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# Datasheet for the decision of 13 July 2023

**Case Number:** T 0887/21 - 3.3.04

**Application Number:** 08847072.9

**Publication Number:** 2217230

**IPC:** A61K31/35, A61K31/702, A61K31/726, C07D309/10, C07D309/14, A61P31/00, A61P31/04, A23L33/21, A23L33/135, A61K31/7016, A61K31/351, A23L33/00

**Language of the proceedings:** EN

**Title of invention:**
Prevention and treatment of secondary infections following viral infection

**Patent Proprietor:**
Société des Produits Nestlé S.A.

**Opponent:**
N.V. Nutricia

**Relevant legal provisions:**
EPC Art. 56

**Keyword:**
Inventive step - (no)

**Decisions cited:**
G 0002/21

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**Case Number: T 0887/21 - 3.3.04**

# D E C I S I O N
# of Technical Board of Appeal 3.3.04
# of 13 July 2023

| | |
|---|---|
| **Appellant:** (Opponent) | N.V. Nutricia<br>Eerste Stationsstraat 186<br>2712 HM Zoetermeer (NL) |
| **Representative:** | Nederlandsch Octrooibureau<br>P.O. Box 29720<br>2502 LS The Hague (NL) |
| **Respondent:** (Patent Proprietor) | Société des Produits Nestlé S.A.<br>Entre-deux-Villes<br>1800 Vevey (CH) |
| **Representative:** | Elkington and Fife LLP<br>Prospect House<br>8 Pembroke Road<br>Sevenoaks, Kent TN13 1XR (GB) |
| **Decision under appeal:** | **Interlocutory decision of the Opposition Division of the European Patent Office posted on 14 April 2021 concerning maintenance of the European Patent No. 2217230 in amended form.** |

**Composition of the Board:**

| | |
|---|---|
| **Chairman** | B. Rutz |
| **Members:** | R. Hauss |
| | L. Bühler |

## Summary of Facts and Submissions

I. European patent No. 2217230 (patent in suit) was granted with a set of 14 claims.

II. The patent in suit was opposed under Article 100(a) and (b) EPC on the grounds that the claimed subject-matter lacked novelty and inventive step and was not disclosed in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art.

III. In the course of the proceedings before the opposition division, the patent proprietor filed amended sets of claims (main request and four auxiliary requests).

IV. Claim 1 of the amended ***main request*** reads as follows:

> *1. A synthetic nutritional composition for use in the prevention of secondary infections following a viral infection characterised by neuraminidase activity comprising a sialylated oligosaccharide and N-acetyl-lactosamine and/or an oligosaccharide containing N-acetyl-lactosamine, and further comprising a probiotic bacterial strain.*

Claim 1 of ***auxiliary request 1*** is identical to claim 1 of the main request except that it further specifies that the secondary infections to be prevented are infections by pathogenic bacteria.

Claim 1 of ***auxiliary request 2*** is identical to claim 1 of the main request except that it further specifies that the secondary infections to be prevented are infections of the respiratory tract by pathogenic bacteria.

Claim 1 of ***auxiliary request 3*** is identical to claim 1 of the main request except that it further specifies that:

- the secondary infections to be prevented are infections of the respiratory tract by pathogenic bacteria
- the sialylated oligosaccharide is selected from the group comprising 3' sialyllactose and 6' sialyllactose

Claim 1 of ***auxiliary request 4*** is identical to claim 1 of auxiliary request 3 except that it further specifies that:

- the oligosaccharide containing N-acetyl-lactosamine is selected from the group comprising lacto-N-tetraose and lacto-N-neotetraose

V. 3' sialyllactose and 6' sialyllactose may be abbreviated as 3'SL and 6'SL. Lacto-N-tetraose may be abbreviated as LNT, and lacto-N-neotetraose as LNnT.

VI. The documents cited in the proceedings before the opposition division included the following:

**D1:** WO 2007/101675 A1

**D9:** US 2006/0018890 A1

**D15:** ANNEX 1 - Experimental data provided by Norbert Sprenger in April 2013

**D16:** Infection and Immunity 66(4), 1439-1444 (1998)

**D17:** JID 176, 704-712 (1997)

VII. The decision under appeal is the opposition division's interlocutory decision, posted on 14 April 2021, finding that the patent as amended in the form of the main request met the requirements of the EPC.

