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**Datasheet for the decision
of 11 December 2019**

Case Number: T 1340/16 - 3.3.01

Application Number: 09800034.2

Publication Number: 2315595

IPC: A61K35/74, A23L1/29, A23L1/30

Language of the proceedings: EN

Title of invention:
PROBIOTICS TO INCREASE IGA SECRETION IN INFANTS BORN BY
CAESAREAN SECTION

Patent Proprietor:
Société des Produits Nestlé S.A.

Opponent:
N.V. Nutricia

Headword:
IgA secretion due to probiotics/NESTLE

Relevant legal provisions:
EPC Art. 56
RPBA Art. 12(4), 13

Keyword:

Main request and auxiliary requests 1 and 3 - inventive step
(no)

Late-filed request auxiliary request 2 - admitted (no)



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Case Number: T 1340/16 - 3.3.01

D E C I S I O N
of Technical Board of Appeal 3.3.01
of 11 December 2019

Appellant: N.V. Nutricia
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Decision under appeal: **Decision of the Opposition Division of the
European Patent Office posted on 11 April 2016
rejecting the opposition filed against European
patent No. 2315595 pursuant to Article 101(2)
EPC.**

Composition of the Board:

Chairman A. Lindner
Members: M. Pregetter
L. Bühler

Summary of Facts and Submissions

- I. European patent No. 2315595 is based on European patent application No. 09800034.2, filed as an international application published as WO2010/010021.

Claim 1 as granted reads as follows:

"1. Use of probiotic bacteria in the manufacture of an infant formula for increasing IgA secretion in an infant delivered by caesarean section during the first four months of the life of the infant, wherein the probiotic bacteria are lactic acid bacteria or Bifidobacteria, and wherein said infant formula contains a protein source in an amount of not more than 2.0g/100kcal, and contains a carbohydrate source, and contains a source of lipids, and wherein the infant formula further comprises a mixture of galacto-oligosaccharide(s), N-acetylated oligosaccharide(s) and sialylated oligosaccharide(s) in which the N-acetylated oligosaccharide(s) comprise 0.5 to 4.0% of the oligosaccharide mixture, the galacto-oligosaccharide(s) comprise 92.0 to 98.5% of the oligosaccharide mixture and the sialylated oligosaccharide(s) comprise 1.0 to 4.0% of the oligosaccharide mixture."

- II. The following documents, cited during the opposition and appeal proceedings, are referred to below:

(5) Bakker-Zierikzee et al., *Pediatr. Allergy Immunol.*, 2006, 17, 134-140

(6) Grönlund et al., *J. Pediatr. Gastroenterol. Nutr.*, 1999, 28(1), 19-25

(7) Fukushima et al., *Int. J. Food Microbiol.*, 1998,

42, 39-44

(8) EP 1 776 877

(12) WO2005/039319

(21) Experimental report, filed on 17 February 2016,
2 pages

(23) WO2007/101675

(29) Huurre et al., Neonatology, 2008, 93, 236-240

III. The appeal lies from the decision of the opposition division to reject the opposition. In the statement setting out the grounds of appeal, the appellant questioned the validity of the priority document, sufficiency of disclosure, and the presence of an inventive step.

IV. With its reply to the statement of grounds of appeal, the respondent provided arguments and submitted auxiliary requests 3 to 5.

With a letter dated 21 August 2017, the appellant filed document (29).

V. Oral proceedings were held on 11 December 2019. In the course of the oral proceedings, the respondent withdrew auxiliary requests 1 to 3, renumbered auxiliary requests 4 and 5 to auxiliary requests 1 and 3, respectively and submitted a new auxiliary request 2.

The respective claims 1 of the auxiliary requests differ from claim 1 of the main request in that the term "use of probiotic bacteria" has been replaced by

definitions concerning particular strains and by deleting the terms "wherein the probiotic bacteria are lactic acid bacteria or Bifidobacteria".

Claim 1 of auxiliary request 1 defines the "use of *Bifidobacterium lactis* CNCM 1-3446 or *Bifidobacterium longum* ATCC BAA-999".

Claim 1 of auxiliary request 2 defines the "use of *Bifidobacterium lactis* CNCM 1-3446".

Claim 1 of auxiliary request 3 defines the "use of *Bifidobacterium longum* ATCC BAA-999".

