Internal distribution code:

(A) [-] Publication in OJ
(B) [-] To Chairmen and Members
(C) [-] To Chairmen
(D) [X] No distribution

Datasheet for the decision of 15 July 2022

Case Number:	T 1683/17 - 3.3.04
Application Number:	08848466.2
Publication Number:	2217246
IPC:	A61K31/7028, A23L1/29, A23L1/30, A23L1/308, A61P37/04, A61P37/08, A61K45/06, A23L1/09, A61K35/74
Language of the proceedings:	EN

Title of invention:
USE OF OLIGOSACCHARIDES CONTAINING N-ACETYLLACTOSAMINE FOR MATURATION OF IMMUNE RESPONSES IN NEONATES

Patent Proprietor:
Société des Produits Nestlé S.A.

Opponents:
ABBOTT LABORATORIES
N.V. Nutricia

Headword:
Oligosaccharides in neonates / NESTLE

Relevant legal provisions:
EPC Art. 100(a), 56

Keyword:
Inventive step - all requests (no) - reasonable expectation of success (yes)

Europäisches Patentamt
European Patent Office
Office européen des brevets

Beschwerdekammern

Boards of Appeal

Chambres de recours

Boards of Appeal of the
European Patent Office
Richard-Reitzner-Allee 8
85540 Haar
GERMANY
Tel. +49 (0)89 2399-0
Fax +49 (0)89 2399-4465

Case Number: T 1683/17 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 15 July 2022

Appellant: (Opponent 1)	ABBOTT LABORATORIES 100 Abbott Park Road Abbott Park IL 60064 (US)
Representative:	Boult Wade Tennant LLP Salisbury Square House 8 Salisbury Square London EC4Y 8AP (GB)
Appellant: (Opponent 2)	N.V. Nutricia Eerste Stationsstraat 186 2712 HM Zoetermeer (NL)
Representative:	Nederlandsch Octrooibureau P.O. Box 29720 2502 LS The Hague (NL)
Respondent: (Patent Proprietor)	Société des Produits Nestlé S.A. Entre-deux-Villes 1800 Vevey (CH)
Representative:	Plougmann Vingtoft a/s Strandvejen 70 2900 Hellerup (DK)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 16 June 2017 rejecting the oppositions filed against European patent No. 2217246 pursuant to Article 101(2) EPC**

Composition of the Board:

Chairman	L. Bühler
Members:	S. Albrecht
	D. Luis Alves

Summary of Facts and Submissions

I. European patent No. 2 217 246 ("patent") was granted on the basis of a set of eight claims.

II. Independent claim 2 as granted reads as follows:

"The use of an oligosaccharide selected from the group consisting of lacto-N-tetraose, lacto-N-neotetraose, lacto-N-hexaose, lacto-N-neohexaose, para-lacto-N-hexaose, para-lacto-N-neohexaose, lacto-N-octaose, lacto-N-neooctaose, iso-lacto-N-octaose, para-lacto-N-octaose and lacto-N-decaose in the manufacture of a medicament or therapeutic nutritional composition for administration to a neonatal infant for reducing the risk of subsequent development of allergy in the infant, wherein the medicament or therapeutic nutritional composition is administered to the infant immediately after delivery and thereafter for at least 2 months."

III. The patent was opposed by two opponents on the grounds that its subject-matter lacked novelty and inventive step and that it did not sufficiently disclose the claimed invention.

IV. The documents filed during the opposition proceedings included the following:

D3: G. Boehm *et al.*, "Prebiotics in Infant Formulas", J Clin Gastroenterol 38 (Supp.2), July 2004, S76-S79

D5: WO 98/43495 A1

D13: G. E. Moro *et al.*, "Reproducing the bifidogenic effect of human milk in formula-fed infants: Why

and how?", *Acta Paediatrica* 94 (Suppl 449), 2005, 14-17

D21: WO 2005/122790 A1

D30: Experimental report by N. Sprenger, filed by the patent proprietor with its letter dated 21 March 2017

V. Both opponents ("appellant I" and "appellant II" respectively) lodged an appeal against the opposition division's decision to reject the oppositions.

