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Datasheet for the decision of 10 August 2017

Case Number: T 0746/14 - 3.3.09

Application Number: 06799537.3

Publication Number: 1940246

IPC: A23L1/29, A23L1/308, A61K31/702, A23C9/20, A61P1/12

Language of the proceedings: EN

Title of invention:
PREVENTING DISEASES IN INFANTS DELIVERED VIA CAESAREAN SECTION

Patent Proprietor:
N.V. Nutricia

Opponent:
United Pharmaceuticals S.A.

Headword:

Relevant legal provisions:
EPC Art. 100(b), 100(c), 54, 56

Keyword:
Inventive step - medical use claims

Decisions cited:
T 0688/13

Catchword:

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Case Number: T 0746/14 - 3.3.09

D E C I S I O N
of Technical Board of Appeal 3.3.09
of 10 August 2017

Appellant: (Patent Proprietor)	N.V. Nutricia Eerste Stationsstraat 186 2712 HM Zoetermeer (NL)
Representative:	Nederlandsch Octrooibureau P.O. Box 29720 2502 LS The Hague (NL)
Respondent: (Opponent)	United Pharmaceuticals S.A. 55 Avenue Hoche 75008 Paris (FR)
Representative:	Starck-Loudes, Anne-Caroline Cabinet Becker & Associés 25, rue Louis le Grand 75002 Paris (FR)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 22 January 2014 concerning maintenance of the European Patent No. 1940246 in amended form.**

Composition of the Board:

Chairman	W. Sieber
Members:	M. O. Müller
	E. Kossonakou

Summary of Facts and Submissions

I. This decision concerns the appeals filed by the opponent and the patent proprietor against the decision of the opposition division finding that European patent No. 1 940 246 as amended met the requirements of the EPC.

II. With the notice of opposition the opponent had requested revocation of the patent in its entirety on the grounds under Article 100(a) (lack of novelty and inventive step), 100(b) and 100(c) EPC.

The documents submitted during the opposition proceedings included:

D2: WO 2005/110121 A1;

D11: S. Håkansson et al., Clinical and Experimental Allergy, volume 33, 2003, pages 757 to 764;

D21: R. Bennet et al., Acta Paediatr., volume 81, 1992, pages 784 to 787;

D24: J. Knol et al., Journal of Pediatric Gastroenterology and Nutrition, volume 40, 2005, pages 36 to 42;

D25: EP 1 634 599 A1; and

D29: B. Laubereau et al., Arch. Dis. Child, volume 89, 2004, pages 993 to 997.

III. The opposition division found auxiliary request 7 allowable, independent claim 1 of which read as follows:

"1. Use of a composition comprising non-digestible oligosaccharides, excluding human milk, for the manufacture of a composition for treatment and/or prevention of a disorder in infants delivered via caesarean section, wherein the disorder is selected from the group consisting of allergy, asthma, and atopic dermatitis, wherein the composition further comprises eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA) and/or arachidonic acid (ARA)."

The request contained six further independent claims, which are, however, not pertinent to this decision.

IV. The opposition division's decision on auxiliary request 7 can be summarised as follows (reasons were partly given already for the higher-ranking main request):

The proviso "excludes human milk" which had been objected to by the opponent under Article 123(2) EPC was based on page 16, lines 24 to 25 of the application as filed.

The invention was sufficiently disclosed. Example 2 showed that the gut flora of infants born via caesarean section was improved by the administration of indigestible oligosaccharides, and the data presented in example 3 showed that the diversity of bifidobacteria was increased as a result of such administration. The contested patent mentioned suitable oligosaccharides, so the skilled person would have been in a position to reproduce the invention without undue burden.

Novelty had not been contested by the opponent.

The claimed subject-matter was inventive. The problem solved in view of the closest prior art D11 or D29 was the provision of a treatment of allergic and infectious diseases in infants born via caesarean section. The claimed solution, namely the use of non-digestible oligosaccharides, excluding human milk, and eicosapentaenoic acid (hereinafter EPA), docosahexaenoic acid (hereinafter DHA) and/or arachidonic acid (hereinafter ARA), was not suggested by the prior art.

