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Datasheet for the decision of 25 June 2015

Case Number: T 0943/13 - 3.3.09

Application Number: 06824315.3

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Language of the proceedings: EN

Title of invention:
COMPOSITION COMPRISING OLIGOSACCHARIDES AS SOLUBLE DIETARY FIBRES FOR USE AGAINST MUSCLE WASTING

Patent Proprietor:
N.V. Nutricia

Opponent:
Fresenius Kabi Deutschland GmbH

Headword:

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

Keyword:
Grounds for opposition - added subject-matter (no)
Grounds for opposition - insufficiency of disclosure (no)
Novelty - (yes)
Inventive step - non-obvious alternative

Decisions cited:
G 0002/88, G 0002/08, T 0219/01, T 0433/05, T 1685/10

Catchword:
The causal relationship between the substance or composition on the one hand and the therapeutic effect achieved on the other hand is decisive for the assessment of inventive step of further-medical-use claims (see point 4.1.5).

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Case Number: T 0943/13 - 3.3.09

D E C I S I O N
of Technical Board of Appeal 3.3.09
of 25 June 2015

Appellant: (Patent Proprietor)	N.V. Nutricia Eerste Stationsstraat 186 2712 HM Zoetermeer (NL)
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Representative:	Fresenius Kabi Deutschland GmbH Patent Department Else-Kröner-Straße 1 61352 Bad Homburg (DE)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 8 February 2013 concerning maintenance of the European Patent No. 1965669 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 that European patent No. 1 965 669 as amended meets the requirements of the EPC.

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

The documents submitted during the opposition proceedings included:

D6: WO 97/39749 A2;

D9: M.V.W. Wijnands et al, Carcinogenesis, volume 22(1), 2001, pages 127 to 132;

D12: WO 02/15720 A2;

D15: I.W. McKinnell et al, Cell, volume 119, 2004, pages 907 to 910;

D17: J. Faber et al, British Journal of Cancer, volume 99, 2008, pages 2029 to 2036;

D18: WO 2009/157759 A1;

D19: WO 2009/157767 A1;

D22: R. Hodin, Gastroenterology, volume 118(4), 2000, pages 798 to 801, and

D23: J.H. Cummings et al, European Journal of Clinical Nutrition, volume 51, 1997, pages 417 to 423.

III. The opposition division's decision was based *inter alia* on the patent as granted (main request), claims 1 and 12 to 15 of which read as follows:

"1. A soluble dietary fibre for use in the treatment or reduction of the incidence of muscle wasting and/or chronic muscle wasting and/or sarcopenia, the dietary fibre comprising at least 30 wt.% of oligosaccharides having a chain length of 3-10 anhydromonose units."

"12. A food supplement containing between 10 and 90 wt.% of the soluble fibre as defined in any one of claims 1-4, and 90-10 wt.% of ribose."

"13. A carbohydrate composition containing 3-40 wt.% of the soluble fibre as defined in any one of claims 1-4, 3-40 wt.% of ribose, 5-40 wt.% of lactose and 20-80 wt.% of other digestible carbohydrates."

"14. A food supplement containing 10-95 wt.% of the soluble fibre as defined in any one of claims 1-4, and 5-90 wt.% of ω-3 fatty acids, the soluble fibre comprising at least 50 wt.% of galacto-oligosaccharides."

"15. A nutritional composition containing the soluble fibre as defined in any one of claims 1-4 and a protein fraction, the weight ratio between the fibre composition and the protein fraction being between 5:95 and 75:25, the protein fraction containing at least 48 wt.% of essential amino acids, the soluble fibre

comprising at least 50 wt.% of galacto-oligosaccharides."

IV. In as far as the main request (the only request relevant to the present decision) is concerned, the decision of the opposition division can be summarised as follows:

The opposition division admitted D15, D17 to D19 and D22 into the proceedings.

As regards the ground under Article 100(c) EPC, the reference to "fibre" in claims 12 to 15 as granted, instead of "fibre composition" as present in claims 12 to 15 as filed, did not extend beyond the content of the application as filed.

The patent as granted also met the requirements of sufficiency of disclosure since, *inter alia*, the questions whether the claimed therapeutic effect was obtained over the whole scope claimed or even obtained at all were inventive-step objections.

The subject-matter of claim 1 as granted was novel over D12. This document did not disclose any specific therapeutic effect of the dietary fibres disclosed therein on muscle wasting or sarcopenia.

However, the subject-matter of claim 1 did not involve an inventive step over the closest prior-art document D12. Basically, the opposition division held that the claimed therapeutic effect had not been proven for oligosaccharides different from galactooligosaccharides and for therapeutic effects different from muscle wasting associated with cancer cachexia. Consequently, the objective technical problem had to be seen in the

provision of a nutritional composition for use in the prevention of muscle loss and acceleration of muscle mass recovery, as an alternative to D12. The solution of said problem was obvious in view of D12 alone since the use of oligosaccharides for their prebiotic properties was already disclosed and no unexpected therapeutic effect resulted therefrom over the whole scope claimed.