VI. In the decision under appeal, the opposition division acknowledged inventive step of claim 2 of the main request starting from document D3 as the closest prior art. The subject-matter of claim 2 differed from this prior art in the type of oligosaccharide used for the purpose recited in this claim. Based on the experimental data disclosed in document D30, the objective technical problem was to be formulated as the provision of an improved oligosaccharide mixture useful for preventing allergy. The solution proposed by the patent was not rendered obvious by the prior art.

VII. With their statements setting out the grounds of appeal, both appellants requested that the decision under appeal be set aside and that the patent be revoked.

VIII. With its reply to these statements dated 9 March 2018, the patent proprietor ("respondent") requested as its main request that the appeals be dismissed (i.e. that the patent be maintained as granted) or, in the alternative, that the patent be maintained as amended on the basis of one of the sets of claims of auxiliary requests 1 to 8 filed with the same reply.

IX. In a letter dated 25 April 2019, appellant I requested that auxiliary requests 1 to 8 not be admitted into the proceedings.

X. In a communication pursuant to Article 15(1) RPBA 2020 dated 27 May 2022, the board addressed, *inter alia*, inventive step for claim 2 of the main request.

XI. Oral proceedings took place before the board on 15 July 2022 as a mixed-mode hearing. Appellant II and the respondent attended the proceedings via videoconference; appellant I and the board were physically present. During these proceedings, the respondent withdrew auxiliary requests 3 to 5. Appellant I subsequently withdrew its request not to admit auxiliary requests 1, 2, 6 to 8 into the proceedings. At the end of the oral proceedings, the Chair announced the board's decision.

XII. The appellants' written and oral submissions relevant to the present decision may be summarised as follows.

Documents D3 or D13 represented the closest prior art. The subject-matter of claim 2 of the main request differed from these documents in the oligosaccharide used, i.e. one of the 11 oligosaccharides listed in claim 2 rather than the mixture of galactooligosaccharides ("GOS") and fructooligosaccharides ("FOS") in a weight ratio of 9:1 used in the closest prior art. In the absence of evidence of a technical effect linked to this difference, the objective technical problem consisted in the provision of an alternative oligosaccharide that stimulated the growth of beneficial intestinal microbiota in the expectation that this would be beneficial for the prevention of allergy. With this

problem in mind, the skilled person would have been aware of document D5 that discussed the bifidogenic effect of lacto-N-neotetraose ("LNnT"). In light of this disclosure, the skilled person would have selected LNnT to solve the technical problem posed and would thus have arrived at the subject-matter of claim 2 without inventive merit.

The same conclusions applied if the objective technical problem were to be considered that of providing an oligosaccharide having improved effects over the oligosaccharide mixture disclosed in the closest prior art since document D5 contained pointers in Tables 3 and 4 that would have prompted the skilled person to select LNnT to solve this technical problem.

Auxiliary requests 1, 2, and 6 to 8 lacked an inventive step for the same reasons as the main request.

XIII. The respondent's written and oral submissions relevant to the present decision may be summarised as follows.

The subject-matter of claim 2 of the main request differed from document D3 or D13 taken as the closest prior art in that the oligosaccharide was one of the 11 oligosaccharides recited in this claim instead of the mixture of GOS and FOS described in the closest prior art. The technical effect linked to this difference was an improvement of the treatment disclosed in the closest prior art, as evidenced by the experimental data of document D30.
The objective technical problem was thus to be worded as improving the preventive treatment disclosed in the closest prior art. The solution proposed in claim 2 would not have been rendered obvious by document D5. This document did not contain any teaching which would

have provided the skilled person with a reasonable expectation that LNnT would give rise to an improvement over the treatment disclosed in the closest prior art. On the contrary, this document was solely concerned with LNnT and its bifidogenic effect and did not even mention the immune system in general terms, let alone allergy. An inventive step had thus to be acknowledged for the subject-matter of claim 2 of the main request.

For the same reasons, auxiliary requests 1, 2, and 6 to 8 fulfilled the requirements of inventive step in so far as these were directed to subject-matter identical to or embraced by the subject-matter of claim 2 of the main request.

XIV. The parties' final requests relevant for the present decision were as follows.

Both appellants requested that the decision under appeal be set aside and that the patent be revoked.

The respondent requested that the appeals be dismissed (main request) or, alternatively, that the patent be maintained on the basis of one of the sets of claims of auxiliary requests 1, 2, or 6 to 8, all filed with the reply to the statements setting out the grounds of appeal.