VIII. According to the decision under appeal, the subject-matter defined in the main request met the requirements of sufficiency of disclosure and novelty (Articles 100(a), 52(1), 54, 100(b) and 83 EPC).

The claimed subject-matter also involved an inventive step (Articles 100(a), 52(1) and 56 EPC). Starting from the technical teaching of document D16, and in view of the experimental data provided in D15, the objective technical problem was to provide an improved synthetic nutritional composition comprising a prebiotic mixture and a probiotic bacterial strain for use in a new specific therapeutic method. The solution to this problem as defined in the claims of the main request could not have been derived in an obvious manner from document D16, alone or in combination with further cited prior art.

IX. The opponent (appellant) filed an appeal against this decision.

X. With its reply to the appellant's grounds of appeal, the patent proprietor (respondent) filed five sets of claims as its main request and auxiliary requests 1 to 4. These are identical to the sets of claims presented in the proceedings before the opposition division (see point IV. above).

XI. Oral proceedings before the board were held on 13 July 2023.

XII. The appellant's arguments may be summarised as follows.

The application as filed provided no experimental data, and the explanation it gave of the claimed composition's postulated activity and therapeutic benefit remained hypothetical. It was mere assertion to state (in the paragraph bridging pages 3 and 4 of the

application as filed) that the co-administration of sialylated oligosaccharides and N-acetyl-lactosamine and/or oligosaccharides containing N-acetyl-lactosamine was "particularly effective". Thus, the application as filed provided no plausible basis, either, for taking post-filed supplementary data (in this case, D15) into account.

The respondent, therefore, had failed to demonstrate the alleged improved efficacy of the composition defined in claim 1 in comparison with what was disclosed in D16.

Document D15 (if it were to be considered) neither confirmed the mechanism of action postulated in the application as filed nor provided evidence of improved efficacy in comparison with the disclosure in D16 on antiadhesive oligosaccharides. If additional technical effects were described in D15, these could not have been derived from the application as filed. It would not be appropriate to take new technical effects into account that were based solely on post-filed evidence. In any case, in view of the teaching of D16, any additional effect that was a synergistic effect (as alleged by the respondent) had to be a bonus effect that could not be the basis for an inventive step.

Starting from the technical teaching of document D16, the objective technical problem was to provide a suitable dosage form for administering sialylated oligosaccharides for preventing secondary infection following a viral infection.

As D16 disclosed a therapeutic benefit in the prevention of secondary infections for both sialylated oligosaccharides and oligosaccharides containing N-acetyl-lactosamine, it would not have required an

inventive step to combine these components for co-administration.

Concerning the dosage form and route of administration, D16 pointed to oral administration in a nutritional composition such as milk or infant formula (see D16: page 1443, last paragraph to page 1444).

Both N-acetyl lactosamine oligosaccharides (in particular LNT and LNnT, which occurred in human milk) and probiotic bacteria were well known as components of nutritional compositions such as infant formula and for their use in preventing infections (e.g. from, *inter alia*, documents D16, D1, D9 and D17).

XIII. The respondent's arguments may be summarised as follows.

It was not contested that D16 was directed to the prevention of secondary bacterial infections following a virus infection. The document provided *in vitro* data that suggested the suitability of sialylated oligosaccharides for this purpose, but it did not disclose the therapeutic use.

The technical features distinguishing the claimed subject-matter from the disclosure of D16 were the combination of the sialylated oligosaccharide with the other two mandatory components, the therapeutic use for preventing secondary infections (which was a functional technical feature of claim 1) and the chosen product form as a nutritional composition.

As the combination of the three active agents provided better efficacy than the use of sialylated oligosaccharides alone, the objective technical problem should be defined as the provision of an improved composition for use in the prevention of secondary

infections following a viral infection characterised by neuraminidase activity.

The technical effect of improved efficacy was made plausible by the mechanistic concept set out in the application as filed, in the paragraph bridging pages 4 and 5 (corresponding to paragraph [0016] of the patent in suit).

In accordance with this, the application as filed stated furthermore that the inventors had surprisingly found that the co-administration of sialylated oligosaccharides and N-acetyl-lactosamine and/or oligosaccharides containing N-acetyl-lactosamine was particularly effective in the prevention of secondary infections following viral infections such as influenza (see the paragraph bridging pages 3 to 4 of the application as filed, corresponding to paragraph [0012] of the patent in suit).