V. This decision was appealed by both the opponent and the proprietor. As the opponent and the proprietor are respectively 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. In its statement of grounds of appeal (letter dated 17 June 2013), the opponent requested that the decision of the opposition division be set aside and that the patent be revoked. The opponent furthermore alleged that in its written decision the opposition division had committed a substantial procedural violation of its right to be heard.

VII. The proprietor's statement of grounds of appeal (letter dated 18 June 2013) contained five claim sets as first to fifth auxiliary requests, the main request being that the patent be maintained unamended.

VIII. Responses to the respective appeals were filed by the the opponent (letter dated 13 August 2013) and the proprietor (letter dated 4 November 2013), the proprietor requesting that the opposition division's decision to admit D15, D17 to D19 and D22 into the proceedings be reversed.

IX. With letter dated 10 January 2014, the proprietor filed

D24: Experimental evidence, Numico Research 2006; and

D25: P.G. Reeves, J. Nutr., volume 127, 1997, pages 838S to 842S.

X. By communication dated 5 January 2015, the board provided its preliminary opinion in which it observed that the subject-matter of claim 1 appeared to be novel over D12, that D9 appeared not to be the closest prior art and that in view of the closest prior-art documents D6, D12 and D15, the objective technical problem appeared to be the provision of an alternative means to obtain the claimed therapeutic effect.

XI. In its response dated 27 March 2015, the proprietor filed new auxiliary requests 1 to 4, replacing former auxiliary requests 1 to 5.

XII. With its letter dated 22 June 2015, the opponent submitted

D24a: D.K. Layman, J. Nutr., volume 133(1), 2003, pages 261S to 267S.

XIII. On 25 June 2015, oral proceedings were held before the board. The opponent declared during the oral proceedings that it was no longer pursuing its objection regarding the alleged procedural violation committed in the decision under appeal. The proprietor withdrew its request that D15, D17 to D19 and D22 not be admitted into the proceedings but maintained that request regarding D24a; no decision on this issue was needed since that document is not relevant to the

present decision. All remaining requests made during the written proceedings were maintained.

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

- The ground under Article 100(c) EPC prejudiced the maintenance of the patent as granted, because the amendment of "fibre composition" in claims 12 to 15 as filed to read "fibre" in claims 12 to 15 as granted extended beyond the content of the application as filed.

- The ground under Article 100(b) EPC prejudiced the maintenance of the patent as granted. The major lines of argument were that firstly the claimed therapeutic effect had not been demonstrated in the opposed patent and could not be obtained as evidenced by D17, secondly the claimed therapeutic effect had not been demonstrated for oligosaccharides other than galactooligosaccharides, and thirdly it was not credible that the claimed therapeutic effect on muscle wasting was likewise obtained for the different condition of sarcopenia.

- The subject-matter of claim 1 lacked novelty over D12, in particular the disclosure of compositions containing prebiotic fibres on page 9 of this document.

- The subject-matter of claim 1 was not inventive in view of D12 as the closest prior art. The objective technical problem in view of this document was the provision of an alternative, and the claimed choice of dietary fibres was an

arbitrary choice already disclosed in this document. There was furthermore no evidence for any effect obtained by the further distinguishing features present in claims 12 and 13, so that the subject-matter of these claims lacked inventive step in view of D12 as well.

The subject-matter of claim 1 furthermore lacked inventive step in view of D15 in combination with D22 and D9 or D23, the subject-matter of claims 12 and 13 was obvious in view of D9 as the closest prior art (argument presented in the written proceedings only), and the subject-matter of claims 14 and 15 was not inventive in view of D6 (example IV) as the closest prior art.

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

- The ground under Article 100(c) EPC did not prejudice the maintenance of the patent as granted. The terms "fibre" and "fibre composition" were used interchangeably in the application as filed and, furthermore, the fibre in the application as filed could contain further components and thus was a fibre composition.

