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**Datasheet for the decision
of 3 November 2015**

Case Number: T 0033/13 - 3.3.09

Application Number: 01910704.4

Publication Number: 1255449

IPC: A23C9/20

Language of the proceedings: EN

Title of invention:

Nutritional formulations containing prebiotic substances

Patent Proprietor:

Nestec S.A.

Opponent:

N.V. Nutricia

Headword:

Relevant legal provisions:

EPC Art. 56

Keyword:

Inventive step - (yes)

Decisions cited:

Catchword:



**Beschwerdekammern
Boards of Appeal
Chambres de recours**

European Patent Office
D-80298 MUNICH
GERMANY
Tel. +49 (0) 89 2399-0
Fax +49 (0) 89 2399-4465

Case Number: T 0033/13 - 3.3.09

D E C I S I O N
of Technical Board of Appeal 3.3.09
of 3 November 2015

Appellant: N.V. Nutricia
(Opponent) Eerste Stationsstraat 186
2712 HM Zoetermeer (NL)

Representative: Nederlandsch Octrooibureau
P.O. Box 29720
2502 LS The Hague (NL)

Respondent: Nestec S.A.
(Patent Proprietor) Avenue Nestlé 55
1800 Vevey (CH)

Representative: Rupp, Christian
Mitscherlich PartmbB Patent- und Rechtsanwälte
Postfach 33 06 09
80066 München (DE)

Decision under appeal: **Decision of the Opposition Division of the
European Patent Office posted on 15 October 2012
rejecting the opposition filed against European
patent No. 1255449 pursuant to
Article 101(2) EPC.**

Composition of the Board:

Chairman W. Sieber
Members: N. Perakis
D. Prietzel-Funk

Summary of Facts and Submissions

- I. This decision concerns the appeal filed by the opponent against the decision of the opposition division to reject the opposition filed against European patent No. 1 255 449.
- II. The patent was granted with 17 claims. Claims 12-14 read as follows:
- "12. Use of oligofructose and sialyllactose in the preparation of a medicament for use as a nutritional composition for feeding to a human for increasing the amount of *Bifidobacteria* and inhibiting the binding of pathogenic bacteria in said human."
- "13. Use according to claim 12, wherein said nutritional composition is for feeding to a human at a concentration containing 0.1 g/L to 10 g/L of oligofructose and 6 mg/L to 10 g/L of sialyllactose."
- "14. Use according to claim 12, wherein said concentration contains 0.3 g/L to 6 g/L of oligofructose and 60 mg/L to 1 g/L of sialyllactose."
- III. A notice of opposition was filed requesting the revocation of the patent in its entirety under Articles 100(a) (lack of novelty and inventive step), 100(b) and 100(c) EPC.

The documents submitted before the opposition division included the following:

- D2: US 5 827 526 A;
D4: WO 98 31241 A1;
D5: WO 99 64022 A1; and

D6: T. Idota *et al.*, "Growth-promoting Effects of N-Acetylneuraminic Acid-containing Substances on Bifidobacteria", *Biosci. Biotech. Biochem.*, 58(9), 1994, pages 1720-1722.

The opposition division rejected the opposition. It considered that the patent was sufficiently disclosed, that the subject-matter of the claims did not extend beyond the content of the application as filed, and that the subject-matter of claim 12 was novel over D4 and D5 and involved an inventive step, the latter also in view of the synergistic effect provided by the combined use of oligofructose and sialyllactose, which had been shown in the patent.

- IV. On 24 December 2012 the opponent (in the following the appellant) filed an appeal against the decision of the opposition division. The statement setting out the grounds of appeal was filed on 25 February 2013. The appellant requested that the decision of the opposition division be set aside and that the patent be revoked in its entirety. The appellant maintained the lack of novelty and lack of inventive step objections raised before the opposition division.
- V. With letter dated 27 October 2015 the patent proprietor (in the following the respondent) withdrew the claims as granted and submitted a new main and a new auxiliary request. The respondent requested that the patent be maintained on the basis of one of these requests. Regarding in particular the new main request, it argued that its subject-matter did not extend beyond the content of the application as filed, was novel and involved an inventive step.
- VI. Claim 1 of the new main request reads as follows:

"1. Use of oligofructose and sialyllactose in the preparation of a medicament for use as a nutritional composition for feeding to a human for increasing the amount of *Bifidobacteria* and inhibiting the binding of pathogenic bacteria in said human, wherein said nutritional composition is for feeding to a human at a concentration containing 0.3 g/L to 6 g/L of oligofructose and 60 mg/L to 1 g/L of sialyllactose."

Claims 2 to 4 are dependent claims.