Thus, the advantage of particularly high efficacy was foreshadowed and also explained convincingly in the application as filed. On this basis, the post-filed data provided in document D15 could be taken into consideration to corroborate the alleged improved efficacy.

D15 did not compare samples containing two or three mandatory components of claim 1 with a sample containing only a sialylated oligosaccharide. Nevertheless, the experimental set-up in D15 still provided a fair comparison with the state of the art according to D16 in so far as a composition containing all three mandatory components required in claim 1 was shown to have better efficacy in inhibiting pathogenic bacteria than a composition containing only the sialylated oligosaccharide in combination with the

probiotic component ("Lnnt+6SL" in comparison with "6SL", as shown in the figure on page 1 of D15).

It was not considered crucial that the pathogenic bacteria in D15 were *Salmonella* and the experimental set-up did not examine the mechanism of bacterial adhesion to epithelial cells since claim 1 did not contain any restrictions on the infectious agent or the mechanism of action. What mattered was the result of improved efficacy shown to be achieved within the scope of claim 1.

As far as obviousness was concerned, the teaching in D16 about low or lacking efficacy of N-acetyl-lactosamine and oligosaccharides containing it would have discouraged the person skilled in the art from including such components in the compositions. Furthermore, D16 did not mention probiotic bacteria at all. While various documents of the prior art mentioned one or more of the mandatory components of claim 1, there was no suggestion to combine these components to prevent infections, let alone with an expectation of improved efficacy.

Claim 1 of each auxiliary request involved an inventive step for the same reasons as claim 1 of the main request.

XIV. The appellant (opponent) requested that the decision under appeal be set aside and that the patent be revoked.

XV. The respondent (patent proprietor) requested that the appeal be dismissed or, in the alternative, that the patent be maintained on the basis of a set of claims of one of auxiliary requests 1 to 4 filed with the reply to the statement setting out the grounds of appeal.

## Reasons for the Decision

1. Admissibility of the appeal

The appeal complies with Articles 106 to 108 EPC and Rule 99 EPC; it is admissible.

2. Inventive step - main request (Articles 100(a), 52(1) and 56 EPC)

*Patent in suit*

2.1 The patent in suit, in its introductory part relating to the background of the invention, discusses the common problem of respiratory infections of bacterial origin. Such infections often follow a viral infection such as influenza, especially in infants and small children. Examples are pneumonia, sinusitis and otitis media. A need for alternatives to therapy with antibiotics is identified. The patent seeks to provide a method for the prevention of secondary infections following viral infections such as influenza which does not rely on the use of antibiotics and which may be conveniently and safely administered (see the patent in suit, paragraphs [0002] to [0011]).

2.2 To solve this problem, the patent proposes the administration of a nutritional composition that comprises a sialylated oligosaccharide in combination with N-acetyl-lactosamine and/or an oligosaccharide containing N-acetyl-lactosamine. Furthermore, the composition comprises a probiotic bacterial strain.

2.3 According to the patent in suit (paragraph [0022]),

> *"[t]he secondary infections which may be prevented according to the invention include infections of the respiratory tract such as pneumonia, sinusitis*

*and otitis media as well as infections of the gastrointestinal tract. The invention is particularly suitable for the prevention of secondary infections of the respiratory tract such as otitis media after influenza in infants and young children."*

2.4 The patent in suit furthermore explains (see paragraph [0016], corresponding to the paragraph bridging pages 4 and 5 in the application as filed) that the oligosaccharides prevent pathogen attachment to host epithelial cells:

*"Without wishing to be bound by theory, the inventors believe that the efficacy of the combination of oligosaccharides described above in the prevention of secondary infections following influenza for example may be a result of disruption of the synergy between the actions of the viral and bacterial pathogens.*

*Specifically, it is known that successful replication of the influenza virus in host epithelial cells relies upon the action of neuraminidases on the surface of the viral particles to free the newly replicated viral particles from the host cell by cleaving the sialic acid residues that bind the particles to the host cell. Indeed, the medicines most [...] commonly prescribed for influenza are neuraminidase inhibitors.*

*Further, it is thought that it is the resulting desialylated epithelial cell surfaces that are particularly vulnerable to adhesion of pathogenic bacteria resulting in secondary infection.*
*By supplying excess sialylated oligosaccharides, the efficiency of the viral neuraminidases can*

*be reduced thus reducing the proportion of desialylated epithelial cell surfaces whilst at the same time neutral oligosaccharides which mimic the preferred epithelial binding sites of pathogenic bacteria are supplied in excess."*

*Starting point in the prior art*

2.5 It was common ground that inventive step was to be assessed starting from the disclosure of document D16. D16 is a scientific journal article with the title "Adherence of *Streptococcus pneumoniae* to Respiratory Epithelial Cells Is Inhibited by Sialylated Oligosaccharides".

