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**Datasheet for the decision
of 10 April 2014**

Case Number: T 1112/10 - 3.3.08

Application Number: 04743163.0

Publication Number: 1644482

IPC: C12N1/20, C12P19/14, C07H3/06,
A61K31/70, A61P1/04

Language of the proceedings: EN

Title of invention:
NOVEL GALACTOOLIGOSACCHARIDE COMPOSITION AND THE PREPARATION
THEREOF

Patent Proprietor:
Clasado Inc.

Opponent:
N.V. Nutricia

Headword:
Galactooligosaccharide/CLASADO

Relevant legal provisions:
EPC Art. 56

Keyword:
Inventive step - (yes)

Decisions cited:
T 0918/05

Catchword:



**Beschwerdekammern
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Chambres de recours**

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Case Number: T 1112/10 - 3.3.08

**D E C I S I O N
of Technical Board of Appeal 3.3.08
of 10 April 2014**

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Decision under appeal: **Decision of the Opposition Division of the
European Patent Office posted on 16 February
2010 rejecting the opposition filed against
European patent No. 1644482 pursuant to Article
101(2) EPC.**

Composition of the Board:

Chairman: M. Wieser
Members: T. J. H. Mennessier
D. Rogers

Summary of Facts and Submissions

- I. The opponent (appellant) lodged an appeal against the decision of the opposition division dated 16 February 2010, whereby the opposition filed against European patent No. 1 644 482, which had been granted on European patent application No. 04743163.0, published as the international application WO 05/03329, was rejected.
- II. The opposition was filed on the grounds of Article 100(a) (lack of inventive step, Article 56 EPC) and 100(c) EPC.
- III. The statement setting out the grounds of appeal was accompanied by four new documents, including documents D8 and D10 (see Section XI below).
- IV. The patent proprietor (respondent) replied by filing submissions.
- V. Oral proceedings were requested by both parties.
- VI. The board issued, as an annex to the summons to oral proceedings, a communication pursuant to Article 15(1) of the Rules of Procedure of the Boards of Appeal (RPBA), expressing its preliminary and non-binding views.
- VII. The respondent replied with letter dated 10 December 2013 and filed auxiliary requests I to III. The appellant filed further submissions with letter dated 7 March 2014.
- VIII. On 10 March 2014 the respondent filed a fourth auxiliary request.

IX. At the oral proceedings, which took place as scheduled on 10 April 2014 in presence of both parties, the respondent withdrew its main request (claims as granted) and filed a new main request which was identical to the first auxiliary request of 10 December 2013.

X. The main request consisted of 17 claims, of which claims 1 and 3 read:

"1. A strain of *Bifidobacterium bifidum* deposited under accession no. NCIMB 41171 at the National Collection of Industrial and Marine Bacteria, Aberdeen, UK on 31 March 2003 that produces a galactosidase enzyme activity that converts lactose to a galactooligosaccharide mixture comprising Gal(α 1-6)-Gal, trisaccharides Gal(β 1-6)-Gal(β 1-4)-Glc and Gal(β 1-3)-Gal(β 1-4)-Glc, tetrasaccharide Gal(β 1-6)-Gal(β 1-6)-Gal(β 1-4)-Glc and pentasaccharide Gal(β 1-6)-Gal(β 1-6)-Gal(β 1-6)-Gal(β 1-4)-Glc."

"3. A galactooligosaccharide composition for promoting specific growth of bifidobacteria comprising, as effective constituents, a mixture comprising Gal(α 1-6)-Gal, trisaccharides Gal(β 1-6)-Gal(β 1-4)-Glc and Gal(β 1-3)-Gal(β 1-4)-Glc, tetrasaccharide Gal(β 1-6)-Gal(β 1-6)-Gal(β 1-4)-Glc and pentasaccharide Gal(β 1-6)-Gal(β 1-6)-Gal(β 1-6)-Gal(β 1-4)-Glc."

Claim 2 was dependent on claim 1. Claim 4 was dependent on claim 3.

Claim 5 was directed to a composition for improving gut health comprising a culture of the strain of *Bifidobacterium bifidum* according to claim 1 or claim 2

in combination with the composition according to claim 3 or claim 4.