V. This decision was appealed by both the opponent and the proprietor. As both parties are each appellant and respondent in the present appeal proceedings, for simplicity the board will continue to refer to them as the opponent and the proprietor.

VI. The opponent's statement of grounds of appeal contained

D38: EP 1 940 250 B1; and

D39: Letter from Mr Jaap Mannaerts, dated 2 March 2011, in the case relating to D38.

The proprietor's statement of grounds of appeal included a main request and first to ninth auxiliary requests.

VII. With letter dated 4 September 2014, third-party observations were filed by Nestec S.A containing

D40: Experimental data headed "Annex 1" signed on 27 June 2013 by R.C. van Duijvenbode;

D41: Copy of the summons to oral proceedings in case T 282/13 including a communication from the board of appeal in that case; and

D42: M. Millar et al., Arch. Dis. Child Fetal Neonatal Ed., volume 88F, 2003, pages 354 to 358.

VIII. A response to the patentee's grounds of appeal was filed by the opponent with its letter of 16 September 2014, together with a copy of D42 and

D43: Internet excerpt relating to "Nutrilon", an infant formula distributed by Nutricia;

D44: Internet excerpt from www.polaris.fr; and

D45: B. Koletzko et al., Journal of Pediatric Gastroenterology and Nutrition, volume 41, 2005, pages 584 to 599.

IX. With letter dated 6 October 2014, the proprietor filed new second, fourth and tenth to twelfth auxiliary requests.

X. With its communication dated 12 January 2017, the board issued its preliminary opinion.

XI. With its letter dated 12 June 2017, the proprietor filed a new main request and new auxiliary requests 1 to 5 and withdrew all previously filed requests.

XII. With its letter dated 23 June 2017, the opponent filed

D46: M. Haarman et al., Applied and Environmental Microbiology, volume 71, number 5, May 2005,

pages 2318 to 2324.

XIII. On 10 August 2017, oral proceedings were held before the board.

XIV. Claim 1 of auxiliary request 1 (the highest-ranking request) reads as follows:

> "1. Use of a composition comprising non-digestible oligosaccharides, excluding human milk, for the manufacture of a composition for treatment and/or prevention of a disorder in infants delivered via caesarean section, wherein the disorder is selected from the group consisting of allergy, asthma, and atopic dermatitis, wherein the composition further comprises eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA) and/or arachidonic acid (ARA), and wherein the composition comprises galacto-oligosaccharides."

Claim 1 of auxiliary request 2 reads as follows (changes to auxiliary request 1 highlighted by the board):

> "1. Use of a composition comprising non-digestible oligosaccharides, excluding human milk, for the manufacture of a composition for treatment and/or prevention of a disorder in infants delivered via caesarean section, wherein the disorder is selected from the group consisting of allergy, asthma, and atopic dermatitis, wherein the composition further comprises eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA) and/or arachidonic acid (ARA), and wherein the composition comprises galacto-oligosaccharides and fructo-oligosaccharides."

XV. So far as relevant to the present decision, the opponent's arguments can be summarised as follows:

Auxiliary request 1

The proviso that the claimed composition was not human milk was not based on the application as filed.

The claimed invention was insufficiently disclosed, since the claimed therapeutic effect could only be obtained with a combination of galacto- and fructooligosaccharides, but not with galactooligosaccharides alone.

The claimed subject-matter lacked novelty over each of D2 and D25.

The subject-matter of claim 1 lacked inventive step over the closest prior art D11 in combination with D25. The skilled person knew from D11 that infants delivered by caesarean section had a disturbed intestinal colonisation, an inferior colonisation resistance to microbial pathogens and an increased risk of allergy, asthma and gastroenteritis. The skilled person looking for a treatment of these disorders would learn from D25 that feeding infants with a composition as defined in claim 1 optimised the infant's intestinal flora, increased its resistance to colonisation by pathogenic bacteria and thereby reduced the risk of allergy and asthma. He would thus apply this composition in D11 and thereby arrive at the claimed subject-matter.

