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Datasheet for the decision of 26 July 2016

Case Number: T 0742/15 - 3.3.09

Application Number: 10165389.7

Publication Number: 2241196

IPC: A61K31/198, A61K31/702, A23L1/29, A61P31/18, A61K31/70

Language of the proceedings: EN

Title of invention:
Nutritional supplement comprising oligosaccharides and cysteine for treating HIV

Patent Proprietor:
N.V. Nutricia

Opponent:
Fresenius Kabi Deutschland GmbH

Headword:

Relevant legal provisions:
EPC Art. 54, 56, 76(1), 83, 84, 123(2)
RPBA Art. 13(1)

Keyword:
Main request: extension beyond the content of the earlier application as filed (yes)
Auxiliary request 1: added subject-matter (no)
Claims - clarity (yes)
Sufficiency of disclosure (yes)
Novelty (yes)
Inventive step (yes)

Decisions cited:
T 0767/13

Catchword:

Europäisches Patentamt
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Case Number: T 0742/15 - 3.3.09

D E C I S I O N
of Technical Board of Appeal 3.3.09
of 26 July 2016

Appellant: (Opponent)	Fresenius Kabi Deutschland GmbH Else-Kröner-Str. 1 61352 Bad Homburg (DE)
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Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 5 February 2015 maintaining European patent No. 2241196 in amended form.**

Composition of the Board:

Chairman	W. Sieber
Members:	J. Jardón Álvarez
	D. Prietzel-Funk

Summary of Facts and Submissions

I. This decision concerns the appeal filed by the opponent against the interlocutory decision of the opposition division that European patent EP-B-2 241 196 as amended met the requirements of the EPC. The granted patent originated from a divisional application of earlier European patent application No. 06733070.4, filed on 19 April 2006 as an international application and published as WO 2006/112716 A2.

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

The documents cited during the opposition proceedings included:

D1: WO 2005/039597 A2;

D2: WO 2005/122790 A1;

D5: US 2003/0124198 A1;

D6: E. Vicenzi *et al.*, "Broad spectrum inhibition of HIV-1 infection by sulfated K5 *Escherichia coli* polysaccharide derivatives", AIDS, 2003, 17(2), pages 177 to 181;

D7: G. Lynch *et al.*, "Sulfated polyanions prevent HIV infection of lymphocytes by disruption of the CD4-gp120 interaction, but do not inhibit monocyte infection", Journal of Leukocyte Biology, 1994, 56, pages 266 to 272;

D8: H. Liu *et al.*, "Multiple and multivalent interactions of novel anti-AIDS drug candidates, sulfated polymannuronate (SPMG)-derived oligosaccharides, with gp120 and their anti-HIV activities", Glycobiology, 2005, 15(5), pages 501 to 510;

D9: US 5 661 123 A;

D13: US 2004/0077590 A1;

D14: WO 99/64022 A1;

D16: P. K. Gopal *et al.*, "Oligosaccharides and glycoconjugates in bovine milk and colostrum" British Journal of Nutrition, 2000, 84, Suppl. 1, pages S69 to S74;

D17: EP 0 626 177 A2;

D18: J. Lange *et al.*, "Nutritional intervention with NR100157 reduces $CD4^+$ T cell decline in HIV-1 positive adults not on antiretroviral therapy"; poster publication, undated;

D19: M. Clerici *et al.*, "Nutritional intervention with NR100157 restores gut microbiota in HIV-1 infected adults not on HAART and reduces systemic immune activation"; poster publication, undated; and

D20: P. Cahn *et al.*, "The Immunomodulatory Nutritional Intervention NR100157 Reduced $CD4^+$ T-Cell Decline and Immune Activation: A 1-Year Multicenter Randomized Controlled Double-Blind Trial in HIV-Infected Persons Not Receiving Antiretroviral

Therapy (The BITE Study)", Clinical Infectious Diseases, 2013, 57(1), pages 139 to 146.

III. The opposition division maintained the patent in amended form on the basis of the claims of the main request filed with letter 20 October 2014. The main request contained fourteen claims; claim 1, the only claim relevant for the present decision, read as follows:

"1. Use of one or more acid and neutral oligosaccharides and of cysteine and/or source of cysteine, in the manufacture of a composition for the treatment of HIV or AIDS in a mammal, said composition comprising a therapeutically effective amount of acid and neutral oligosaccharides wherein the acid oligosaccharides are prepared from pectin, pectate, alginate, chondroitine, hyaluronic acids, heparine, heparane, sialoglycans, fucoidan, fucooligosaccharides or carrageenan and the neutral oligosaccharide is selected from the group consisting of galactooligosaccharide, fructooligosaccharide, transgalactooligosaccharide, xylooligo-saccharide, lactosucrose and arabinooligosaccharides, and wherein said source of cysteine is selected from casein proteins, plant proteins selected from pea, potato, soy and rice, N-acetylcysteine and/or diacetylcysteine, whey, colostrum, egg proteins or a combination thereof, and wherein the cysteine and/or source of cysteine provide at least 100 mg cysteine equivalent in a daily dose."