VII. On 3 November 2015 oral proceedings were held before the board. At them, the appellant did not object to the admission of the new main request into the proceedings. Nor did it raise any objection under Articles 123(2), 83 and 54 EPC against the claims of the main request, but argued that the subject-matter of claim 1 lacked inventive step. However the appellant objected to the admission of the new auxiliary request into the proceedings.

VIII. The relevant arguments put forward by the appellant in its written submissions and during the oral proceedings may be summarised as follows:

- The subject-matter of claim 1 lacked inventive step. D2 was considered as the closest prior-art document, although D4 and D5 could also be thus regarded. D2 disclosed nutritional compositions comprising indigestible oligofructoses and aimed to achieve the same effects of improving the growth of *Bifidobacteria* and inhibiting the binding of pathogenic bacteria (column 1, lines 41-50). Thus, the composition of claim 1 differed from D2 only in that it further contained a sialyllactose.

- The technical problem in view of D2 was the provision of a composition which showed an improved gastrointestinal effect. The solution to this problem was obvious in view of D6, which disclosed the contribution of sialyllactose to the growth effect on some *Bifidobacteria*, such as *B. breve*, and to the prevention of pathogenic micro-organisms from binding to human tissues (table 2). Thus the skilled person would obviously combine D2 with D6 and would arrive at the claimed subject-matter without the need to exercise any inventive skill. If any additional effect was present, it was merely a bonus effect resulting from the obvious combination.

- Even if the technical problem was formulated as suggested by the respondent, namely to provide an improved nutritional composition which promoted the growth of *Bifidobacteria* and prevented the growth of less beneficial bacteria, the solution was obvious in view of the combination of D2 with D6. Figure 2 in the patent in suit did not show any synergistic effect and figure 3 did not show any growth-promotion effect regarding *Bifidobacteria*.

- Furthermore, the patent did not contain any evidence regarding the prevention of the growth of less beneficial bacteria. On the one hand, the results in figure 1 were not conclusive. On the other hand, paragraph [0020] of the patent, commenting on figure 1, disclosed that reduced growth was not obtained for the less beneficial bacteria.

- Lastly, there was no evidence that the technical problem was solved over the entire scope of the claim, because the examples of the patent were carried out with one specific concentration of 3'-sialyllactose and one specific concentration of oligofructose.

IX. The relevant arguments put forward by the respondent in its written submissions and during the oral proceedings may be summarised as follows:

- The subject-matter of claim 1 of the main request involved an inventive step. Any of D2, D4 or D5 or even paragraph [0003] of the patent could be considered to represent the closest prior art. These known nutritional compositions contained oligofructose but not sialyllactose. The combination of oligofructose with sialyllactose provided an unexpected synergy in the growth of *Bifidobacteria* on the one hand and the prevention of the growth of less beneficial bacteria on the other hand (figure 1 of the patent).
- D6 related to the use of sialyllactose in nutritional compositions. However, it did not disclose that sialyllactose promoted the growth of *Bifidobacteria*. In fact, D6 disclosed that sialyllactose at the claimed concentration had no effect on the growth of *B. infantis* (Table II). As regards the effect of sialyllactose on less beneficial, pathogenic bacteria, D6 disclosed that it suppressed their binding activity on human tissues (page 1722, last paragraph).

- Thus, even if the skilled person considered combining D6 with any of D2/D4/D5, he would not have expected the synergistic effect on the promoting the growth of Bifidobacteria and preventing that of the pathogenic bacteria.
 - The above synergistic effect was shown in the experimental part of the patent for *B. infantis*. Moreover, the skilled person would legitimately expect this synergy to be more pronounced in the case of the other *Bifidobacteria* of D6, such as *B. bifidum* and *B. breve*, whose growth according to table II had been promoted in the presence of sialyllactose.
 - Regarding the effect on the growth of the less beneficial micro-organisms, figure 1 of the patent did not provide the necessary evidence; this was however confirmed in the corresponding part of the patent, namely paragraph [0020].
- X. The appellant requested that the decision under appeal be set aside and that the patent be revoked.
- XI. The respondent requested that the patent be maintained on the basis of the claims of the new main request or the new auxiliary request filed with the letter dated 27 October 2015.

Reasons for the Decision

1. The sole issue in the present appeal regarding the new main request is inventive step.

2. The claimed invention

The invention according to claim 1 of the new main request relates to the use of oligofructose and sialyllactose at specific amounts in the preparation of a medicament for use as a nutritional composition for feeding to a human (for the exact wording of claim 1 see point VI above). The combined use of oligofructose and sialyllactose enhances the growth of *Bifidobacteria* beyond the expected level and and inhibits the binding of pathogenic bacteria to human tissues (second medical use formulation of claim 1). It has been found that this combination provides a synergistic prebiotic effect, namely promotion of the beneficial *Bifidobacteria*, while having no effect on the growth of pathogenic bacteria such as *E. coli* or *Bacteroides* (page 2, lines 5-6; page 3, lines 28-31 and 34-35; page 4, lines 51-52; figure 1).