Auxiliary request 2

Also the subject-matter of claim 1 of auxiliary request 2 lacked inventive step in view of D11 in combination with D25. The objective technical problem stayed the same and, for the same reasons as for auxiliary request 1, the skilled person would apply the composition disclosed in D25 and thereby arrive at the subject-matter of claim 1 of auxiliary request 2. The proprietor's attempt to reformulate the objective technical problem had to fail, since the data of the patent did not support it. In fact a proper comparison of these data showed the opposite of what the proprietor asserted, namely that by replacing a standard formula by a formula as defined in claim 1 the percentage of bifidobacteria in infants delivered by caesarean section increased less rapidly than in infants born via the vaginal route. Irrespective of this, the skilled person reading D25 would anyway have applied the composition disclosed therein, even in view of the proprietor's reformulated problem. Hence, even in view of this problem, the subject-matter of claim 1 was rendered obvious by D11 in combination with D25.

XVI. So far as relevant to the present decision, the proprietor's arguments can be summarised as follows:

Auxiliary request 1

The subject-matter of claim 1 of auxiliary request 1 was inventive. It differed from the closest prior art D11 in that the formula defined in this claim additionally contained galactooligosaccharides and any of EPA, DHA and

ARA. The problem solved in view of D11 was the provision of a treatment that prevented the kind of disorders faced by infants delivered by caesarean section. The skilled person would not expect that the composition disclosed in D25 for infants in general and preterm infants in particular would work as well for infants delivered by caesarean section. More specifically, as had been shown in example 1 of the opposed patent, this type of infant had no beneficial bifidobacteria at all and thus the skilled person would not expect that feeding the composition of D25 would result in the growth of these bacteria. Furthermore, D21 taught the skilled person to administer bifidobacteria to infants delivered by caesarean section, since in these infants bifidobacteria would not reach normal levels for four to eight weeks. So, it would have been much more logical to administer bifidobacteria to these infants, rather than the composition disclosed in D25.

Auxiliary request 2

In view of the amendments made to claim 1 of this request, the data in the patent now reflected exactly the embodiments covered by claim 1. Based on these data, the problem solved in view of the closest prior art D11 had to be reformulated as how to achieve a growth of bifidobacteria at a rate at least as fast as that achieved by infants born via the vaginal route. Since infants delivered by caesarean section were known to have no or very few bifidobacteria, the skilled person would not expect that if they were fed a composition as disclosed in D25 these bifidobacteria would grow at least as fast as those in infants delivered by the vaginal

route. Therefore, the skilled person would not use the composition disclosed in D25 to treat infants delivered by caesarean section as dealt with in D11. Hence, the subject-matter of claim 1 was inventive over D11 in combination with D25.

XVII. The opponent requested that the decision under appeal be set aside and that European patent No. 1 940 246 be revoked.

The proprietor requested that the patent be maintained on the basis of auxiliary requests 1 or 2, both filed with letter dated 12 June 2017.

Reasons for the Decision

Auxiliary request 1 (highest-ranking request)

1. Amendments (Article 100(c) and (b) EPC) and novelty

1.1 The opponent's sole objection under Article 100(c) EPC related to the proviso in independent claims 1 to 3 and 10 that the claimed composition was not human milk. During the oral proceedings, the board reached the conclusion that this proviso was based on page 16, lines 24 to 25 of the application as filed and that thus the ground for opposition under Article 100(c) EPC did not prejudice the maintenance of the patent on the basis of auxiliary request 1.

1.2 The opponent's sole objection under Article 100(b) EPC was based on the argument that the claimed therapeutic effects could only be obtained with a combination of galacto- and fructooligosaccharides, but not with galactooligosaccharides alone, as covered *inter alia* by

claim 1 of auxiliary request 1. During the oral proceedings, the board reached the conclusion that in view of the examples of the patent and the experimental results in D40, it was credible that the claimed therapeutic effects could also be achieved with galactooligosaccharides alone and that thus the ground for opposition under Article 100(b) EPC did not prejudice the maintenance of the patent on the basis of auxiliary request 1.