2.6 According to D16, the rising incidence of respiratory infections caused by multiple-antibiotic-resistant strains of *Streptococcus pneumoniae* presents an ever-increasing therapeutic challenge. Viral infection of the upper respiratory tract may compromise host resistance and enable virulent strains of *S. pneumoniae* to progress to clinical infection (see D16: page 1439, left column, first and second paragraph; page 1443, right column, last paragraph).

2.7 As set out in D16, the hypothesis that one might apply the isolated and purified bacterial adhesin membrane receptors or analogues of these substances as competitive inhibitors of bacterial adherence to prevent or treat bacterial infection was known (page 1442, right column, "Discussion"). The agents of interest prevent or disrupt the adhesion of *S. pneumoniae* to the airway and thus permit the *Streptococci* to be effectively cleared by mucociliary action (page 1439, left column, first paragraph).

2.8 The *in vitro* experiments described in D16 explore the efficacy of free oligosaccharides as inhibitors of *S. pneumoniae* adherence to cells of respiratory ("NHBE cells") and conjunctival ("Chang cells") origin (abstract: first sentence; page 1442, right column, "Discussion"; page 1440, left column: "Epithelial cells and cell lines").

2.9 Thus, it was not in dispute that D16 relates to the same therapeutic indication as current claim 1, namely preventing secondary infection after a viral infection. The stated goal is developing possible therapeutic uses of soluble carbohydrate receptors as antiadhesive agents for respiratory pathogens (D16: page 1439, right column, first paragraph).

2.10 The findings in D16 were that the adherence of pathogenic *S. pneumoniae* bacteria to respiratory epithelial cells is inhibited preferentially by sialylated oligosaccharides and is also - more weakly - inhibited by N-acetyl lactosamines (see D16: abstract, title).

2.10.1 Sialylated epitopes appear to represent possible adherence targets for *S. pneumoniae* colonisation of the upper airway (see D16: page 1443, left column, lines 19 to 20). It was shown that sialylated oligosaccharides inhibit adherence of *S. pneumoniae* to a cell line derived from conjunctival epithelium and to primary explants of NHBE cells (page 1443, left column, second paragraph). The antiadhesive effects of nonsialylated oligosaccharides were observed to be weaker, and transient during growth of *S. pneumoniae* in suspension culture (page 1443, left column, lines 2 to 5, right column, lines 18 to 25).

2.10.2 The sialylated oligosaccharides tested according to D16 and showing the desired antiadhesive activity included 3'SL and 6'SL (see D16: page 1440, right column, second paragraph to page 1441, right column, line 2; see also Table 1, Figure 1; Table 2).

*Technical problem and solution*

2.11 As set out above, D16 seeks to develop possible therapeutic uses of soluble oligosaccharide receptors as antiadhesive agents for respiratory pathogens. Among the oligosaccharides tested, D16 identifies sialylated oligosaccharides as the most promising candidates, which *in vitro* showed good antiadhesive activity against *S. pneumoniae* strains.

2.12 Claim 1 of the main request differs from the disclosure in D16 by combining the sialylated oligosaccharide(s) with N-acetyl-lactosamine compounds and with a probiotic strain, and by requiring this combination to be provided in a synthetic nutritional composition. Furthermore, since D16 restricts itself to *in vitro* experiments, it does not disclose the therapeutic use of claim 1, although such a use is expressly envisaged and is mentioned as the ultimate goal in D16 (see point 2.9 above).

2.13 Thus, starting from the disclosure of D16, the technical problem to be solved is to provide a composition and route of administration (in other words, a specific product type or dosage form) for sialylated oligosaccharides for use in the prevention of secondary infection after a viral infection, in implementation of the teaching in D16. This encompasses the secondary problem of identifying further suitable components for such a composition.