IV. The decision can be summarised as follows:

- There was sufficient basis in the parent application as filed in support of sources of

cysteine as defined in claim 1, including their combinations, when taking into account the disclosure of the invention as a whole.

- The presence of a range of "between 15 and 50 en% lipid" and the condition "wherein the composition comprises at least 25 en% of a fat blend comprising n-3 and n-6 fatty acids" did not result in a lack of clarity of the subject-matter of claims 11 and 12. The claims could not be understood in any other way than to comprise two cascading definitions of the fat content.

- The invention was sufficiently disclosed in view of the experiments of example 1 of the patent and the lack of experimental evidence to the contrary.

- None of D1, D2, D5, D14 or D17 anticipated the claimed subject-matter.

- Lastly, the claimed subject-matter involved an inventive step starting from D14 as closest prior-art document. The opposition division saw the objective technical problem to be solved over D14 in the provision of an alternative medicament and its use for the treatment of HIV or AIDS in a mammal. It acknowledged an inventive step because the skilled person would not consider it obvious to combine the disclosure of D14, directed to an improvement of the immune system, with the disclosure of either D7 or D8, directed to blocking HIV entry into target cells by interacting with gp120, since D14 was silent about the effect exhibited by the compounds of D7 and D8.

V. On 14 April 2015 the opponent (in the following: the appellant) lodged an appeal against this decision. The statement setting out the grounds of appeal and requesting the revocation of the patent in its entirety was filed on 15 June 2015. It included the following further documents:

D33: C.R. Scholfield, "Composition of Soybean Lecithin", Journal of the American Oil Chemists' Society, 1981, 58(10), pages 889 to 892;

D34: M. Meyrand *et al.*, "Comparison of milk oligo-saccharides between goats with and without the genetic ability to synthesize α_{s1}-casein", Small Rumin Res. 2013, 113(2-3), pages 411 to 420; and

D35: Four abstracts of articles concerning sialyl oligosaccharides in colostrum of different sources; taken from Pub Med.gov (4 pages).

VI. On 20 October 2015 the appellant filed further submissions and referred to decision T 767/13 of 13 October 2015 concerning the parent patent.

VII. With its reply dated 27 October 2015 the patent proprietor (in the following: the respondent) disputed the arguments submitted by the appellant and requested as main request that the appeal be dismissed. It also filed seven auxiliary requests.

VIII. In response to the board's communication in preparation for the oral proceedings and taking into account decision T 767/13, the respondent filed with letter dated 7 January 2016 a new main request and eight auxiliary requests to replace its previous requests.

IX. On 6 July 2016 the appellant filed further submissions in preparation of the oral proceedings.

X. During the oral proceedings held on 26 July 2016, the patent proprietor filed a new auxiliary request 1 and withdrew all its previous auxiliary requests.

The claims relevant for the present decision are the claims of the main request, claim 1 being identical to claim 1 as maintained by the opposition division (see point III above), and the claims of auxiliary request 1.

Auxiliary request 1 contains nine claims including three independent claims, namely claims 1, 8 and 9. Claims 1 and 8 read as follows:

"1. Use of one or more acid and neutral oligosaccharides and of cysteine and/or source of cysteine, in the manufacture of a composition for the treatment of HIV or AIDS in a mammal, said composition comprising a therapeutically effective amount of acid and neutral oligosaccharides wherein the acid oligosaccharides are prepared from pectin, pectate, alginate, chondroitine, hyaluronic acids, heparine, heparane, sialoglycans, fucoidan, fucooligosaccharides or carrageenan and the neutral oligosaccharide is selected from the group consisting of galactooligosaccharide, fructooligosaccharide, transgalactooligosaccharide, xylooligo-saccharide, lactosucrose and arabinooligosaccharides, and wherein said source of cysteine is selected from N-acetyl-cysteine, whey, colostrum, egg proteins or a combination thereof, and wherein the cysteine and/or source of cysteine provide at least 100 mg cysteine equivalent in a daily dose."

"8. A food composition comprising between 15 and 50 en% lipid, between 25 and 60 en% protein, between 15 and 45 en% carbohydrate, acid oligosaccharide prepared from pectin, pectate, alginate, chondroitine, hyaluronic acids, heparine, heparane, sialoglycans, fucoidan, fucooligosaccharides or carrageenan, preferably pectin hydrolysate and neutral oligosaccharide selected from the group consisting of galactooligosaccharide, fructooligosaccharide, transgalactooligosaccharide, xylooligo-saccharide, lactosucrose and arabinooligosaccharides, and cysteine and/or source of cysteine selected from N-acetylcysteine whey, colostrum, egg proteins or combinations thereof, wherein the composition comprises at least 25 en% of a fat blend comprising n-3 and n-6 fatty acids."