1.3 The opponent's sole novelty objections were based on documents D2 and D25. During the oral proceedings, the board reached the conclusion that, assuming that claim 10 was deleted, the subject-matter of all remaining independent claims of auxiliary request 1 would be novel over these documents. The board was of the opinion that D2 did not disclose the presence of any of EPA, DHA and ARA as required by all independent claims of auxiliary request 1, and that D25 did not disclose the patient group of infants delivered by caesarean section as defined in these claims.

1.4 Since auxiliary request 1 was eventually rejected for lack of inventive step, there is no need to give a detailed reasoned decision on the conclusions reached by the board during the oral proceedings on the above issues (points 1.1 to 1.3).

2. Inventive step

2.1 Claim 1 refers to the use of a composition comprising galactooligosaccharides and any of EPA, DHA and ARA for the manufacture of a composition for the treatment and/or prevention of allergy, asthma or atopic dermatitis in infants delivered by caesarean section (for the exact wording of claim 1, see point XIV above).

2.2 Both parties agreed that D11 was the closest prior art.

2.2.1 D11 is a study investigating whether caesarean section increases the risk of childhood asthma and gastroenteritis compared to children born via the vaginal route (section "Objective" in the summary on page 757). The study was based on an analysis of data from Swedish medical service registers (section "Methods" in the summary on page 757). It was found that there was a fairly strong correlation between caesarean section and treatment as an inpatient in childhood with a diagnosis of asthma or gastroenteritis (second sentence of the second full paragraph on the left-hand column of page 760). More specifically, the study showed that there was a 30% increase in the risk of developing asthma or gastroenteritis in infants older than 1 year who had been delivered by caesarean section (first sentence in the section "Discussion" on page 761). According to D11, this result supported the hypothesis that caesarean section was associated with an increased risk of subsequent allergic manifestations in the child and that disturbance of the intestinal colonisation could be a common contributive pathogenic factor (first paragraph of the section discussion on page 761). The increased occurrence of gastroenteritis in infants delivered by caesarean section was explained in D11 by an altered intestinal flora that showed lower colonisation resistance to microbial pathogens (first two sentences of the first full paragraph in the left-hand column on page 762).

2.2.2 So the skilled person knows from D11 that infants delivered by caesarean section have disturbed intestinal colonisation, inferior colonisation

resistance to microbial pathogens and an increased risk of allergy, asthma and gastroenteritis.

D11 does not disclose the type of food the infants in the study had received. It must therefore be assumed that these infants had received a standard formula without any galactooligosaccharides and any of EPA, DHA and ARA. As was common ground between the parties, the presence of these components in the composition to be used according to claim 1 of auxiliary request 1 is thus a distinguishing feature.

2.3 During the oral proceedings, the proprietor considered the problem solved in view of D11 to be the provision of a treatment that prevented the kind of disorders faced by infants delivered by caesarean section, i.e., in the language of D11, disturbed intestinal colonisation, less resistance to colonisation by microbial pathogens and an increased risk of allergy, asthma and gastroenteritis.

2.4 As a solution to this problem, claim 1 proposes a treatment with a composition containing galactooligosaccharides and any of EPA, DHA or ARA.

2.5 It needs to be examined whether the above problem is indeed solved by the claimed treatment.

2.5.1 Example 2 of the patent describes an experiment which studies the effect of a mixture of galacto- and fructooligosaccharides on the microbial flora of infants delivered by caesarean section. In this experiment, two groups of such infants were fed with a standard formula (SF) or an infant formula supplemented with galacto- and fructooligosaccharides (GFSF). It was found that in the first week after delivery, the

percentage of bifidobacteria detected in faecal samples of these infants was 4.3% in both groups (compared to 19.8% for infants delivered via the vaginal route). After 6 weeks of feeding, the faecal samples of the infants fed with the standard formula contained 12.3% bifidobacteria, while the samples of those who received the infant formula supplemented with galacto- and fructooligosaccharides contained a much higher amount, namely 17.2% (table 3). At the same time the percentage of the undesired pathogen escherichia coli was 11.8% for the group fed the standard formula and 0% for that fed the supplemented formula.