Reasons for the Decision

1. The appeals comply with Articles 106 to 108 EPC and Rule 99 EPC and are thus admissible.

Main request (patent as granted) - claim 2 - Article 100(a) EPC in conjunction with Article 56 EPC

2. Claim 2 is drafted in the Swiss-type format and relates to, *inter alia*, the use of LNnT in the manufacture of a medicament or therapeutic nutritional composition for administration to a neonatal infant for reducing the risk of subsequent development of allergy in the infant, wherein the medicament or therapeutic nutritional composition is administered to the infant immediately after delivery and thereafter for at least 2 months.

The closest prior art

3. The opposition division, appellant I and the respondent identified document D3 as the closest prior art. In appellant II's view, document D3 and document D13 qualified as equally suitable starting points for the assessment of inventive step of the subject-matter of claim 2.

Document D3

3.1 Document D3 (see abstract) pertains to a study on the prebiotic effect of an oligosaccharide mixture in preterm and term infants. According to the teaching of page S77, left-hand column, second full paragraph, this mixture consists of 90% GOS and 10% FOS ("mixture of GOS/FOS in a weight ratio of 9:1"). The study results are summarised in the section of the abstract entitled "Results". This section teaches that the mixture of GOS/FOS in a weight ratio of 9:1 significantly increases the number of *Bifidobacteria* and reduces the number of pathogens when compared with a group of infants fed an unsupplemented formula. In the final

paragraph of document D3, reference is made to evidence that these *Bifidobacteria* and their metabolites play an important role in the postnatal development of the immune system. The authors of document D3 conclude by stating that prebiotics may play an important role as a new concept in allergy prevention.

Document D13

3.2 Like document D3, document D13 (see abstract in conjunction with page 16, left-hand column, first full sentence) discloses that supplementation of infant formulas with a mixture of GOS/FOS in a weight ratio of 9:1 stimulates the growth of *Bifidobacteria* in term and preterm infants. Page 16 (see final paragraph) teaches that the observed modification of the intestinal flora in neonates was of great importance and very promising for the future prevention of allergic diseases when considering trials documenting the lower *Bifidobacteria* content in the gut in allergic infants.

Conclusion on the closest prior art

4. Hence, documents D3 and D13 both teach that the mixture of GOS/FOS in a weight ratio of 9:1 stimulates the growth of *Bifidobacteria* (i.e. it has bifidogenic effects) in preterm and term infants and underline the importance of this finding for the prevention of allergic diseases in this subject group. In view of the foregoing, the board agrees with appellant II that both these documents represent suitable starting points for the assessment of inventive step of the subject-matter of claim 2. This has not been disputed by the respondent.

Distinguishing feature(s) vis-a-vis the closest prior art

5. It was common ground between the parties that the only difference between the disclosure of each of documents D3 and D13 ("document D3/D13") and the subject-matter of claim 2 is the choice of one of the 11 oligosaccharides recited in this claim rather than the oligosaccharide mixture of GOS/FOS in a weight ratio of 9:1 used in document D3/D13. The board has no reason to take a different view.

Objective technical problem and solution

6. The respondent defined the objective technical problem as an improvement of the preventive treatment disclosed in document D3/D13 (see point XIII. above).

7. In the following assessment of inventive step, the board, for the sake of argument and in the respondent's favour, accepts the respondent's formulation of the technical problem.

8. The proposed solution to this problem is one of the 11 oligosaccharides listed in claim 2.

Obviousness of the proposed solution

9. In the board's judgement, the proposed solution would have been obvious in view of document D3/D13 taken in combination with document D5. The reasons are as follows.

9.1 Document D5 (see title) generally relates to nutritional formulations containing LNnT, i.e. one of the 11 oligosaccharides listed in claim 2 of the main request. In a preferred embodiment, these formulations

are infant feeding formulas (see page 4, lines 6 to 13). Page 5, lines 6 to 7 teaches that LNnT stimulates the growth and/or metabolic activity of bacteria of the genus *Bifidobacterium*.

9.2 Thus, documents D3, D13 and D5 all relate to oligosaccharide-supplemented formulas and their bifidogenic effects in infants.

9.3 In the respondent's view, the skilled person faced with the technical problem of improving the treatment disclosed in document D3/D13 would not have consulted document D5 and taken its content into consideration. Document D5 solely referred to the bifidogenic properties of LNnT in the context of preventing bacterial infections. No mention was made of the immune system in general and allergy in particular.