Claim 9 differs from claim 8 only in that the energy percentage for protein is defined as being "between 35 and 60 en%" (instead of between 25 and 60).

Claims 2 to 7 are dependent claims.

XI. The arguments presented by the appellant, insofar as they are relevant for the present decision, may be summarised as follows:

- The objections filed three weeks before the oral proceedings had been filed in due time because there was no time limit in the board's communication. The respondent had enough time to react to them and they should be admitted into the proceedings.

- The amendments made to the claims of the main request extended beyond the content of the parent

application as filed. There was no support in the application as filed for either the wording "N-acetyl-cysteine and/or diacetylcysteine" or the combinations of cysteine sources now claimed. At the same time, the amendment "wherein the composition comprises at least 25 en% of a fat blend" in claims 8 and 9 introduced a lack of clarity concerning the energy percentage of the lipid in the claim.

- There was no experimental evidence in the patent showing that the compositions used were indeed effective in treating HIV or AIDS. The only example in the specification was a binding experiment. Moreover, there was no information concerning how the glutathione status had to be measured and how the "cysteine equivalent" had to be calculated when the cysteine source was a protein. Lastly, there was no evidence showing that the invention could be carried out over the whole scope of the claim.

- The subject-matter of claim 1 of auxiliary request 1 was not novel in view of the disclosures of D1, D5 and D14. D1 was also novelty-destroying for the subject-matter of claims 8 and 9.

- The claimed subject-matter lacked inventive step starting from example 3 of D14 as closest prior art. The use of oligosaccharides for the treatment of HIV/AIDS was already known from D6 or D8, and in the absence of any unexpected effect the claimed subject-matter was an obvious alternative lacking inventive step.

XII. The relevant arguments of the respondent may be summarised as follows:

- There was no justification for admitting into the appeal proceedings the new attacks filed on 6 July 2016.

- The claims of the main request were supported by the parent application as filed. Although there was no explicit mention of the "combination" of all the cysteine sources therein mentioned, the skilled person would not exclude combining sources, because the important feature was the amount of cysteine, not its source.

- The claims were novel over D1 because, in order to arrive at an embodiment as claimed, several selections were needed (multiple selection). The subject-matter of claim 1 was also novel over D5 and D14 because no acid oligosaccharide was used in these documents. Even if acid oligosaccharides were present in colostrum, as maintained by the appellant, the claimed subject-matter would still be novel because the acid oligosaccharides would not be present in the required therapeutically effective amount.

- Concerning sufficiency of disclosure and inventive step the respondent relied on the findings of the board in case T 767/13 that applied equally to the claims now under consideration.

XIII. The appellant requested that the decision under appeal be set aside and that the patent be revoked in its entirety.

The respondent requested that the patent be maintained on the basis of the claims of the main request filed

with letter dated 7 January 2016, or alternatively on the basis of the set of claims of auxiliary request 1 filed on 26 July 2016 during the oral proceedings.

Reasons for the Decision

MAIN REQUEST

1. *Amendments - Articles 100(c) and 76(1) EPC*

1.1 The patent in suit was granted on a divisional application of earlier European patent application No. 06733070.4 (filed on 19 April 2006 as an international application and published as WO 2006/112716 A2). In respect of Articles 100(c) and 76(1) EPC, the subject-matter of the patent in suit may not therefore extend beyond the content of the earlier (parent) application as filed.

The relevant criterion in this context is whether the skilled person can derive the claimed subject-matter directly and unambiguously, using common general knowledge, from the parent application as filed as a whole, either explicitly or implicitly.

1.2 The only objection under Articles 100(c) and 76(1) EPC raised in the statement of grounds of appeal against the claims maintained by the opposition division concerned the definition of the source of cysteine in claim 1 and the other independent claims. This definition of the source of cysteine was already present in granted claim 1 and reads as follows:

"wherein said source of cysteine is selected from casein proteins, plant proteins selected from pea,

potato, soy and rice, N-acetyl-cysteine and/or diacetylcysteine, whey, colostrum, egg proteins or a combination thereof".

In particular, the appellant objected to the wording "N-acetyl-cysteine and/or diacetylcysteine" and "a combination thereof".

1.2.1 The respondent relied in part on claim 7 of the parent application as filed as support for the definition of the source of cysteine as:

"N-acetyl-cysteine, whey, colostrum, egg proteins or a combination thereof",

and in part on page 12, lines 17 to 23 stating that:

"Suitable sources of cysteine according to the invention are, for example, proteins in denatured and/or undenatured form such as milk proteins e.g. whey or casein proteins. Egg proteins are rich in cysteine and are therefore also suitable. Plant proteins such as pea, potato, soy and rice can also be used to provide cysteine. [...]. Furthermore, synthetic cysteine equivalents, e.g. derivatives of cysteine, such as cysteine, cysteine salts, N-acetylcysteine and/or diacetylcysteine can be used".