2.5.2 The experimental data in D40 show a similar result for feeding with galactooligosaccharides alone, namely that the number of bifidobacteria increases from 5.3 to $29*10^4$.

2.5.3 It can therefore be assumed in the proprietor's favour that feeding infants delivered by caesarean section a composition supplemented with galactooligosaccharides, instead of a standard formula as applied in D11, increases the amount of beneficial bifidobacteria and decreases that of pathogenic bacteria. It is also plausible that this leads to a reduced risk of allergy, asthma and gastroenteritis.

2.5.4 The supplemented formulae fed in example 2 of the patent and D40 did not contain any of EPA, DHA or ARA, even though these fatty acids are mandatory in claim 1. In the proprietor's favour, it is assumed that the above findings would apply also if these fatty acids had been additionally present in the supplemented formulae of example 2 or D40.

2.5.5 It can thus be assumed in the proprietor's favour that the problem it referred to is solved by feeding infants delivered by caesarean section a composition as defined in claim 1, instead of the standard formula of D11. Therefore, this problem, i.e. the provision of a treatment for infants delivered by caesarean section that prevents disturbed intestinal colonisation, increases resistance to colonisation by microbial pathogens and reduces the risk of allergy, asthma and gastroenteritis (see point 2.3 above), is the objective technical problem.

2.6 It needs to be examined whether the skilled person faced with this problem and starting from D11, would have arrived in an obvious way at the subject-matter of claim 1. In this respect, the opponent relied *inter alia* on D25.

As not disputed by the proprietor, D25 (both claim 2, dependent upon claim 1, and example 1) discloses an infant formula composition containing trans-galactooligosaccharides, fructooligosaccharides and at least one of EPA, DHA and ARA. This composition is as defined in claim 1 of auxiliary request 1.

In paragraph [0008], D25 states that this composition leads to the development of an optimal intestinal flora and stimulates the immune system, resulting in a better defence if an allergen, pathogen or toxin crosses the intestinal barrier and/or enters the circulation system. In paragraph [0010], D25 discloses that oligosaccharides stimulate the formation of low-risk intestinal flora and in particular reduce the count of pathological intestinal bacteria and stimulate colonisation of the intestine by bifidobacteria. In paragraphs [0011] and [0012], D25 goes on to say that a

further improvement of the immune system and/or gut maturity is achieved by the inclusion of EPA, DHA or ARA. In example 2 of D25 a liquid infant nutrition containing trans-galactooligosaccharide, fructopolysaccharide, EPA, DHA and ARA is put in a package with a label indicating that the formula is suitable for preventing or treating allergy.

Thus, the skilled person would learn from D25 that feeding infants with a composition as defined in claim 1 of auxiliary request 1 optimises their intestinal flora, increases resistance to colonisation by pathogenic bacteria and reduces the risk of allergy and asthma.

The skilled person starting from D11 and knowing that infants delivered by caesarean section suffer from disturbed intestinal colonisation, reduced resistance to colonisation by microbial pathogens and a higher risk of allergy and asthma (point 2.2.2 above) would thus have known that all this could be treated by feeding a composition as defined in claim 1.

2.6.1 The proprietor argued that the skilled person would not have expected that the composition disclosed in D25 for infants in general and preterm infants in particular would work also for infants delivered by caesarean section. More specifically, as had been shown in example 1 of the opposed patent, infants delivered by caesarean section had no beneficial bifidobacteria at all and thus the skilled person would not have expected that feeding the composition of D25 would result in the growth of these bacteria.

The board accepts that feeding a chemical composition cannot generate living organisms such as bacteria out

of nothing. However, as was acknowledged by the proprietor during the oral proceedings, infants delivered by caesarean section come into contact with bifidobacteria present in the environment. So these infants do not remain devoid of bifidobacteria; the growth of these bacteria is merely delayed compared to infants born via the vaginal route. There is no reason to assume that once these bacteria are present, the skilled person would not expect them to grow if the infants were fed a composition as disclosed in D25.