2.14 The respondent argued that, in view of the mechanistic concept set out in the application as filed and the experimental data presented in the (post-filed) test report D15, the objective technical problem should instead be defined as the provision of an improved composition for use in the prevention of secondary infections following a viral infection characterised by neuraminidase activity.

2.15 The board arrived at a different conclusion for the following reasons.

2.15.1 The application as filed contains no experimental data. The mechanistic concept that the respondent relied on (see paragraph bridging pages 4 and 5 in the application as filed; see point 2.4 above) is mentioned in the context of the prevention of secondary infections following viral infections such as influenza (see paragraph bridging pages 3 and 4). It is merely asserted by way of a hypothesis and is not backed up by any corroborative data. Thus, the information provided in the application as filed does not amount to evidence of an "improvement" (see point 2.14 above) in comparison with the starting point in the prior art (i.e. D16).

2.15.2 D15 describes a test that involves conditioned media obtained by culturing probiotic bifidobacteria overnight in a medium containing glucose and either LNnT, 6'SL or a combination of both. After sterile filtration, these conditioned media are incubated with a strain of *Salmonella typhimurium*. After two hours, the *Salmonella* are plated at different dilutions on selective media, and the number of colony-forming units is assessed after overnight incubation.
D15 concludes that a medium conditioned with a

bifidobacterium and a mixture of 6'SL and LNnT showed superior inhibition of the model pathogen.

2.15.3 The respondent argued that the fact that the application as filed included a mechanistic concept at least provided justification for submitting additional evidence with D15. The relevant point here is, however, that the test described in D15 relates to inhibition of *Salmonella typhimurium* (known for causing gastroenteritis) in a culture medium, without the involvement of epithelial host cells. This is not corroborative evidence of the concept taught in the application as filed, but entirely new information both on the mechanism of action and the pathogenic organism involved.

Firstly, D15 relates to a presumed synergistic effect that is independent of epithelial binding. This is not derivable from the application as filed. Contrary to the respondent's view, the fact that a mechanistic concept of the antiadhesive activity of oligosaccharides is set out in the application as filed cannot justify introducing new experimental data that is manifestly based on a different mechanism of action.

Secondly, the application as filed mentions only once, in a general way, that the infections which may be prevented, apart from infections of the respiratory tract, also include infections of the gastrointestinal tract (page 7, lines 14 to 18 of the application as filed, corresponding to paragraph [0022] of the patent in suit). This site of activity is not discussed any further, no mechanism is proposed, and no mention at all is made of *Salmonella* species as a putative pathogenic target organism of the claimed composition.

An invention cannot be based solely on knowledge made available only after the effective date. In the case

in hand, it could not have been derived from the application as filed that the envisaged compositions were supposed to inhibit *Salmonellae*, and this independently of any antiadherence mechanism.

2.15.4 In the terms used in decision G 2/21 (OJ EPO 2023, A85), in these circumstances, the skilled person, having the common general knowledge in mind, and based on the application as originally filed, would not have derived the technical effect examined in D15 and relied on by the respondent for inventive step as being encompassed by the technical teaching and embodied by the same originally disclosed invention.

In this regard, it is not sufficient that a technical effect can be achieved by a composition which in terms of technical features corresponds to compositions in the application as filed. In order to be taken into account in the formulation of the objective technical problem, the alleged technical effect that is supposedly shown by the post-filed evidence (in the present case, the inhibition of *Salmonellae* outside the context of epithelial adherence) must also be encompassed by the technical teaching of the application as filed, i.e. the technical effect in question must in the first place be disclosed or be at least derivable from the technical teaching of the application documents (G 2/21, Reasons 72). As set out in paragraph 2.15.3 above, already this first requirement is not met in the case in hand.

2.15.5 Moreover, D15 cannot, in any case, provide a conclusive comparison of the claimed composition with the disclosure in D16, already because it cannot be verified on the basis of the available information that any of the tested compositions conform to claim 1.

As correctly pointed out by the appellant, the composition of the samples tested according to D15 is not known, because the initially prepared formulations were exposed to the metabolic activity of the probiotic *Bifidobacterium* strain (see the description of the test in point 2.15.2 above). It is unknown whether LNnT and 6'SL were still present in their initial concentrations (or present at all) in the filtered conditioned media that were used in the test and what other compounds may have been present. Furthermore, the *Bifidobacteria* were removed from the compositions by sterile filtration.