VI. The appellant's arguments, insofar as they are relevant to the present decision, may be summarised as follows.

Admission of requests

Auxiliary requests 1 and 3 were filed with the reply to the grounds of appeal without providing arguments concerning the reasons for filing these requests. Both requests were *prima facie* not allowable under Article 123(2) EPC and thus introduced new issues. Auxiliary request 2 was filed during the oral proceedings. Claim 1 of auxiliary request 2 defined a certain, specific strain of Bifidobacteria. The subject-matter of auxiliary request 2 could not be dealt with during the oral proceedings since it necessitated a completely new review of the prior art and probably the selection of a different closest prior art.

Inventive step

The closest prior art was document (8). It described the stimulation of a healthy intestinal flora of

infants born by caesarean section by probiotics and the consequence thereof, i.e. the stimulation of a healthy immune system (paragraph [0063]). Example 3 of document (8) disclosed an infant formula comprising, *inter alia*, *Bifidobacterium longum*. Differences between the claimed subject-matter and the disclosure of document (8) were the prebiotic mixture, which had never been linked to a surprising effect and which was similar to the mixture in document (23), and the claimed effect of increased IgA secretion. The technical problem could be seen to be what further specific effect could be expected from a dietary composition such as the one disclosed in document (8). Document (8) taught that the administration of probiotics to infants delivered by caesarean section would lead to stimulation of the immune system due to the stimulation of a healthy intestinal flora. The skilled person was thus aware that they were dealing with a healthy intestinal flora and would consult document (6). Document (6) stated that a normal intestinal flora went hand in hand with IgA secretion and thus provided a pointer to what could be achieved in infants delivered by caesarean section. No inventive step was present.

The same line of argument applied to the subject-matter of auxiliary requests 1 and 3. Document (8) taught that *Bifidobacterium longum* could be relied upon. A commercially available strain of *Bifidobacterium longum* was ATCC BAA-999 (see claim 11 of document (23)). It would have been used by the skilled person when trying to rework example 3 of the closest prior art. No change of effect would be expected when using the now claimed strain.

VII. The respondent's arguments, insofar as they are relevant to the present decision, may be summarised as follows.

Admission of requests

Auxiliary requests 1 and 3 were filed together with the reply to the statement of grounds of appeal taking into account objections concerning the scope of the claims. Auxiliary request 2 was a reaction to developments during oral proceedings. The filing of a further converging auxiliary request, strongly backed up by document (21), was meant to be a *bona fide* attempt to overcome the remaining objections.

Inventive step

Document (8) was the closest prior art. Its general teachings could be found in paragraphs [0003], [0010] and [0063]. The main difference between the subject-matter of claim 1 of the main request and document (8) was the fact that document (8) merely mentioned the immune system in general. It did not point to the humoral part thereof. The further differences in the composition of the prebiotics were not crucial for the assessment of inventive step. In line with the impugned decision, the problem was seen to be the provision of a targeted therapeutic application of a probiotic composition known to stimulate the immune system in infants delivered by caesarean section.

Document (8) did not mention IgA secretion at all. Other documents on file taught away from such an effect. According to document (12), immune effects due to the administration of probiotics were the inhibition of a Th2 type immune response (i.e. the inhibition of

an immune response linked to the humoral immune system where IgA secretion might be expected) and a stimulation of a Th1 type immune response. Document (5) found no increase in IgA levels in infants receiving Bb-12 probiotic bacteria. Document (7) was of no relevance since it concerned older children. Finally, it had to be noted that document (6) did not deal with the administration of probiotics, but merely discussed the development of the intestinal flora of newborn infants. Therefore, it could not lead the skilled person to the claimed subject-matter.

The same line of argument applied to the auxiliary requests. These requests defined specific strains, the immune response of which could not have been predicted. The mere fact that a certain strain was commercially available could not lead to the assumption that it would work.

VIII. The final requests of the parties were as follows.

The appellant (opponent) requested that the decision under appeal be set aside and that the European patent No. 2315595 be revoked.

The respondent (patent proprietor) requested that the appeal be dismissed (main request). Alternatively, it requested that the patent be maintained on the basis of one of the following sets of claims:

- auxiliary request 1 filed as auxiliary request 4 with the reply to the statement of grounds of appeal;
- auxiliary request 2 filed during the oral proceedings; and
- auxiliary request 3 filed as auxiliary request 5 with the reply to the statement of grounds of appeal.

