(4) RPBA provides guidance on criteria boards should consider when exercising their discretion

with respect to the admittance of amendments, including the complexity of the amendment, the suitability of the amendment to address the issues which led to the decision under appeal, and the need for procedural economy. However, Article 12(6) RPBA additionally stipulates that boards shall not admit, *inter alia*, requests which should have been submitted in the proceedings leading to the decision under appeal, unless the circumstances of the appeal case justify their admittance.

17. In the case at hand, auxiliary request 1 should have been submitted in the opposition proceedings. The reason for this is that two objections concerning unallowable amendments in claim 1 of the patent as granted were raised in the notice of opposition, the first with respect to an expression in item (i) and the second with respect to ManA in the enzyme list in item (ii) (section 4. on pages 6 and 7 of the notice of opposition). These two objections were hence raised at the very start of the proceedings and, consequently, an auxiliary request addressing the two objections should have been submitted in response at that time.

18. The respondent pointed to the fact that auxiliary request 3 as filed in the opposition proceedings contained the same amendment in item (ii) of the claim as the present auxiliary request 1, and that a claim request identical to the present auxiliary request 1 could not have been filed in the opposition proceedings since the opposition division had dealt with the two objections simultaneously at the oral proceedings.

19. This line of argument is not persuasive, however, since the two objections were raised at the start of the proceedings, and therefore suitable auxiliary requests

dealing with both objections could have been submitted in a timely manner, especially as only two objections concerning unallowable amendments had been raised. Submitting auxiliary requests dealing with each possible outcome would thus have been a simple task and could have been expected well before the opposition division considered the merits of these objections in the oral proceedings, particularly as auxiliary requests filed only in response to the opposition division's opinion at the oral proceedings would also have been considered late-filed.

20. The respondent cited decisions T 2011/21 and T 738/20 as evidence that boards had previously admitted auxiliary requests on appeal and remitted the cases to the opposition division for further prosecution. However, the circumstances of these cases are different from the case at hand and therefore they are not relevant.

21. In T 2011/21, the board decided to admit an auxiliary request into the proceedings which, contrary to the case at hand, had been filed during the opposition proceedings (see Reasons 3), and the board hence assessed whether this request had been admissibly raised and maintained during the opposition proceedings under Article 12(4) RPBA and not, as in the case at hand, whether it should have been filed in the opposition proceedings under Article 12(6) RPBA (Reasons 3.2.2).

22. In T 738/20, the board decided to admit an auxiliary request under Article 13(1) and (2) RPBA in view of new evidence introduced by the board in its communication under Article 15(1) RPBA (Reasons 5.3 and 5.4). Under such circumstances, the question of whether or not the

request at issue should have been filed in the opposition proceedings does not arise.

23. In view of the above considerations, no special circumstances are apparent that could justify considering this claim request on appeal, despite the fact that it should have been submitted in the opposition proceedings. Auxiliary request 1 has therefore not been admitted into the appeal proceedings (Article 12(6) RPBA).

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