Claim 6 was directed to a composition according to any one of claims 3 to 5 for use in a method of treatment.

Claims 7 to 9 were each directed to the use of the composition according to any one of claims 3 to 5 in the preparation of a medicament.

Claim 10 was directed to the use of a strain according to claim 1 or claim 2 for producing the mixture of galactooligosaccharides as defined in claim 3 or claim 4.

Claims 11 to 13 were dependent on claim 10.

Claim 14 was directed to a method for the manufacture of a substance for promoting the growth of bifidobacteria characterized in that lactose or lactose-containing material was treated with a strain according to claim 1 or claim 2.

Claims 15 to 17 were dependent on claim 14.

XI. The following documents are referred to in the present decision:

(D4) R. Tanaka et al., *Bifidobacteria Microflora*, Vol. 2, No. 1, 1983, pages 17 to 24

(D5a) H. Hashimoto et al., *Journal of Applied Glycoscience*, Vol. 48, No. 3, 2001, pages 279 to 285, together with the corresponding STN database summary sheet (AN: 2001:504348)

- (D5b) H. Hashimoto et al., *Journal of Applied Glycoscience.*, Vol. 41, No. 2, 1994, pages 143 to 150, together with the corresponding STN database summary sheet (AN: 95:136681)
- (D7) D. Roy et al., *Milchwissenschaft*, Vol. 47, No. 1, 1992, pages 18 to 21
- (D8) M. Ito et al., *Microbial Ecology in Health and Disease*, Vol. 3, 1990, pages 285 to 292
- (D9) M. Ito et al., *Journal of Nutritional Science and Vitaminology*, Vol. 39, 1993, pages 635 to 640
- (D10) "Oligosaccharides, production, Properties and Applications", in "Japanese Technology Reviews", Edited by Teruo Nakakuki, Gordon and Breach Science Publishers, 1993, pages 90 to 94
- (D12) Experimental report attached to the respondent's letter of 23 September 2009

XII. The submissions made by the appellant, insofar as they are relevant to the present decision, may be summarised as follows:

Document D7 which evaluated the properties of α - and β -galactosidase from crude extracts of a *Bifidobacterium infantis* isolate represented the closest prior art with respect to the subject-matter of claim 1. The technical problem to be solved was the provision of an alternative *Bifidobacterium* strain having the same properties. Knowing from document D7 (see the first sentence of the second paragraph of the introduction) that bifidobacteria of human origin possessed α - and β -galactosidase activities, it would

have been obvious to the skilled person to identify the strain of claim 1.

Each of documents D4, D8, D9 and D10 qualified as the closest state of the art with respect to the subject-matter of claim 3. They also described preparations of transgalactosylated oligosaccharides consisting of tri-, tetra-, penta-, and hexasaccharides which showed prebiotic properties.

The technical problem to be solved was the provision of an alternative prebiotic composition.

Documents D5a, D5b and D6 taught that the disaccharide Gal-(α 1-6)-Gal promoted the specific growth of bifidobacteria.

There was no evidence on file showing that the claimed composition had a synergistic effect going beyond the effect of the individual components contained therein. A skilled person by incorporating Gal-(α 1-6)-Gal into the composition of any of documents D4, D8, D9 and D10 would have arrived at the solution according to claim 3 in an obvious way. This was in line with decision T 918/05 of 11 February 2009 (see point 7.1.2 of the reasons) where the competent board found that, in a situation where individual components were known to have a prebiotic effect, a skilled person would have combined them and no inventive step could be attributed to the obtained composition.

XIII. The submissions made by the respondent, insofar as they are relevant to the present decision, may be summarised as follows:

Document D7 failed to provide the slightest hint that a transglycosylating activity could occur in a strain of *Bifidobacterium*. Furthermore, it did not teach that the described α - and β -galactosidases even had such an activity. Therefore, relying on document D7, the skilled person would have had no expectation to arrive at a *Bifidobacterium* strain being capable of digesting lactose to produce a mixture of α - and β -galactosaccharides, let alone at the specific strain of claim 1.