In this context, the board observes that if a party wishes to rely on comparative tests, it is for that party to provide the necessary information on the relevant qualitative and quantitative composition of the samples tested.

2.15.6 For these reasons, the improvement alleged by the respondent cannot be taken into account in the formulation of the objective technical problem, which remains the same as as defined in point 2.13 above.

2.16 It will be assumed that the solution to this problem is as defined in claim 1.

*Obviousness of the solution*

2.17 The person skilled in the art seeking to solve the objective technical problem and the secondary problem defined in point 2.13 above would have arrived at the subject-matter of claim 1 without the exercise of inventive skill, for the following reasons.

Product type and route of administration

2.18 Based on the teaching of D16 and D17 (reference [16] in D16), it would have been an obvious choice to incorporate the oligosaccharides, which are known components of human milk, into a nutritional composition such as infant formula.

2.18.1 On page 1443, right column, last paragraph, D16 mentions that the well-documented beneficial effects of breast-feeding for prevention of pneumococcal infection might well be due in large part to antiadherence effects of sialylated and lactosamine-terminated oligosaccharides and glycoproteins.

The authors regard their findings as consistent with the existing notion, in the context of breast-feeding, that frequent bathing of the nasopharyngeal mucosa with milk containing sialylated oligosaccharides and glycoproteins at concentrations in the millimolar range might interrupt adherence of *S. pneumoniae* to epithelial cells of the upper respiratory tract, thus reducing the load of colonising organisms and diminishing the risk of infection (D16: sentence bridging paragraphs 1443 and 1443).

They conclude that the use of orally or nasally administered milk oligosaccharides as prophylactic and/or therapeutic agents to promote clearance of *S. pneumoniae* from the nasopharyngeal mucosa may have value as a means of reducing the risk of developing otitis media (see D16: page 1444).

2.18.2 Thus, D16 teaches that oral administration of the oligosaccharides in the form of a milk-type product (i.e. a nutritional product) is expected to be effective in diminishing the risk of *S. pneumoniae* infection.

2.18.3 As it was well known that such infections, e.g. otitis media infections, are frequent and particularly relevant in infants, and since D16 discusses mechanism in the context of breast-feeding, the person skilled in the art would have considered infant formula as an obvious choice for a dosage form. Infant formula is a milk-based or milk-like nutritional composition suitable for the administration of the antiadherent oligosaccharides. Supplementation of [infant] formula with antiadherent oligosaccharides such as LNnT is also suggested in D17 (see page 712, last paragraph).

Further components

2.19 Contrary to the respondent's view, D16 does not teach away from the use of the second mandatory component (N-acetyl lactosamine and/or oligosaccharides containing N-acetyl lactosamine).

2.19.1 Firstly, D16 mentions previous reports in the scientific literature that the human milk oligosaccharide LNnT can inhibit binding of *S. pneumoniae* to epithelial cells (see page 1439, left column, third paragraph):

*"Evidence for adherence of S. pneumoniae to the human airway via carbohydrate receptors on respiratory epithelial cells was first presented by Andersson et al. (2, 3), who showed that the human milk oligosaccharide lacto-N-neotetraose (LNnT) (Galβ1-4GlcNAcβ1-3Galβ1-4Glc) could effectively inhibit binding of S. pneumoniae to desquamated cells of the human nasopharynx and oropharynx."*

The same references are mentioned again in connection with the fact that certain complex sugar sequences had been proposed in the pertinent literature as targets

to which *S. pneumoniae* specifically adheres (see page 1442, right column, second paragraph).

D16 also contains a reference to document D17 (reference [16] of D16, see the paragraph bridging pages 1443 and 1444), which reports that LNnT, in addition to showing *in vitro* anti-adherence properties, acted directly on cultured lung epithelial cell lines to induce changes such that pneumococcal adherence was prevented for prolonged periods. LNnT was found to be active to lower the bacterial load and ameliorate pneumococcal pneumonia in a rabbit model (see D17: abstract and Results).

2.19.2 Secondly, while the N-acetyl lactosamine-type compounds were not always active in the experiments described in D16, they were still found to inhibit the adherence of some of the *S. pneumoniae* strains tested.