9.4 The board does not agree. As submitted by the appellants at the oral proceedings, document D3 (see abstract, section "Conclusion", first sentence in conjunction with page S78, right-hand column, last paragraph) and document D13 (see point 3.2 above) both establish a link between, on the one hand, the ability of the tested oligosaccharide mixture to stimulate the development of a microbial flora similar to that of breast-fed infants and, on the other hand, the prevention of allergy. As a consequence, the skilled person starting from document D3/D13 and seeking to reduce the risk of developing allergy even further would have consulted document D5 because - like document D3/D13 - document D5 refers to oligosaccharide-supplemented infant formulas with stimulatory effects on the growth and/or metabolic activity of beneficial biota of the microbial flora, specifically *Bifidobacteria*.

9.5 In reading document D5, the skilled person would have paid particular attention to the bacterial assays disclosed in Example 1 of this document. In these assays, several carbohydrate preparations - including LNnT, FOS and GOS - were tested for their abilities to promote metabolic activity and the growth of *Bifidobacterium infantis.* The results are reported in Tables 3 and 4 respectively (see pages 10 and 11 of document D5).

9.6 In favour of the respondent, the board accepts its oral submission that the data of Table 4 are more relevant than those of Table 3. These data stem from assays in which the growth of the tested bacteria were measured based upon the lactic acid produced per bacterial cell. To this end, bacteria of the species *Bifidobacterium infantis* were cultured in a medium containing either no carbohydrate or one of the carbohydrate preparations displayed in the left-hand column of Table 4. These carbohydrates included the following:

(a) LNnT at concentrations of 0.1 and 1 mg/ml respectively

(b) FOS at concentrations of 0.1 and 1 mg/ml respectively

(c) GOS at concentrations of 0.1 and 1 mg/ml respectively

9.7 After approximately 24 to 48 hours, carbohydrate fermentation was measured by, *inter alia*, lactic acid production. The corresponding lactic acid concentrations are set out in the right-hand column of Table 4, entitled "Lactic Acid Concentration Less

Background". In this regard, the following is undisputed:

(a) At concentrations of 1 mg/ml, LNnT gives rise to the highest lactic acid concentration of all tested carbohydrates, i.e. it has a value of 0.070 (see Table 4, third column, second row). In contrast, no or only very little lactic acid is produced by the bacteria in the presence of 1 mg/ml FOS and 1 mg/ml GOS respectively (see Table 4, third column, third and fourth rows indicating values of 0.000 and 0.010 respectively).

(b) At concentrations of 0.1 mg/ml, the outcome for LNnT, GOS and FOS is the opposite, i.e. FOS achieves the highest lactic acid production having a value of 0.050, followed by GOS and LNnT exhibiting values of 0.030 and 0.020 respectively.

9.8 At first sight, these data might be considered unclear in that sometimes LNnT gives rise to a higher lactic acid production by the tested bacteria than GOS alone and FOS alone, and sometimes it does not.

9.9 However, on closer inspection, the skilled person would have realised that the effects of LNnT, GOS and FOS on lactic acid production by the tested bacteria are in fact concentration-dependent and that the highest lactic acid concentration is obtained with LNnT at a concentration of 1 mg/ml (see point 9.7(a) above). In light of this teaching, the skilled person would have selected this oligosaccharide at sufficiently high concentrations in the expectation that it would be more effective than GOS and FOS individually in stimulating the growth of *Bifidobacteria* in infants.

9.10 Undoubtedly, the oligosaccharides tested in Example 1 of document D5 do not include the mixture of GOS/FOS in a weight ratio of 9:1 described in the closest prior art (document D3/D13). Accordingly, the question arises whether, based on the prior art on file, the skilled person would have reasonably expected LNnT to be more effective also compared to this mixture.