Regarding claim 3, the technical problem to be solved over document D4 taken as the closest prior art was the provision of a galactooligosaccharide composition which had a strong prebiotic activity and an anti-adhesion effect.

There was no teaching in document D5a that Gal-(α 1-6)-Gal functioned as a bifidus growth factor. Neither was it suggested that it could have the specified activities. Document D5b did not provide a clear teaching that the α -linked galactooligosaccharides mixture α -GOS A and α -GOS B were prebiotics. Furthermore, D5b did not attribute any particular significance to the galactooligosaccharide composition component of α -GOS A. The results presented in Table 3 of D5b related to an *in vitro* study which established only whether the different species tested could utilise the sugars or galactooligosaccharide mixtures as an energy source when grown as a monoculture *in vitro*. Document D6 mentioned that an α -galactooligosaccharide prepared from galactose through the action of α -galactosidase was "utilizable by *Bifidobacterium bifidum*" but failed to disclose the structure of this oligosaccharide. Thus, none of documents D5a, D5b and

D6 taught that Gal-(α 1-6)-Gal functioned as a prebiotic.

Moreover, neither the galactooligosaccharide composition of document D4 nor Gal-(α 1-6)-Gal had been shown to have anti-adhesion properties.

There was therefore no reason why a person skilled in the art would have considered it obvious to combine the β -linked TOS composition of document D4 with Gal-(α 1-6)-Gal in order to obtain a composition having both, a strong prebiotic activity and an anti-adhesion effect.

- XIV. The appellant (opponent) requested that the decision under appeal be set aside and the patent be revoked.
- XV. The respondent (patent proprietor) requested that the decision under appeal be set aside and the patent be maintained on the basis of claims 1 to 17 of the main request filed at the oral proceedings on 10 April 2014.

Reasons for the Decision

Admissibility of documents D8 to D10

1. Exercising the discretion conferred on it by Article 12(4) RPBA, the board admits into the proceedings documents D8 to D10, whose admission has not been objected to by the respondent, as well as the main request which only contains amendments that are straightforward and do not raise any new issues.

Article 123(2) and (3) EPC

2. The main request differs from the set of claims as granted in so far as in claims 1 and 3 the presence of the two trisaccharides mentioned has become compulsory. Support for this feature is found in particular on page 4, lines 14 to 17 of the application as filed (see WO 05/03329). The respondent, who raised an objection under Article 123(2) EPC against claims 1 and 3 as granted, does not raise any objection in this respect against claims 1 and 3 of the main request. These amendments do not extend beyond the content of the application as filed and do not extend the protection conferred by the patent. Therefore, the main request complies with the requirements of Article 123(2) and (3) EPC.

Article 56 EPC

3. Document D7 is the only document cited by the appellant in its arguments concerning inventive step of the subject-matter of claim 1. This document reports on a study whose purpose was to evaluate the properties of α -and β -galactosidase preparations from the *Bifidobacterium infantis* ATCC 27920 strain. The effect of temperature on the enzymatic activities and the effects of metal ions and other reagents on α -and β -galactosidase activities of crude enzyme preparations were determined (see page 20). No decisive conclusion is reached by the authors who only hypothesize that the consumption of live bifidobacteria, such as *Bifidobacterium infantis*, may provide α -and β -galactosidase activities for hydrolysis of complex carbohydrates which are not normally ingested in the intestinal tract of humans.