Reasons for the Decision

1. The appeal is admissible.
2. *Inventive step - main request*
 - 2.1 The object of the patent in suit is the increase of IgA secretion during the first four to six months of life by administering probiotic bacteria to infants delivered by caesarean section (paragraph [0001]). The administration of probiotic bacteria primes the gastrointestinal tract of the infants in favour of subsequent colonisation by those species of Bifidobacteria which are commonly found in the tracts of healthy, vaginally-delivered, breast-fed infants. The beneficial colonisation increases total IgA secretion (paragraph [0018]).
 - 2.2 It was common ground that document (8) represents the closest prior art and that the differences in the definition of the prebiotics were not crucial.

Document (8) relates to methods for feeding and in particular to compositions to be administered to infants delivered via caesarean section. These infants lack biodiversity in their intestinal flora. The document states that the intestinal flora plays a crucial role in the development of the infant. The stimulation of the healthy development of the intestinal flora of infants born by caesarean section stimulates the immune system and provides resistance to infections (paragraphs [0001],[0003],[0010],[0011] and [0063]). The administration of microorganisms will increase the biodiversity of the infants' flora (paragraphs [0016], [0017] and [0063], claim 14).

Example 3 discloses a nutritional composition to be administered to infants born by caesarean section comprising protein, fat, digestible carbohydrates, non-digestible carbohydrates (prebiotics) and Bifidobacteria, *inter alia* *Bifidobacterium longum*, and lactic acid bacteria.

- 2.3 The subject-matter of claim 1 of the main request differs from the disclosure of document (8) in the prebiotics and the definition of a specific immunological effect in the form of IgA secretion.

Example 2 of the patent in suit shows that the administration of the *Bifidobacterium longum* strain ATCC BAA-999 leads to an increase in IgA secretion of infants delivered by caesarean section when compared to such infants receiving a formula not containing the probiotic strain.

- 2.4 Starting from the closest prior art identified by both parties, the technical problem is the provision of a further, specific immunological effect in infants delivered by caesarean section due to the administration of probiotics in an infant formula comprising alternative prebiotics.

The solution is the administration of a composition comprising probiotics as defined in claim 1 of the main request for increasing IgA secretion.

The problem has been solved as shown by example 2 of the patent in suit.

- 2.5 The person skilled in the art, confronted with the problem of identifying and providing specific immunological effects associated with a healthy

intestinal flora of newborn infants, would consider all immunological effects discussed in the context of the intestinal flora of newborn infants.

Document (6) relates to the intestinal flora of infants delivered by caesarean section. It is thus a document the skilled person would have had relied on when starting from document (8) as the closest prior art. After discussing the intestinal flora and its development, document (6) concludes by examining facts reported in literature as being associated with the intestinal flora. Firstly, it is stated that normal intestinal flora has an immunostimulatory function. Lack of intestinal flora is linked to a deficit of mucosal IgA plasma cells. Secondly, it is reported that the administration of probiotic bacteria to children in association with diarrhoea or mucosal vaccination has been shown to lead to an increase in IgA response. IgA is identified as an important mediator of mucosal immunity in cooperation with a variety of innate protective mechanisms (page 24, last paragraph). Document (6) thus suggests a direct link between the intestinal flora, probiotics and IgA secretion. This link would have led the skilled person to expect that IgA secretion forms part of the immunological effects elicited by the administration of probiotics and thus to the subject-matter claimed. No inventive step is present.

- 2.6 The respondent has argued that the expectation of IgA secretion due to the administration of probiotics from the documents on file amounted to hindsight. It has identified various documents that "teach away" from the claimed subject-matter. Furthermore, some of the documents on file would not be consulted by the skilled person.

It has to be borne in mind that the subject-matter under consideration does not define an effect that is independent from the effect of the closest prior art but an effect that is potentially comprised within the ambit of the teaching of the closest prior art. The question to be answered is thus merely whether the skilled person would have considered carrying out tests to identify IgA secretion when trying to determine the effects probiotics have on the immune system of infants in their first months of life. The closest prior art already provides the teaching that the administration of probiotics leads to a healthy intestinal flora. Such a healthy intestinal flora has been linked to IgA secretion, see document (6) discussed above. It is thus merely necessary to briefly discuss whether the further documents relied on by the opponent can question the conclusion based on document (6).