1.2.2 There is undisputedly no explicit support in the parent application as filed for the cysteine sources listed on page 12, such as casein proteins and plant proteins, to be used in combination.

1.2.3 There is also no implicit disclosure of these combinations in the parent application as filed. On the contrary, the use of the wording "or a combination

thereof" for the cysteine sources listed in claim 7 of the parent application as filed, and the lack of such a wording for the list of cysteine sources on page 12, hints rather at a deliberate differentiation between both lists.

1.2.4 Although the board agrees with the respondent that the parent application as filed does not exclude the combination of sources now claimed, it is noted that this is not the criterion for an implicit disclosure. Implicit means that it is directly and unambiguously derivable from the specification as filed, not that it is not excluded from the specification as filed. This is not the case here.

1.2.5 Also the combination of "N-acetyl-cysteine and diacetylcysteine" as cysteine source is not supported by the parent application as filed. The passage on page 12 cited above includes a list of four possible cysteine sources, namely "cysteine, cysteine salts, N-acetylcysteine and/or diacetylcysteine". It is not apparent from the wording or the context whether "and/or" relates to the whole list (generic disclosure for all possible combinations) or only to the last two members of the list (specific disclosure). However, if the wording is to be interpreted generically, this disclosure cannot provide a basis for the specific combination N-acetyl-cysteine and diacetylcysteine envisaged by claim 1. Thus, this combination too is not directly and unambiguously derivable from the application as filed.

1.3 For these reasons, claim 1 of the main request contains subject-matter which extends beyond the content of the parent application as filed (Articles 100(c) and 76(1) EPC). This objection applies also to the other

independent claims which define the source of cysteine in the same way.

1.4 Consequently, the main request is not allowable.

1.5 By letter dated 6 July 2016, i.e. about three weeks before the oral proceedings, the appellant filed a submission including several new objections under Articles 100(c), 76(1) and 123(3) EPC. The respondent requested that the new objections not be admitted into the proceedings since they would have to be dealt with for the first time at the oral proceedings. As to the reasons for filing them at such a late stage in the proceedings, the appellant argued that no time limit had been set in the communication of the board and that the respondent had enough time to study the objections and react to them. Moreover, some of the objections had already been presented in the notice of opposition.

1.5.1 Article 12(2) RPBA requires that the statement of the grounds of appeal contains the appellant's complete case. However, as pointed out above, in its statement of grounds of appeal the appellant objected under Articles 100(c) and 76(1) EPC only to the wording "N-acetylcysteine and/or diacetylcysteine" and "a combination thereof" in the context of the definition of the cysteine source. Moreover, no objection under Article 123(3) EPC had been raised.

1.5.2 The new objections mentioned above represent in fact an amendment to the appellant's case which could, and should, have been filed earlier in the proceedings. Apart from that, the objections were rather subtle, which appeared to increase the complexity of the case at this late stage.

1.5.3 Under these circumstances the board exercised its discretion under Article 13(1) RPBA not to admit into the proceedings those objections raised for the first time in the letter of 6 July 2016. Consequently, only the objections raised with the statement of grounds of appeal and objections arising from the amendments made by the respondent on 7 January 2016 (basically associated with dependent claim 14 of the main request) were admitted into the proceedings.

AUXILIARY REQUEST 1

2. Amendments - Articles 100(c) and 76(1) EPC

2.1 The claims of auxiliary request 1 basically correspond to the claims of the main request, except for the definition of the cysteine source and the deletion of previous independent claim 2 and dependent claims 3, 4, 13 and 14.

2.2 The cysteine source in claim 1 is now defined as being "selected from N-acetylcysteine, whey, colostrum, egg proteins or a combination thereof", as disclosed in claim 7 of the parent application as filed.

A corresponding amendment has been made to independent product claims 8 and 9.

2.3 As a result of this amendment, the objections to the definition of the cysteine source discussed above in relation to the main request no longer apply.

2.4 The objections raised against claim 14 of the main request became moot, since this claim was deleted from auxiliary request 1.

3. Amendments - Clarity

3.1 Apart from the definition of the cysteine source, independent claims 8 and 9 have been amended by introducing at the end of the claim the further requirement "wherein the composition comprises at least 25 en% of a fat blend comprising n-3 and n-6 fatty acids" (see point X above). The appellant did not contest the support for this amendment (actually 2nd paragraph of page 15 of the parent application as filed) but argued that the amendment caused a lack of clarity. The range of between 15 and 50 en% lipid would be incompatible with the added further requirement of at least 25 en% of a fat blend comprising n-3 and n-6 fatty acids. Furthermore, it was not clear how the energy percentage of the fat blend should be calculated.