3. Closest prior art

3.1 The patent in suit acknowledges in paragraphs [0003] to [0007] that the beneficial effects of oligofructose and sialyllactose on human health were known in the art. Thus, oligofructose was known to be fermented in the large intestine only by a limited range of micro-organisms that included most species of *Bifidobacteria* - beneficial to human health - while other bacteria present in the "mixed population" of this part of the intestine either did not grow or were inhibited from growing. Sialyllactose was known to have anti-adhesive properties for specific pathogenic bacteria and was used to treat a number of medical conditions.

- 3.2 The appellant cited D2, D4 and D5 and argued that any of them could be considered to represent the closest prior art.
- 3.2.1 D5 discloses prophylactic and therapeutic nutritional compositions for the creation or maintenance of health-protective intestinal microflora which comprise fructo-oligosaccharides (FOS) such as oligofructose (page 8, lines 12-13) and bovine or caprine colostrum (see page 1, lines 6-12; page 15, lines 18-23) which represent a unique combination of beneficial nutrients, including carbohydrates, fats and amino acids (page 8, lines 16-18; page 22, lines 10-14). According to D5, FOS are good substrates for *Bifidobacteria* and selectively encourage their growth (see page 8, lines 13-15). Regarding colostrum, D5 discloses that it comprises oligosaccharides which may prevent attachment of pathogenic bacteria to human tissues (page 22, line 22 to page 23, line 1). D5 neither discloses the presence of sialyllactose in colostrum, let alone in the claimed amount, nor deals with the effect of sialyllactose on *Bifidobacteria* or pathogenic bacteria.
- 3.2.2 D2 discloses the use of specific indigestible FOS such as the oligofructoses 1-kestose, nystose and $1^F\text{-}\beta\text{-}$ fructofuranosyl nystose in nutritional compositions for enteral administration to humans (see column 2, lines 25-33; column 3, lines 44-46; column 7, lines 41-44; column 8, lines 45-49; claims). The biological effect of these fructo-oligosaccharides was to increase the *Bifidobacteria* in the enteral tract (see column 1, lines 39-59; column 3, lines 17-24) and to prevent excessive growth of harmful bacteria (column 1, lines 45-50). D2 does not disclose the use of sialyllactose in the nutritional composition.

- 3.2.3 D4 discloses mixtures of mono-, oligo- and polysaccharides for dietetic foods and for pharmaceuticals with both nutritional and biological or prebiotic effects which are considerably greater than the effect of the individual components (abstract; page 2, lines 18-21). The disclosed effects concern the prevention of pathogenic substances from adhering to human tissues and the stabilisation of the natural microflora (see page 2, lines 21-25 and 29; page 7, lines 8-15). The compositions of D4 can additionally contain 1-5 wt% of sialyllactose (page 4, line 24 to page 5, line 5; examples 2-4) which influences the biological activity of the oligo- and polysaccharides (page 7, lines 16-17). D4 does not clearly and unambiguously disclose that the biological effects derive from the combination of oligofructose and sialyllactose in the claimed amounts, nor that these effects concern *Bifidobacteria*. Moreover, D4 does not relate to preventing the growth of harmful bacteria.
- 3.3 It is apparent from the above analysis that D2, D4 and D5 do not disclose more than what was already acknowledged in the patent in suit, namely the known effects of oligofructose on the growth of *Bifidobacteria* and of sialyllactose on the anti-adhesive properties for specific pathogenic bacteria. The board concluded that the prior art cited in the patent was an appropriate starting point for the examination of inventive step.
- 3.4 The subject-matter of claim 1 of the main request differs from the prior art in that the nutritional composition contains a combination of oligofructose and sialyllactose in specified amounts.

4. Technical problem and solution

4.1 The respondent accepted that the effects of oligofructose and sialyllactose per se were known. For the formulation of the technical problem over the closest prior art it relied upon the synergistic effect provided by the combination of oligofructose and sialyllactose. In particular it saw the technical problem in the provision of an improved nutritional composition that promoted growth of *Bifidobacteria* but not that of pathogenic bacteria.

4.2 The solution is provided by the combination of the oligofructose with sialyllactose in the amounts specified in claim 1.

The technical evidence in the patent shows that problem as formulated by the respondent is indeed the objective technical problem and has indeed been solved.

4.2.1 Reference is made to figure 1 of the patent, which shows that the composition of example 1, which is within the scope of claim 1, not only contributes to the growth of *Bifidobacteria infantis*, as would normally be expected in view of the prior art, but has a synergistic effect in that the growth of *B.infantis* significantly exceeds the sum total of the individual contributions made by each component of the nutritional composition.