4. The technical problem underlying the patent according to claim 1 is seen as the provision of a *Bifidobacterium* strain displaying both α - and β -galactosidase activities which is capable of transglycosylation for the production of a galactooligosaccharide composition (which is a composition according to claim 3) comprising disaccharide Gal(α 1-6)-Gal, trisaccharides Gal(β 1-6)-Gal(β 1-4)-Glc and Gal(β 1-3)-Gal(β 1-4)-Glc, tetrasaccharide Gal(β 1-6)-Gal(β 1-6)-Gal(β 1-4)-Glc and pentasaccharide Gal(β 1-6)-Gal(β 1-6)-Gal(β 1-6)-Gal(β 1-4)-Glc. As a solution the patent proposes the *Bifidobacterium bifidum* NCIMB 41171 strain. In view of the disclosure of the patent at issue (see in particular the experimental part of the description disclosing the production by a *Bifidobacterium bifidum* NCIMB 41171 of a galactooligosaccharide mixture as defined in claim 1, which mixture exhibits anti-adhesion properties), the claimed subject-matter credibly solves this technical problem.
5. It remains to be answered whether a skilled person, as argued by the appellant, in the light of document D7 alone, would have arrived at the claimed strain in an obvious way.
6. Despite the statement - expressly relied on by the appellant - made in the second sentence of the introduction on page 18 of document D7, that bifidobacteria of human origin possess α - and β -galactosidase activities, document D7 only points to the potential use of α - and β -galactosidase activities for hydrolysis of complex carbohydrates. It does not contain any hint that would have encouraged a skilled person to look for a bifidobacterium strain capable of

transglycosylation which is able to produce a galactooligosaccharide composition comprising disaccharide Gal(α 1-6)-Gal, trisaccharides Gal(β 1-6)-Gal(β 1-4)-Glc and Gal(β 1-3)-Gal(β 1-4)-Glc, tetrasaccharide Gal(β 1-6)-Gal(β 1-6)-Gal(β 1-4)-Glc and pentasaccharide Gal(β 1-6)-Gal(β 1-6)-Gal(β 1-6)-Gal(β 1-4)-Glc.

7. Therefore, the skilled person facing the objective problem underlying the invention according to claim 1 (see point 4 above), when starting from the disclosure in document D7, would not have arrived at the solution provided in claim 1 in an obvious way. Therefore, the subject-matter of claim 1 involves an inventive step.
8. When considering the disclosure in documents D4, D8, D9 and D10, all referring to transgalactosylated oligosaccharides, document D4 is regarded as the closest state of the art with respect to the subject-matter of claim 3. In contrast to the product 'Oligomate-50', described in documents D8, D9 and D10, the composition TOS, described in document D4, does not contain transglycosylated disaccharides (see document D10, page 93), which are also not present in the composition according to claim 3.
9. Document D4 describes the effects of the administration of a composition of transgalactosylated oligosaccharides (TOS) on the fecal flora of normal subjects. The TOS composition of document D4 consists of tri-, tetra- and penta- and hexasaccharides and is produced by subjecting lactose to an enzymatic hydrolysis by the β -galactosidase produced by *Aspergillus oryzae*. Its molecular formula is Gal-(Gal) n -Glu, wherein Gal, Glu and n denote a

galactose residue, a glucose residue and an integer between 1 and 4 (see Figure 1 on page 18). The structure of the TOS compositions produced by the β -galactosidase of *Aspergillus oryzae* is shown in Table 30 on page 93 of document D10, where it is also shown that they contain the two trisaccharides, the tetrasaccharide and the pentasaccharide of the composition of claim 3. The authors of document D4 concluded that the TOS composition promoted the growth of both, resident and administered, *Bifidobacterium* strains *in vivo* (see page 20, right-hand column), a finding which indicates that the TOS composition of document D4 had a prebiotic effect. However, the document does not mention any anti-adhesion properties of the TOS composition.

10. The technical problem underlying the patent according to claim 3 is defined as the provision of a composition which, in addition to its prebiotic activity, inherently provides an anti-adhesion effect on intestinal bacteria such as *Escherichia coli* and *Salmonella typhimurium*. As a solution the patent proposes a composition according to claim 3. In view of the disclosure of the patent at issue (see in particular Example 3) which describes an *in vitro* gut model used to establish the prebiotic properties of the claimed composition and Example 5 which describes anti-adhesion properties of the tested composition), the claimed subject-matter credibly solves this technical problem.
11. It remains to be answered if a skilled person starting from document D4 would have arrived at the claimed composition in an obvious way.