3.2 Concerning the first objection, the board accepts that the two cascading definitions for lipid and fat content may not be optimal claim wording, but this does not mean that the claim is unclear. The board has already decided in decision T 767/13 relating to the parent patent that the introduction of the lower limit of 25 en% for the fat blend in addition to the given lipid content did not create a lack of clarity, because the added feature automatically restricts the energy percentage of (total) lipid in the claim. Thus, if no other lipid but the fat blend is in the food composition, then the lower limit of at least 25 en% for the fat blend (comprising n-3 and n-6 fatty acids) is also the lower limit of (total) lipids. If, in addition to the fat blend, other lipids are present, the lower limit of (total) lipids would still be above 25 en%, namely 25 en% plus the contribution of the other lipids (see T 767/13, point 1.4 of the reasons).

3.3 The second objection is based on an alleged discrepancy between two passages in the parent application as filed.

The sentence bridging pages 17/18 states: "In the context of this invention it is to be understood that the oligosaccharides in the compositions of the present invention do not deliver calories and are therefore not included in the en% mentioned herein."

Page 15, lines 8-12, states: "In one embodiment at least about 25 en% ... of a fat blend comprising n-3 and/or n-6 fatty acids is used (en% is short for energy percentage and represents the relative amount each constituent contributes to the total caloric value of the preparation)".

According to the appellant, the skilled person would not know how to calculate the en% of the fat blend of claims 8 and 9 as it could be made (i) based on the total caloric value of the preparation as indicated on page 15, lines 11/12, i.e. including oligosaccharides, or (ii) excluding oligosaccharides as indicated on pages 17/18.

3.3.1 In the board's view there is no discrepancy between the two statements in the parent application as filed. Page 15 makes it quite clear that only those constituents are taken into account that contribute to the total caloric value. Since, however, oligosaccharides are considered not to deliver calories, as stated at pages 17/18, logically enough they are not taken into account when calculating the energy percentage of the fat blend. The board is therefore unable to follow the appellant's argument

that pages 15 and 17/18 define the energy percentages differently.

3.3.2 This view is corroborated by the historical background given by the respondent at the oral proceedings. The statement at pages 17/18 reflects the common understanding in the food industry at the time of filing the parent application, namely that oligosaccharides do not deliver calories. Only later on was the small contribution of dietary fibres, such as oligosaccharides, included for calculating the total caloric value. Thus, it is quite clear for the person skilled in the art that the energy percentage of the fat blend required in claims 8 and 9 has to be calculated as set out in the parent application, namely without the oligosaccharides.

3.4 For these reasons, the amendments made to the claims fulfil the requirements of Article 84 EPC.

4. Sufficiency

4.1 The opponent had contested sufficiency of disclosure of the parent patent because in its view there was not enough information in the patent to show that the compositions used were indeed effective in the treatment of HIV or AIDS. In particular, the opponent noted that the claims were directed to the treatment of HIV or AIDS, while the only working example merely showed that some specific oligosaccharides bound to DC-SIGN.

The appellant further argued that the invention was not sufficiently disclosed because there was no information in the specification about how to measure the reduction of the glutathione status and how to calculate the

cysteine equivalent when proteins were used as cysteine source.

4.2 Concerning the first objection the board has already held in decision T 767/13 relating to the parent patent that, in order to meet the requirements of sufficiency, it is not mandatory that results of applying the claimed composition in clinical trials, or at least to animals, are reported. The patent must provide information showing that the composition has a direct effect on a metabolic mechanism specifically involved in the disease (see Case Law of the Boards of Appeal of the EPO 8th edition 2016, Chapter II.C.6.2).

This is indeed the case here, as already outlined in the previous decision. Example 1 shows that acid and neutral oligosaccharides bind to and can block DC-SIGN receptors with differing efficacy. In view of this information in the specification, and taking into account that it is known that blocking the DC-SIGN receptor can prevent the receptor from first adhering to and then internalising HIV and thus from translocation to CD4 cells, example 1 renders it plausible that the used compositions containing acid and neutral oligosaccharides provide a treatment for HIV or AIDS (see paragraph [0025]). In any case, binding experiments are also used in D7 and D13 to study the anti-HIV activity of oligosaccharides.

4.3 Concerning the determination of the glutathione status, the board considers that this is within the knowledge of the skilled person. Several documents in the proceedings refer to glutathione, for instance D5 stating that improved resistance to infections, chronic stress or other traumas are believed to be attained "by increasing glutathione concentration in body

tissues" (see paragraph [0027]). The determination of the glutathione level would therefore be within the knowledge of the skilled person.

4.4 Lastly, concerning the calculation of the cysteine equivalent, the specification discloses on paragraph [0052] that "hereinbelow 'cysteine equivalent' refers to an amount of cysteine as such or to an amount of cysteine that is present in a source of cysteine", gives an example of how to calculate it and in the same paragraph states that the method can be applied similarly to proteins or peptides. Peptides are then exemplified. Concerning the possible lack of information about the cysteine amount of a given protein, the board agrees with the respondent that this information can also be retrieved by the skilled person from the literature. D5, for example, provides the relevant information for whey products.