Document (12) states that probiotics inhibit the Th2 type immune response. There are however no data in document (12) to back up this statement. Also, there is no reference to literature in this respect.

Document (5) stresses the importance of IgA secretion and the link between IgA secretion and the gut flora (see introductory paragraphs, page 134, left-hand column, first paragraph, to page 135, right-hand column, first paragraph). Based on these ideas, document (5) performs feeding tests with newborn infants and provides data for IgA secretion after feeding with probiotics, see Table 3. The values measured for IgA secretion vary considerably over time. The authors come to the conclusion that there is no significant increase of IgA secretion due to the feeding of probiotics. The skilled person, bearing in

mind the extremely large variations of IgA secretion over time and the information provided in the introductory parts of document (5), would not have considered that the data of document (5) were more significant than the findings of the literature relied on by document (6).

The respondent considers document (7) to be irrelevant. It therefore does not merit analysis.

Consequently, the skilled person would not have considered the mere statement in document (12) or the data of Table 3 of document (5) to provide serious doubts that the literature discussed in document (6) was in error.

- 2.7 The parties have indicated that the type of prebiotics were not crucial.

Prebiotic ingredients as defined in claim 1 of the main request are described for example in claim 1 of document (23). The optimisation of amounts of ingredients used in a composition constitutes a routine task for the person skilled in the art.

- 2.8 The subject-matter of claim 1 of the main request lacks an inventive step (Article 56 EPC).

3. *Admission of requests*

3.1 *Auxiliary requests 1 and 3*

Auxiliary requests 1 and 3 were submitted together with the reply to the statement setting out the grounds of appeal. They represent a valid response to the appellant's line of argument relating to the scope of

the claims in relation to an effect shown for only two bacterial strains.

Auxiliary requests 1 and 3 were thus admitted in accordance with Article 12(2) and (4) RPBA.

3.2 *Auxiliary request 2*

Auxiliary request 2 was filed at an advanced stage of the appeal proceedings, namely towards the end of the oral proceedings before the board, after the discussion on inventive step of the main request had been completed. No new aspects were raised during oral proceedings before the board, beyond those already addressed during the written phase of the appeal proceedings. Therefore, the filing of auxiliary request 2 cannot be seen as a timely or appropriate reaction to new developments during oral proceedings. Claim 1 of auxiliary request 2 has been limited to a further single specific strain. The shift in subject-matter gave rise to issues that could not be dealt with without an adjournment of the oral proceedings. When considering issues relating to the admission of claim requests, it is irrelevant that post-published evidence, such as document (21), has been presented for the specific strain of auxiliary request 2. Consequently, the board decided not to admit auxiliary request 2 into the appeal proceedings (Article 13(1) and (3) RPBA).

4. *Inventive step - auxiliary requests 1 and 3*

As already stated above, see point 2.2, the closest prior art discloses an infant formula comprising *Bifidobacterium longum*. In order to prepare an actual infant formula, the person skilled in the art has to

make use of an actually existing probiotic strain. A commercially available strain of *Bifidobacterium longum* is ATCC BAA-999, which is described as being probiotic (see document (23), claim 11).

While strain specificity in terms of effects has been discussed in the context of strains belonging to different probiotic genera and species, no substantiated reasons or evidence of major differences linked to strains within one species have been provided. Furthermore, taking into account the theoretical explanation provided in the introductory parts of the patent in suit (paragraph [0018]), the actual secretion of the IgA is not due to the probiotic strain administered, but to unspecified strains that colonise the gastrointestinal tract after priming with this probiotic strain.

The selection of the *Bifidobacterium longum* strain ATCC BAA-999 is one of the options available to the skilled person when faced with the need to choose an actual strain of *Bifidobacterium longum* and consequently cannot lead to the acknowledgement of an inventive step.

The arguments provided for claim 1 of the main request apply mutatis mutandis to the subject-matter of auxiliary requests 1 and 3 which is also not inventive (Article 56 EPC).

5. Having come to a negative conclusion on inventive step for claim 1 of all requests admitted into the appeal proceedings, it is not necessary to provide reasons concerning the further independent claims and for issues relating to priority, sufficiency of disclosure and extension of subject-matter.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.
2. The patent is revoked.

The Registrar:

The Chairman:



M. Schalow

A. Lindner

Decision electronically authenticated