4.2.2 Figure 1 also illustrates the absence of bacterial growth with respect to *Clostridia*, a class of pathogenic bacteria. The board accepts that such an absence of growth is *prima facie* not apparent for the other pathogenic bacteria investigated, namely *Bacteroides*. Thus the results after 11.5 and 36 hours

manifestly show a reduction in bacteria growth, whereas at 24 hours no growth effect is clearly discernible. It is, however, stated in corresponding paragraph [0020] of the patent specification that "(T)he combination of oligofructose and sialyllactose had no effect on the growth of Clostridia or Bacteroides". In view of this statement and in the absence of any evidence to the contrary the board accepts that the absence of growth has also been plausibly shown for *Bacteroides*.

4.2.3 The appellant objected to this interpretation on the basis of another part of paragraph [0020] which states: "However, the growth of Clostridia and *B.infantis*, but not Bacteroides, in the presence of oligofructose was similar to that seen in the presence of glucose". However, this statement is irrelevant since it is comparing bacterial growth in oligofructose with that in glucose, and the latter is not a component of the nutritional composition of the claimed invention.

4.3 Obviousness

4.3.1 The skilled person starting from the closest prior art and seeking to improve the growth of beneficial *Bifidobacteria* while at the same time preventing or reducing the growth of harmful bacteria would not find any hint in the available prior art that the combination of oligofructose and sialyllactose in the claimed amounts would lead to such an unexpected enhancement of beneficial bacterial growth while preventing the growth of pathogenic bacteria.

4.3.2 The appellant referred to D6, which is a study related to the growth-promoting effect of sialyllactoses 3'-SL and 6'-SL on various *Bifidobacteria*, and argued that it hinted at combining oligofructose with sialyllactose in

order to enhance the growth of *Bifidobacteria*. However, the results presented in Table II of D6 (see page 1721), confirmed in the text of D6 (see page 1721, right column), do not establish a general trend when sialyllactose is used as substrate for a *Bifidobacteria* species and the skilled person would not be motivated to combine it with the closest prior art. Furthermore, D6 contains no hint that sialyllactose combined with oligofructose would have a synergistic growth-promoting effect on *Bifidobacteria*. The synergistic effect is demonstrated in the patent in suit for *B. infantis* (see figure 1), while D6 does not show any growth-promotion effect for this type of bacteria. The synergistic effect was thus contrary to the normal expectation of the skilled reader of D6. The respondent argued during the oral proceedings that if a synergistic effect was shown over the normal expectation of the skilled person for *B. infantis*, for which there was no growth-promoting effect, then an analogous synergistic effect would legitimately be expected for the other *Bifidobacteria* of D6, i.e. for those which do show a growth-promoting effect. The board accepts this argument, in the absence of any evidence to the contrary.

In summary, the combination of the prior art with D6 would not be expected to lead to a synergistic effect regarding the growth-promotion of *Bifidobacteria*.

- 4.3.3 Furthermore, D6 gives no hint that sialyllactose has any blocking effect on the growth of less beneficial, pathogenic bacteria. What D6 discloses is that sialylated oligosaccharides suppress the binding activity of pathogenic bacteria on human tissues (page 1722, left column, lines 25-26), which is an effect related to the activity of these bacteria but

not to their growth. Thus the skilled person would not expect that the combination of the sialyllactose of D6 with the oligofructose of the prior art would inhibit or reduce the growth of the pathogenic bacteria. In fact, this confirms that the results illustrated in figure 1 of the patent concerning the harmful bacteria are surprising.

4.4 No other conclusion with regard to inventive step would be reached when starting from D2, D4 or D5 as the closest prior art, since those documents, as shown above, do not go beyond the prior art acknowledged in the patent in suit and used by the board as the starting point for the assessment of inventive step.

4.5 In view of the above, the subject-matter of claim 1 of the main request involves an inventive step.

5. Dependent claims

Claims 2 to 4 are specific embodiments of claim 1 and for the reasons set out above also involve an inventive step.

6. In view of the above, the main request is allowable.

7. Amended description

The respondent submitted a description adapted to the claims of the main request. The appellant did not raise any objections. The board is satisfied that the amended description satisfies the requirements of 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 opposition division with the order to maintain the patent on the basis of the following documents:
 - claims 1 to 4 filed as main request with letter dated 27 October 2015;
 - pages 2 to 5 of the description as filed during the oral proceedings before the board;
 - figures 1 to 3 of the patent specification.

The Registrar:

The Chairman:



M. Cañueto Carbajo

W. Sieber

Decision electronically authenticated