2.6.2 The proprietor further argued that D21 (fourth paragraph of the left-hand column on page 787) taught the skilled person to administer bifidobacteria to infants delivered by caesarean section, since bifidobacteria might not reach normal levels for four to eight weeks in these infants. According to the proprietor, it would therefore have been much more logical to administer bifidobacteria to these infants, rather than the composition of D25.

This argument is not convincing. If a certain claimed solution, in the present case the one suggested by D25, is obvious, it can normally not be rendered non-obvious by another document that suggests another solution, however obvious that may be.

2.6.3 The subject-matter of claim 1 therefore lacks inventive step in view of D11 in combination with D25. Auxiliary request 1 is thus not allowable.

2.7 During the oral proceedings, the opponent also presented an inventive-step attack starting from D24 as the closest prior art. Since this was a new attack raised for the first time during the oral proceedings, the board, at the proprietor's request, did not admit

it into the proceedings. Since however auxiliary request 1 was rejected for lack of inventive step in view of D11 as the closest prior art, no reasoned decision is needed on this issue.

Auxiliary request 2

3. Inventive step

3.1 Claim 1 of auxiliary request 2 differs from claim 1 of auxiliary request 1 in that the composition additionally contains fructooligosaccharides.

3.2 It was common ground between the parties that D11 remained the closest prior art and that the subject-matter of claim 1 differed therefrom by the type of composition to be used, i.e. that instead of a standard formula as applied in D11 (see point 2.2.2. above) a composition was applied that additionally contained galacto- and fructooligosaccharides as well as EPA, DHA and/or ARA.

3.3 It was however a matter of dispute between the parties whether the objective technical problem needed to be formulated more ambitiously and whether the claimed solution was obvious in view of D25.

3.3.1 The proprietor argued in this respect as follows:

The data provided in example 2 of the opposed patent now became relevant, since the oligosaccharides now required by claim 1, i.e. galacto- and fructooligosaccharides, were exactly those applied in this example. A comparison of the data of this example showed that feeding infants delivered by caesarean section with a formula containing a mixture of the two

oligosaccharides increased the percentage of bifidobacteria by a factor of 4.0, compared with a factor of only 3.4 for infants born via vaginal delivery. So, the increase in the number of bifidobacteria achieved with the supplemented formula was higher in infants delivered by caesarean section than in infants born via the vaginal route. The problem solved in view of the closest prior art D11 had therefore to be reformulated more ambitiously, as the provision of a growth rate of bifidobacteria in infants delivered by caesarean section that was at least as fast as that achieved with infants born via the vaginal route.

Since infants delivered by caesarean section were known to have no or very few bifidobacteria, the skilled person would not expect that applying a composition as disclosed in D25 would cause these bifidobacteria to grow at least as fast as in infants born via the vaginal route. Therefore, in view of the above reformulated problem, the skilled person would not use the composition disclosed in D25.

3.3.2 The board does not agree.

D25 states in paragraph [0008] that the composition described in this document stimulates the development of an optimal intestinal flora. The skilled person aiming at fast and thus optimal growth of bifidobacteria in the infants disclosed in D11 would thus have been motivated by D25 to feed them the composition disclosed in this document. Since this composition is as defined in claim 1, he would thereby arrive at the subject-matter of this claim. This does not change even if, as asserted by the proprietor, the growth were faster than the skilled person would

expect. As set out above, the skilled person would apply the composition of D25 and thus find himself in a "one-way street" that would - without any additional technical measure - lead him to the fast growth found in the patent. Hence, even if the objective technical problem was as defined by the proprietor, the claimed solution would still be obvious in view of D11 in combination with D25 (see T 688/13, point 1.5.3).

3.4 Consequently, auxiliary request 2 is not allowable.

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. Cañueto Carbajo W. Sieber

Decision electronically authenticated