12. In contrast to the TOS composition of document D4 which does not contain any disaccharide (see Figure 1 on page 18), the composition of claim 3 does contain one disaccharide, namely the α -galactobiose isomer of formula Gal(α 1-6)-Gal).
13. Document D5a (published after D5b and co-authored by four authors of D5b) provides some information with respect to **α -GOS A**, an α -linked galactooligosaccharide synthesized from galactose by the reverse reaction of α -galactosidase from *Candida guilliermondii* H-404, which contains Gal(α 1-6)-Gal.
14. Document D5b is a paper in the Japanese language, only the abstract is written in English. The abstract provides information focusing on α -GOS B, a α -linked galactooligosaccharide also produced by the α -galactosidase from *Candida guilliermondii* H-404, which is said to be acknowledged to have strong selective growth activity for *Bifidobacterium*. No further details are given to substantiate this statement. In its last but one sentence the abstract states further that " **α -GOS A** was also produced from only galactose, and was compared with α -GOS B". From the very last sentence of the abstract which reads "But there were no large differences with respect to all properties tested.", the appellant concludes that also **α -GOS A** had a strong selective growth activity for *Bifidobacterium*. Furthermore the appellant argues that the results presented on Table 3 on page 150 of document D5b, showing that **α -GOS A** was utilised by five species of *Bifidobacterium*, support this assumption.

15. **α -GOS A** is described on page 283, right-hand column of document D5a. It consists of 21% oligosaccharides other than disaccharides and 79% disaccharides including Gal(α 1-6)-Gal (representing 68% of the disaccharides).
16. Document D5b does not establish that Gal(α 1-6)-Gal is responsible for the strong selective growth activity of **α -GOS A** for *Bifidobacterium*. Furthermore, the mere observation that bacteria grew in presence of **α -GOS A** does not mean that it exhibits prebiotic activity in a *in vitro* gut model as disclosed in Example 3 of the patent and in document D12.
17. The board notes that document D5a does not contain any explicit information referring to prebiotic properties of Gal(α 1-6)-Gal. In this respect, it would have been clear to a skilled person that the sentence on page 279 - reading "*These oligosaccharides have attracted attention as a strong bifidus growth factor [...]*", relied on by the appellant, does not relate to disaccharides such as Gal(α 1-6)-Gal but to α -linked galactooligosaccharides such as raffinose and stachyose, as referred to in the preceding sentence.
18. Both documents D5a and D5b are, moreover, silent as to anti-adhesion properties of **α -GOS A** and/or Gal(α 1-6)-Gal.
19. Regarding document D6 which was also referred to by the appellant, the board notes that it does not refer to any definite galactooligosaccharide, let alone to Gal(α 1-6)-Gal. Consequently said document is irrelevant for the present assessment.

20. The above analysis leads to the conclusion that the state of art had not established that Gal(α 1-6)-Gal had prebiotic properties or anti-adhesion properties.
21. The board concludes that a skilled person facing the objective problem to be solved (see point 10 above) would not have had any incentive to combine the disclosure in document D4 with the disclosure in document D5b and/or document D5a.
22. The reasoning arrived at by the competent board in decision T 918/05 of 11 February 2009 does not apply to the present case. While in the case underlying this decision the single components contained in the claimed composition were known to show the desired activities, in the present case one component, Gal(α 1-6)-Gal was not known to have prebiotic activity and both components (TOS and Gal(α 1-6)-Gal) were not known to have anti adhesion properties.
23. Therefore, as for claim 1 the subject-matter of claim 3 involves an inventive step. The same conclusion applies to the subject-matter of claims 2 and 4 to 17.

Adaptation of the description

24. The board considers that, by filing amended page 3 at the oral proceedings, the description has been satisfactorily amended in accordance with the EPC.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.
2. The case is remitted to the department of first instance with the order to maintain the patent as amended in the following version:

Description:

Pages 2 and 4 to 15 of the patent specification.

Page 3 of the amended patent specification received during the oral proceedings of 10 April 2014.

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Claims:

Claims 1 to 17 of the Main Request received during the oral proceedings of 10 April 2014.

Drawings:

Fig. 1 and Fig. 2 of the patent specification.

The Registrar:

The Chairman:



A. Wolinski

M. Wieser

Decision electronically authenticated