4.5 The board is therefore satisfied that the invention can be carried out by the skilled person without undue burden. Moreover, the opponent did not show that an embodiment of the invention could not be carried out. The onus of proof in this respect lies with the opponent.

4.6 For these reasons, the board concludes that the requirements of sufficiency of disclosure are met.

5. Novelty

5.1 Claim 1 is drafted as a second medical use claim and comprises the following features:

(a) use, in the manufacture of a composition for the treatment of HIV or AIDS in a mammal, of a composition comprising:
(b) a therapeutically effective amount of acid oligosaccharides prepared from pectin, etc.;
(c) a therapeutically effective amount of neutral oligosaccharides selected from the group consisting of galactooligosaccharide, etc.; and
(d) cysteine and/or source of cysteine selected from N-acetylcysteine, etc.; and
(e) wherein the cysteine and/or source of cysteine provide at least 100 mg cysteine equivalent in a daily dose.

5.2 Claims 8 and 9 are directed to food compositions comprising:

(f) between 15 and 50 en% lipid, between 25/35 (25 in claim 8, 35 in claim 9) and 60 en% protein, between 15 and 45 en% carbohydrate,
(g) acid oligosaccharide prepared from pectin, etc.;
(h) neutral oligosaccharide selected from the group consisting of galactooligosaccharide, etc.; and
(i) cysteine and/or source of cysteine selected from N-acetylcysteine, whey, colostrum, egg proteins or combinations thereof, wherein
(j) the composition comprises at least 25 en% of a fat blend comprising n-3 and n-6 fatty acids.

5.3 The novelty of the subject-matter of claims 1, 8 and 9 was challenged by the appellant in view of D1 (a document under Article 54(3) EPC). Additionally, it contested the novelty of the subject-matter of claim 1 in view of D5 and D14.

5.4 Document D1

5.4.1 D1 is directed to the use of acid oligosaccharide and neutral oligosaccharide for the treatment and/or prevention of an immune system related disorder in a mammal (see claim 1). The treatment of HIV/AIDS is disclosed on page 8, lines 13 to 24. Although there is no disclosure of a daily dose of at least 100 mg/ cysteine equivalent in D1, the appellant maintained that this feature was implicitly disclosed in D1. Cow milk proteins were particularly preferred in D1 (see page 19, lines 17 to 21) and the compositions of D1 included sufficient calories to feed the subject (see page 20, lines 3 to 6), thus ensuring that at least 100 mg cysteine equivalent would be present.

5.4.2 The board disagrees. There is no clear and unambiguous disclosure in D1 of feature (e) of claim 1, namely of the use of a daily dose of at least 100 mg of cysteine equivalents. In order to arrive at the claimed cysteine daily dose, it would be necessary to make several selections within the disclosure of D1, namely to select:

(i) whey protein or another protein with a high content of cysteine from the list of preferred proteins disclosed on page 19, lines 17 to 21 of D1;

(ii) the amount of protein in the composition by choosing appropriate values for the en% and the caloric density from the general ranges disclosed on page 18, lines 21 to 24 and on page 20, lines 4 to 6, respectively; and

(iii) the amount of the food composition to be consumed.

5.4.3 The subject-matter of claim 1 thus results from a multiple selection within the teaching of D1. The skilled person would have no reason to select the combination of features now claimed. Such a combination is neither explicitly disclosed nor implicitly hinted at in D1. On the contrary, it requires combining separate embodiments within the teaching of D1, namely the caloric densities disclosed in relation to infant foods (see page 19, line 28 to page 20, line 6) with the use for the treatment of HIV/AIDS, which is a separate embodiment in D1.

5.4.4 For these reasons the board concludes that the subject-matter of claim 1 is novel over D1.

5.4.5 Similar considerations apply to the subject-matter of claims 8 and 9, which cannot be derived in a clear and unambiguous manner from the disclosure of D1. In particular, there is no disclosure in D1 of feature (j) of claims 8 and 9, i.e. the specific fat blend. The passage on page 19, lines 12 to 15 cited by the appellant in this context is completely silent about the mandatory use of a fat blend comprising n-3 and n-6 fatty acids and contributing to at least 25 en% of the caloric content of the composition.

5.4.6 The subject-matter of claims 8 and 9 is also novel over the disclosure of D1.

5.5 Document D5

5.5.1 D5 discloses nutritional compositions containing selenium, colostrum and whey to increase the

concentration of glutathione in the mammalian body to enhance the response of the mammal's immune system to infection (see abstract).

5.5.2 Although D5 does not disclose the use of acid oligosaccharides (feature (b) of claim 1), the appellant maintained that D5 anticipated the subject-matter of claim 1 because neutral and acidic oligosaccharides were present in colostrum, as shown in D16 (see abstract and tables 2 and 3).