The N-acetyl-lactosamine compounds tested according to D16 include LNnT. LNnT was observed to inhibit adherence of radiolabeled *S. pneumoniae* R-6 to Chang cells (page 1440, right column, second paragraph) and to inhibit the adherence of three of eight *S. pneumoniae* clinical isolates tested with Chang cells (page 1442, left column, penultimate sentence). LNnT did not inhibit adherence to NHBE cells in primary culture, although it did show activity for three of nine *S. pneumoniae* isolates in the type screen survey. According to the authors of D16, results may depend on the adhesins present on the specific *S. pneumoniae* strains tested or the sugar chain sequences present on the specific target cells tested (page 1443, left column, fourth paragraph).

2.19.3 All this cannot be considered to be teaching away from N-acetyl lactosamine-type compounds such as LNnT, let alone to be evidence of an existing technical prejudice

against them. The person skilled in the art would instead have considered using LNnT in addition to sialylated oligosaccharides as there was a chance of obtaining complementary activity, depending on the bacterial strains and types of epithelial cells involved and the interactions between their adhesins and sugar chain sequences.

The combination of sialylated oligosaccharides with lactosamine-containing oligosaccharides and the suitability of lactosamine-containing oligosaccharides as a component of infant formula is also suggested by the passage in D16 relating to the effects of breast-feeding (page 1443, right column, last paragraph), which recalls that both types of oligosaccharides are components of human milk:

*"In infants, the well-documented beneficial effects of breast-feeding for prevention of pneumococcal infection [...] might well be due in large part to antiadherence effects of sialylated and lactosamine-terminated oligosaccharides and glycoproteins."*

2.19.4 As already mentioned, the use of LNnT in infant formula is also suggested in D17 (see point 2.18.3 above).

2.20 While probiotic bacterial strains are not mentioned in document D16, they were well-known food ingredients, and their incorporation into the claimed compositions would not have required inventive skill.

2.20.1 The probiotic bacterial strain was originally mentioned merely as an optional ingredient in the application as filed. The application and the patent in suit mention known beneficial effects on well-being and general health and list a number of commercially available strains of probiotic bacteria (see paragraph [0027]

of the patent in suit and the paragraph bridging pages 8 and 9 in the application as filed).

2.20.2 The person skilled in the art seeking to solve the objective technical problem and following the pointers in the prior art towards milk-type compositions and infant formula would have been aware that probiotic strains were well-known ingredients of such products and would have considered incorporating such strains into the compositions for their known general health benefits, without the exercise of inventive skill

2.20.3 To create suitable product formulations, the person skilled in the art would also have consulted prior-art disclosures on this general type of product.

Document D1 discloses food products comprising a probiotic bacterial strain and a prebiotic mixture of oligosaccharides that includes, *inter alia*, at least one sialylated oligosaccharide selected from 3'SL and 6'SL (D1: claims 12 and 1). The food product may be an infant formula (D1: claim 13) and may be a therapeutic nutritional composition for preventing infections, including infections of the respiratory tract (D1: claims 15 to 18). D1 mentions the known health-promoting effects of the probiotic strains based on improvement of the intestinal microbial balance.

Document D9 relates to the treatment and prevention of respiratory infections and otitis media in infants by administration of probiotic strains (in particular, Bifidobacteria, combined with Lactobacteria). These may be administered in an infant formula (D9: claims 1, 11, 14 and 23; paragraph [0024]).

These prior-art disclosures confirm that probiotic bacteria were known as suitable and generally

beneficial components of similar nutritional compositions, including infant formula.

2.21 For these reasons, the subject-matter of claim 1 of the main request does not involve an inventive step within the meaning of Article 56 EPC.

3. Inventive step - auxiliary requests

3.1 Claim 1 in each of auxiliary requests 1 to 4 does not contain any further technical feature that distinguishes the claimed subject-matter from the disclosure in D16.

3.2 As a consequence, the objective technical problem and reasoning set out in section 2 for claim 1 of the main request apply equally to claim 1 of each of the auxiliary requests. It follows that the subject-matter of claim 1 in each of auxiliary requests 1 to 4 does not involve an inventive step within the meaning of Article 56 EPC.

**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:

B. Atienza Vivancos B. Rutz

Decision electronically authenticated