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**Datasheet for the decision
of 23 June 2009**

Case Number: T 0649/07 - 3.3.09

Application Number: 98913279.0

Publication Number: 0973413

IPC: A23L 1/09

Language of the proceedings: EN

Title of invention:

Nutritional formulations containing Lacto-N-neotetraose

Patentee:

ABBOTT LABORATORIES

Opponent:

Numico Research B.V.

Headword:

-

Relevant legal provisions:

EPC Art. 56

Keyword:

-

Decisions cited:

-

Catchword:

"Inventive step - yes"



Case Number: T 0649/07 - 3.3.09

D E C I S I O N
of the Technical Board of Appeal 3.3.09
of 23 June 2009

Appellant: Numico Research B.V.
(Opponent) P.O. Box 7005
NL-6700 CA WAGENINGEN (NL)

Representative: Meekel, Arthur Augustinus P.
Nederlandsch Octrooibureau
P.O. Box 29720
NL-2502 LS Den Haag (NL)

Respondent: ABBOTT LABORATORIES
(Patent proprietor) CHAD 0377/AP6D-2
100 Abbott Park Road
Abbott Park IL 60064-3500 (US)

Representative: Modiano, Micaela Nadia
Modiano Josif Pisanty & Staub Ltd
Thierschstraße 11
D-80538 München (DE)

Decision under appeal: Interlocutory decision of the Opposition
Division of the European Patent Office posted
10 January 2007 concerning maintenance of
European patent No. 0973413 in amended form.

Composition of the Board:

Chairman: P. Kitzmantel
Members: J. Jardón Álvarez
M-B. Tardo-Dino

Summary of Facts and Submissions

I. The grant of European patent No. 0 973 413 in respect of European patent application No. 98913279.0 in the name of Abbott Laboratories, which had been filed on 30 March 1998 as International application PCT/US98/06217 (WO - 98/43495), was announced on 28 July 2004 (Bulletin 2004/31) on the basis of 12 claims. Independent Claims 1 and 12 read as follows:

"1. A synthetic nutritional composition comprising a *Bifidobacterium infantis* stimulating amount of Lacto-N-neo Tetraose and further comprising edible macronutrients.

12. Use of Lacto-N-neo Tetraose for manufacturing a nutritional formulation for inhibiting Bacteroides, Clostridium and E. coli infection in a subject by feeding the subject an effective anti-bacterial amount of Lacto-N-neo Tetraose."

Claims 2 to 11 were dependent claims.

II. Notice of Opposition requesting the revocation of the patent in its entirety on the grounds of lack of novelty and inventive step (Article 100(a) EPC), was filed by Numico Research B.V. on 27 April 2005.

During the opposition proceedings *inter alia* the following documents were cited:

D2: WO - 95/24495

- D4: A. Cravioto *et al.*, "Inhibition of Localized Adhesion of Enteropathogenic *Escherichia coli* to HEP-2 Cells by Immunoglobulin and Oligosaccharide Fractions of Human Colostrum and Breast Milk" *J. Infections Diseases* 1991, pages 1247 - 1255; and
- D10: T. Idota *et al.*, "Growth-promoting Effects of N-Acetylneuraminic Acid-containing Substances on Bifidobacteria." *Biosci. Biotech. Biochem.*, 58(9), 1994, pages 1720 - 1722.
- III. By its interlocutory decision announced orally on 9 November 2006 and issued in writing on 10 January 2007, the Opposition Division held that the grounds for opposition raised by the Opponent did not prejudice the maintenance of the patent in amended form on the basis of the claims according to the then pending auxiliary request.

Independent Claims 1, 11 and 12 as maintained by the Opposition Division read as follows:

"1. A synthetic nutritional composition comprising a *Bifidobacterium infantis* stimulating amount of Lacto-N-neo Tetraose of from about 0.075 to about 2.0 mg/ml and further comprising edible macronutrients.

11. Use of Lacto-N-neo Tetraose for manufacturing a nutritional formulation for inhibiting Bacteroides, Clostridium and E. coli infection in a subject by feeding the subject an effective anti-bacterial amount of Lacto-N-neo Tetraose.

12. Use of Lacto-N-neo Tetraose for manufacturing a synthetic nutritional composition for stimulating *Bifidobacterium infantis*, said composition further comprising edible macronutrients."

The Opposition Division acknowledged the novelty of Claim 1 because the prior art did not disclose a nutritional composition comprising the specified amounts of lacto-N-neo-tetraose and edible macronutrients and the novelty of Claim 11 because D4 failed to identify lacto-N-neo-tetraose as the active agent responsible for the antibacterial effect of the tested lacto-N-neo-tetraose-containing oligosaccharide fraction.