5.5.3 The board agrees with the respondent that there is no disclosure in D5 of the use of "a therapeutically effective amount of acid oligosaccharides" for the treatment of HIV/AIDS, as required by feature (b) of claim 1. As indicated in the abstract of D16, levels of oligosaccharides in bovine milk are very low; the acidic oligosaccharides are said to be present in bovine colostrum in "trace" amounts (see table 4). D5 does not disclose the use of acid oligosaccharides for the treatment of HIV/AIDS; the fact that trace amounts of acid oligosaccharides may be present in bovine colostrum does not represent a direct and unambiguous disclosure of the use of the therapeutically effective amount of acid oligosaccharides now claimed.

5.5.4 For these reasons, D5 does not anticipate the subject-matter of claim 1.

5.6 Document D14

5.6.1 D14 discloses a nutritive composition comprising whey, selenium and colostrum for creating and maintaining healthy intestinal flora and for enhancing the immune system (see claim 1).

5.6.2 The novelty objection of the appellant based on D14 relies *inter alia* on the assumption that the presence of acidic oligosaccharides in colostrum amounts to a disclosure of feature (b) of claim 1.

5.6.3 As explained above in relation to D5, the board finds this argument unconvincing, and novelty of claim 1 has to be acknowledged over D14 at least for the same reasons already given for D5, namely that no therapeutically effective amount of acid oligosaccharides is used in D14. In fact, D14 does not concern compositions for the treatment of HIV or AIDS, as explained in point 6.2.1 below.

6. Inventive step

6.1 The invention aims to provide nutritional compositions for treating HIV patients, in order to improve their nutritional status and to reduce HIV-infection-related dysfunctions, in particular immune dysfunction, intestinal dysfunction and/or low glutathione status (see paragraphs [0021] and [0022]).

The set of claims of auxiliary request 1 includes three independent claims, namely claim 1 drafted as a second medical use claim and directed to the use of acid and neutral oligosaccharides and of cysteine in the manufacture of a composition for the treatment of HIV or AIDS, and claims 8 and 9, both directed to food compositions comprising lipid, protein and carbohydrate in given energy percentages comprising acid oligosaccharide, neutral oligosaccharide, cysteine and a fat blend comprising n-3 and n-6 fatty acids.

6.2 Claim 1

6.2.1 Closest prior art

The only inventive-step attack maintained by the appellant during the oral proceedings was based on D14 as closest prior art.

D14 discloses nutritional compositions that are useful in the creation and/or maintenance of health-protective intestinal bacterial flora and simultaneously in the enhancement of the immune system. The nutritional compositions of D14 contain whey protein concentrates or isolates, fructooligosaccharides, and bovine or caprine colostrum (page 1, lines 6 to 12). These ingredients in combination are said to have a prophylactic and therapeutic effect in maintaining and enhancing beneficial gastrointestinal microflora (page 15, lines 21 to 23).

More specifically, the fructooligosaccharides and oligosaccharides naturally present in colostrum are said to help in maintaining healthy gastrointestinal microflora (see paragraph bridging pages 22 and 23) and the whey protein is said to be useful in weight control and in enhancing the immune system (page 18, lines 13 to 16) due to its ability to enhance glutathione levels (see page 19, lines 16 to 21).

D14 does not specifically concern compositions for the treatment of HIV or AIDS, it merely notes that HIV-seropositive persons suffering from chronic diarrhea and malabsorption of nutrients may benefit from the immune-enhancing effects of whey protein (see page 20, last paragraph, in particular, lines 18 to 19; see also page 4, lines 4 to 10).

6.2.2 Problem and solution

According to the respondent, the technical problem underlying the patent in view of D14 is the provision of a nutritional composition for immune improvement achieved by acting on glutathione levels and decreasing systemic $CD4^+$ T cell activation in HIV infection (see first paragraph of page 9 of the reply to the grounds of appeal).

This problem is solved by using compositions as defined in claim 1 which contain, in addition to whey/cysteine to improve glutathione levels, acid oligosaccharides and neutral oligosaccharides to improve immune dysfunction. In particular, the invention is said to be based on the finding that certain acid and neutral oligosaccharides can block DC-SIGN preventing viral translocation from dendritic cells to $CD4^+$ T-cells, preventing further spread of the virus and development of HIV-infection-related dysfunctions (see paragraph [0089]; see also paragraphs [0024] and [0025]).

Example 1 in the patent shows that the acid and neutral oligosaccharides are indeed effective in the treatment of HIV, since they bind to and block the DC-SIGN receptor. The further experimental evidence filed during the opposition proceedings, namely documents D18 to D20, confirm these results. In particular D18 shows that a composition comprising acid and neutral oligosaccharides and a source of cysteine is indeed effective in the treatment of HIV infection. CD4+ T-cell decline in HIV patients to which such a composition was administered was significantly reduced

compared to a control group of HIV patients (see conclusion).