9.11 In the board's judgement, this is indeed so. The mixture of GOS/FOS in a weight ratio of 9:1 described in the closest prior art differs from GOS used in Example 1 of document D5 solely in that 10% of this oligosaccharide is replaced by FOS. As argued by the appellants and explained in point 9.7(a) above, the skilled person would have learned from Table 4 of document D5 that 1 mg/ml of FOS does not cause the tested bacteria to produce any lactic acid and that GOS at the same concentration exhibits only very little activity in this regard. In light of these facts, the board agrees with the appellants that the skilled person would have reasonably expected a mixture of GOS/FOS in a weight ratio of 9:1 at a concentration of 1 mg/ml to give rise to levels of lactic acid production in Example 1 of document D5 which do not differ significantly from those obtained with 1 mg/ml of GOS alone and which are lower than those achieved by 1 mg/ml of LNnT.

9.12 The respondent contested this. Citing document D21, page 19, lines 5 to 9, the respondent argued that the skilled person would have been aware that mixtures of GOS and FOS act synergistically in promoting the growth of *Bifidobacteria*. As a consequence, the skilled person would have considered the mixture of GOS/FOS disclosed in document D3/D13, on the one hand, and GOS and FOS individually, on the other hand, to be distinct

entities and hence would not have had any reasonable expectation, based on the teaching of document D5, that LNnT would provide an improved treatment of allergy compared to the mixture of GOS/FOS described in document D3/D13.

9.13 The board does not endorse the respondent's view.

9.13.1 The passage of document D21 relied on by the respondent forms part of Example 3 of this document. This example aims at determining the effects of different oligosaccharides on the production of short chain fatty acids ("SCFA") resulting from the fermentation of these oligosaccharides by micro-organisms of fresh faecal samples of infants. Page 19, lines 5 to 9 of document D21 refers to Figure 3a as showing that a mixture of a specific GOS
(i.e. transgalactooligosaccharides or "TOS") and inulin (identified as a type of FOS by the respondent and appellant I) results in a significantly and synergistically increased amount of SCFA (particularly acetate) per gram fibre compared to the single components.

9.13.2 The board does not have any reason to doubt the validity of the teaching of the aforementioned passage of document D21. However, this teaching only addresses the synergism relied on by the respondent under specific experimental conditions, in relation to a specific oligosaccharide mixture. Hence, from document D21's disclosure on page 19, lines 5 to 9 alone, it cannot be concluded that the synergistic effects reported are of general applicability. Absent any evidence in support of this general applicability, the respondent's argument must fail.

9.13.3 Furthermore, appellant I correctly noted at the oral proceedings with respect to Figure 3a of document D21 that the increased amount of SCFA achieved by the mixture of TOS and inulin versus TOS and inulin alone is of significantly lower magnitude than the increase in lactic acid production obtained with 1 mg/ml of LNnT versus 1 mg/ml of GOS alone and 1 mg/ml of FOS alone in Example 1 of document D5 (i.e. 0.070 versus 0.010 and 0.000 respectively, see point 9.7(a) above). Therefore, the board, in agreement with the appellants, finds that document D21's disclosure on page 19, lines 5 to 9 would not have diminished the skilled person's degree of confidence in successfully solving the underlying technical problem based on the teaching of document D3/D13 taken in combination with the teaching of document D5.

Overall conclusion on inventive step of claim 2 of the main request

10. In view of the foregoing considerations, the board concludes that the subject-matter of claim 2, as far as it relates to LNnT, would have been obvious in light of the closest prior art (document D3/D13) taken in combination with document D5.

11. Consequently, the ground of opposition under Article 100(a) in conjunction with Article 56 EPC prejudices the maintenance of the patent as granted.

Auxiliary requests 1, 2, 6 to 8 - Article 56 EPC

12. Claim 2 of auxiliary request 1 and claim 1 of auxiliary request 7 are identical to claim 2 of the main request with the exception that the claimed oligosaccharides have been restricted to lacto-N-tetraose and LNnT.

13. Claim 2 of auxiliary request 2 and claim 1 of auxiliary request 8 are identical and differ from claim 2 of the main request in that the claimed oligosaccharides have been limited to LNnT.

14. Claim 1 of auxiliary request 6 is identical to claim 2 of the main request.

15. Hence, the subject-matter of claim 2 of each of auxiliary requests 1 and 2 as well as the subject-matter of claim 1 of each of auxiliary requests 6 to 8 does not fulfil the requirements of Article 56 EPC for the same reasons as set out for claim 2 of the main request.

Overall conclusion

16. Since none of the claim requests is allowable, the patent has to be revoked.

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:

I. Aperribay L. Bühler

Decision electronically authenticated