Concerning inventive step, the Opposition Division considered that the disclosure of D10 would not suggest the surprisingly high efficacy of lacto-N-neo-tetraose in promoting the growth of *Bifidobacterium infantis* as established by the patent in suit. As to Claim 11, the Opposition Division held that there was no hint in D4 motivating the skilled person to investigate a possible antibiotic effect against *E. coli* of lacto-N-neo-tetraose; this isomer being present in the oligosaccharide fraction together with the isomer lacto-N-tetraose known from EP - 0 313 533 to be active in this respect.

IV. On 9 March 2007 the Opponent (Appellant) lodged an appeal against the decision of the Opposition Division and paid the appeal fee on the same day.

In the Statement of Grounds of Appeal filed on 16 May 2007, the Appellant requested the revocation of

the patent in its entirety. It contended that the claims allowed by the Opposition Division lacked clarity (Article 84 EPC), did not fulfil the requirements of Article 123(2) and (3) EPC, and lacked novelty (Article 54 EPC) and inventive step (Article 56 EPC).

V. The Respondent (Patent Proprietor) presented its counterstatement by letter dated 5 December 2007. It requested that the appeal be dismissed and the patent be maintained with the claims in accordance with an amended set of claims filed therewith.

VI. On 12 January 2009 the Board dispatched a summons to attend oral proceedings on 23 June 2009. In the attached annex to the summons the Board drew the attention of the parties to the points to be discussed during the oral proceedings.

VII. By letter dated 20 May 2009, the Respondent filed further arguments in support of its main request and filed sets of claims for two auxiliary requests.

VIII. During the oral proceedings held on 23 June 2009, after the discussion of the main request, the Respondent withdrew its previous main request and filed as its sole request an amended main request consisting of Claims 1 to 10 of its previous first auxiliary request.

Claim 1 of this request reads as follows:

"1. A synthetic nutritional composition for use in stimulating *Bifidobacterium infantis* comprising a

Bifidobacterium infantis stimulating amount of Lacto-N-neo tetraose of from about 0.075 to about 2.0 mg/ml and further comprising edible macronutrients."

Claims 2 to 10 are dependent claims.

IX. The arguments presented by the Appellant insofar as they are relevant for the present decision may be summarized as follows:

- The Appellant contested the novelty of nutritional compositions comprising lacto-N-neo-tetraose as ingredient because this compound was to be found in human milk as well as in transgenic non-human mammal milk, (processed) human milk and/or fortified human milk. It admitted however, during the oral proceedings, that its use for stimulating *Bifidobacterium infantis* as presently claimed was novel over this state of the art.

- Concerning inventive step, the Appellant regarded the disclosure of D10 relating to the growth-promoting effects of oligosaccharides present in human milk on *Bifidobacteria* as the closest prior art. In its opinion the claimed subject-matter was distinguished from the disclosure of D10 only by the fact that D10 did not specifically disclose lacto-N-neo-tetraose as one of these oligosaccharides. The Appellant saw the problem underlying the patent in suit as being to identify suitable oligosaccharides having this effect. The solution to this problem, namely the use of lacto-N-neo-tetraose, a known oligosaccharide of human milk, lacked inventive step. In its opinion it was obvious based on the teaching

of D10 to try out the oligosaccharides of human milk in order to discover suitable ones having the required growth-promoting effect.

- The Appellant did not raise any formal objections against the claims and did not contest the admittance of the set of claims into the proceedings.

X. The arguments presented by the Respondent, insofar as they are relevant for the present decision, may be summarized as follows:

- The Respondent agreed with the Appellant that D10 represented the closest prior art document. It justified an inventive step of the claimed subject-matter by the unexpected high bifido-stimulating effect of lacto-N-neo-tetraose when compared to that of the N-acetylglucosamine, a compound disclosed in D10 as particularly active in that respect, or to that of other saccharides as shown by the results in Table 3 of the patent in suit. In particular a purposive selection had to be acknowledged with respect to the many oligosaccharides of human milk which bear an N-acetylglucosamine moiety, many of which are present there in a much larger amount than lacto-N-neo-tetraose.

XI. The Appellant requested that the decision under appeal be set aside and that the European patent No. 0 973 413 be revoked.

The Respondent requested that the patent be maintained on the basis of the set of Claims 1 to 10 of the sole

request filed on 24 June 2009 during the oral proceedings.

Reasons for the Decision

1. The appeal is admissible.

MAIN REQUEST

The Respondent withdrew the claims on which the decision under appeal was based and filed during the oral proceedings a new main request.

2. *Novelty (Article 54 EPC).*

- 2.1 Claim 1 is essentially directed to:

- an edible composition comprising 0.075 to 2.0 mg/ml of lacto-N-neo-tetraose (a known tetrasaccharide found in human milk in amounts of ca. 0.060 mg/ml: cf. Table 1 of D2) and edible macronutrients,
- for use in stimulating *Bifidobacterium infantis*

- 2.2 The subject-matter of this claim is novel because there is no disclosure in the cited prior art either of nutritional compositions comprising lacto-N-neo-tetraose in the specified amounts or of its use for stimulating *Bifidobacteria*. As the novelty of this purpose-related subject-matter was also acknowledged by the Appellant no further comments are needed in this respect.