The board is therefore satisfied that the above problem has been credibly solved by the measures taken.

6.2.3 Obviousness

It remains to be decided whether, in view of the available prior art, it would have been obvious for the skilled person to solve this technical problem by the means claimed.

D14 itself gives no hint towards the claimed solution. As pointed out above, the oligosaccharides in D14 are exclusively used to maintain healthy gastrointestinal microflora. D14 is completely silent about any positive influence of acid and neutral oligosaccharides on $CD4^+$ T-cell decline.

The appellant argued that the skilled person would arrive in an obvious manner at the claimed subject-matter by combining the teaching of D14 with the teaching of D6 and/or D8, because these documents disclosed the anti-HIV activity of certain oligosaccharides. Thus, D6 disclosed on page 179, right column, lines 13 to 15 that "highly sulfated K5-OS(H) inhibited the replication of T-cell line adapted TCLA X4 strains with an IC_{50} similar to that of heparin". D8 disclosed interactions of sulfated polymannuronate (SPMG)-derived oligosaccharides and stated on page 507, right column, second full paragraph, that "Anti-HIV activities started from 8-mer, and 10-20-saccharide residues or higher units confer to potential antagonists, with 8-mer oligosaccharide the minimum size requirement for combating HIV infection", and in

the third full paragraph that "All these findings, particularly with the potent anti-HIV activity of SPMG and its oligos in HIV-IIIB-infected cells, ...".

Although D6 and D8 indeed show that certain oligosaccharides are able to inhibit HIV infections, the oligosaccharides in these documents are not the ones present in the compositions of D14. Moreover, acid oligosaccharides are not mentioned at all in D14, even if they could be present in bovine colostrum. The skilled person had no motivation from these citations to use the compositions of D14, or to add other oligosaccharides to the compositions of D14, to treat further HIV-related symptoms, because, as explained in point 7.2.1 above, the main aim of D14 is to maintain health-protective microflora in the intestinal tract of mammals. It appears that the appellant's argument is made with the knowledge of the invention and therefore cannot call into doubt the inventiveness of claim 1.

6.2.4 In summary, there is no incentive in the prior art for the skilled person to modify the compositions of D14 to solve the above-mentioned problem, namely to provide compositions that are useful for the treatment of HIV or AIDS by improving not only the low glutathione status but also immune dysfunctions.

6.2.5 For these reasons, the subject-matter of claim 1, and by the same token that of dependent claims 2 to 7, involves an inventive step.

6.3 Claims 8 and 9

6.3.1 The subject-matter of claims 8 and 9 is directed to a food composition defined by stating the energy

percentage of lipid, protein and carbohydrate and comprising the same components used in claim 1, namely:

- acid oligosaccharides prepared from pectin, etc.;
- neutral oligosaccharides selected from the group consisting of galactooligosaccharide, etc.; and
- cysteine and/or source of cysteine,

and further comprising;

- at least 25 en% of a fat blend comprising n-3 and n-6 fatty acids.

6.3.2 The inventive step of these claims was contested by the appellant, starting from D14 as closest prior art and combining it with D9. The appellant argued essentially that D14 already discloses a food composition including all the components of claims 8 and 9, the only distinguishing feature being the defined energy percentages, and these percentages could not justify an inventive step because they were standard in the field, as shown for instance in D9 (see column 3, lines 32 to 35, 56 to 58 and column 3, line 66 to column 4, line 3).

6.3.3 The compositions of claims 8 and 9 have the same use as the compositions used in claim 1, namely the treatment of HIV patients in order to improve infection-related dysfunctions (see point 6.2.2 above). The additional presence of the fat blend comprising omega-3 and omega-6 fatty acids is said to reduce inflammatory intestinal dysfunction (see paragraph [0061]). The reasoning above for the use claims applies equally to the composition claims. The subject-matter of claims 8

and 9 therefore involves an inventive step for the same reasons given above for claim 1.

6.3.4 The fact that the claimed compositions might be closely related to those already known from D14 cannot call the above finding into question. The board acknowledges an inventive step for the composition claims basically because the effect associated with the use of the compositions in the treatment of HIV is not suggested by the cited prior art, as explained in detail above in relation to claim 1.

7. The respondent had initially requested that D33 to D35 and the inventive-step attack based on D17 not be admitted into the proceedings. Since, however, the appellant no longer relied on these documents, there was no need for the board to decide on these requests.

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 9 of auxiliary request 1 filed on 26 July 2016 during the oral proceedings before the board; and

   - pages 1 to 26 of the description filed on 20 November 2014 during the oral proceedings before the opposition division.

The Registrar: The Chairman:

M. Cañueto Carbajo W. Sieber

Decision electronically authenticated