3. *Inventive step (Article 56 EPC).*

3.1 Closest prior art.

3.1.1 The Board concurs with the parties to the proceedings in that the closest prior art is represented by document D10.

3.1.2 D10 relates, like the patent in suit, to the growth of *bifidobacteria*. It indicates in its introduction (page 1720, left column, first paragraph after the abstract, especially lines 11 to 18) that oligosaccharides containing N-acetylglucosamine promote the growth of *Bifidobacterium bifidum* and that other oligosaccharides such as fructo-oligosaccharide, isomalto-oligosaccharide, and galacto-oligosaccharide have been also reported as *bifidus* factors.

The examples in D10 investigate the growth-promoting effect of N-acetylneuraminic acid-containing oligosaccharides derived from cow's milk, such as sialyl-lactose and glycomacropeptide on *Bifidobacteria* (see Table 2).

3.1.3 The subject-matter of Claim 1 of the patent in suit differs from the disclosure of D10 by the use of lacto-N-neo-tetraose as the active ingredient for stimulating *Bifidobacteria*.

3.2 Problem to be solved and its solution.

3.2.1 According to the specification of the patent in suit, by using lacto-N-neo-tetraose a higher stimulating effect is achieved than by using N-aceytglucosamine itself or other oligosaccharides. The results in

Table 3 of the patent demonstrate that lacto-N-neo-tetraose is an excellent metabolic stimulant of *Bifidobacterium infantis*. The β -galactosidase utilization index BGUI of lacto-N-neo-tetraose at a concentration of 0.1 mg/ml is 83.9, well above the value for N-acetylglucosamine (10.8 for GlcNAc-Sucrose) and for the other tested saccharides. Similar results are obtained when measuring the acetate utilization index AUI.

3.2.2 Thus, taking account of the advantageous effect of lacto-N-neo-tetraose over that to be expected on the basis of the disclosure of D10, the technical problem to be solved by the patent can be formulated as being the provision of an improved composition for stimulating the growth of *Bifidobacterium infantis*.

3.2.3 This problem is solved by using a composition comprising 0.075 to 2.0 mg/ml of lacto-N-neo-tetraose as active ingredient.

3.2.4 The results of the examples and comparative examples in Table 3 of the patent as discussed above under 3.2.1 show that the above mentioned problem has been credibly solved. This finding was not disputed by the Appellant.

3.3 Obviousness.

3.3.1 It remains to be decided whether, in view of the available prior art documents, it would have been obvious for the skilled person to solve this technical problem by the means claimed, namely by using lacto-N-neo-tetraose.

3.3.2 Document D10 cannot give any hint to this solution as no mention is made of lacto-N-neo-tetraose in the document. In fact D10 concentrates on the study of the activity of N-acetylneuraminic acid containing oligosaccharides, that is to say, oligosaccharides structurally quite different from the one now claimed. There is also no hint in the other documents cited by the Appellant, none of them dealing with the problem of stimulating the growth of *Bifidobacteria*.

3.3.3 The Appellant did not dispute that lacto-N-neo-tetraose is not suggested by D10 but argued that in view of the teaching of D10 that several oligosaccharides of human milk were known to promote the growth of *Bifidobacteria* it would have been obvious for the skilled person to try other such oligosaccharides and thus arrive at the claimed invention.

3.3.4 This Board cannot accept this argument of the Appellant for the following reasons:

- There is no specific suggestion or guidance in D10 towards any particular oligosaccharide out of the many (human breast milk contains more than 100 different oligosaccharides) present in human milk. As pointed out above, D10 concentrates on the study of substances derived from cow's milk.
- Moreover there is no suggestion in D10 or in the other cited documents towards the choice of lacto-N-neo-tetraose in order to achieve an improved growth-promoting effect on *Bifidobacterium infantis*.

3.3.5 It follows that the finding according to the claimed subject-matter that lacto-N-neo-tetraose gives a higher *Bifidobacterium infantis* stimulating effect than other structurally close oligosaccharides is not a teaching the skilled person being confronted with the task of finding a solution to the existing technical problem would find in the available prior art or within his general common knowledge.

3.4 The subject-matter of Claim 1 therefore involves an inventive step within the meaning of Article 56 EPC. This conclusion extends *a fortiori* to Claims 2 to 10, appendant to Claim 1.

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 Claims 1 to 10 of the sole request filed during oral proceedings after any necessary consequential amendments of the description.

The Registrar

The Chairman

G. Röhn

P. Kitzmantel