- The ground under Article 100(b) EPC did not prejudice the maintenance of the patent as granted:

  - The claimed therapeutic effect of a reduction or treatment of muscle wasting was obtained with galactooligosaccharides. In this respect, the probative value of D17 was less than that of example 1 of the patent or D24, since D17 relied

on qualitative statements only. The opponent's argument that example 1 of the patent had no probative value since the diets used in this example consisted of carbohydrates only and thus were not balanced was not convincing. It belonged to the skilled person's common general knowledge that in tests such as the one of example 1, balanced foods were used. The opponent's reference to an alleged lack of information in example 1 was not persuasive either. Firstly, the opponent had not provided any evidence that the information that was allegedly missing from example 1 was decisive for the question of whether or not the claimed therapeutic effect was obtained. Secondly, the opponent had given no reasons why the fact that data on body and tumour weight were lacking in example 1 disqualified the findings in this example as regards muscle weight. Thirdly, the lack of information about the statistical method in example 1 was less of a problem than the fact that D17 did not contain any data at all. Fourthly, the results of example 1 of the patent were confirmed by D24, the data of which clearly showed a trend towards a reduction in muscle wasting for galactooligosaccharide-containing diets. It was in this respect not relevant that galactooligosaccharides led to a reduction of lean body mass, as this did not correlate with muscle mass. As could be deduced from the fact that the experimental section of the patent contained data on muscle mass only, the patent was about reduction of muscle wasting rather than the reduction of the loss of lean body mass.

- The opponent's second insufficiency argument, namely that it was not plausible that the claimed therapeutic effect was obtained for oligosaccharides other than galactooligosaccharides, was not persuasive, since no experimental evidence had been provided by the opponent to back up its argument.

- The opponent's third insufficiency argument, namely that it was not plausible that the effect on muscle wasting in cancer was likewise observed in sarcopenia, was not persuasive either. In this respect, it was irrelevant that D9 and D23 described dietary fibres as suitable to treat cancer, and thereby possibly indirectly to treat muscle wasting, since this did not exclude the dietary fibres from also being directly effective against muscle wasting.

- The subject-matter of claim 1 was novel over D12 since this document did not disclose any dietary fibre for use in the treatment of muscle wasting.

- The subject-matter of claims 1 and 12 and 13 was inventive over D12 as the closest prior art. The objective technical problem was the provision of an alternative means to treat muscle wasting. The solution to this problem was the use of dietary fibres as defined in claim 1. In D12, whey protein was disclosed as the active ingredient for the treatment of muscle wasting, and dietary fibres as defined in claim 1 were disclosed only as stimulating bacterial growth in the colon.

  The subject-matter of claim 1 was also inventive in view of D15 as the closest prior art. The

distinguishing feature was the dietary fibres as defined in claim 1 and the objective technical problem solved thereby was the provision of an alternative means for treating muscle wasting. The claimed solution was not obvious in view of D15 and the opponent's arguments as regards a combination of D15 with D22 and D9 or D23 were based on hindsight.

Finally, the subject-matter of claims 14 and 15 was inventive in view of D6. Here too, the objective technical problem was to provide an alternative treatment for muscle wasting. The only place where dietary fibres were mentioned in D6 was example IV and no explanation was given as to why these dietary fibres were included, let alone any connection made to the treatment of muscle wasting.

XVI. The final requests of the parties were as follows:

The opponent requested that the decision under appeal be set aside and that the patent be revoked.

The proprietor requested that the decision under appeal be set aside and that the patent be maintained

- as granted (main request), or

- on the basis of any of auxiliary requests 1 to 4 filed with letter of 27 March 2015,

- on the basis of auxiliary request 5, which consists of the claims found allowable by the opposition division and actually amounts to a request that the opponent's appeal be dismissed.

Reasons for the Decision

Main request (claims as granted)

1. Amendments - Article 100(c) EPC

1.1 Claims 12 to 15 as filed refer to a composition ("food supplement", "carbohydrate composition" and "nutritional composition") containing a certain amount of the "fibre composition as defined in any one of claims 1-4". Granted claims 12 to 15 differ from claims 12 to 15 as filed in that the wording "**fibre composition** as defined in any one of claims 1-4" has been replaced by "**fibre** as defined in any one of claims 1-4" (emphasis added by the board). The opponent argued that this amendment was not based on the application as filed.

1.2 The board does not agree. As set out above, claims 12 to 15 as filed refer to a fibre composition and specify it by reference *inter alia* to claim 1 as filed. This claim, however, is not directed to a fibre composition but to a fibre ("soluble dietary fibre"). Consequently, the terms "fibre composition" and "fibre" are used interchangeably in the application as filed for one and the same thing. In fact, they both mean the same thing, namely a fibre composition comprising at least 30 wt% of specific oligosaccharides but which may comprise further components. This is corroborated by the "comprising"-language in claim 1 as filed: "fibre comprising at least 30 wt.% of oligosaccharides having a chain length of 3-10 anhydromonose units". The replacement of "fibre composition" by "fibre" in claims 12 to 15 as granted therefore does not introduce any new subject-matter.

1.3 In the absence of any further objections from the opponent's side, the board is convinced that the ground under Article 100(c) EPC does not prejudice the maintenance of the patent as granted.

2. Sufficiency - Article 100(b) EPC

2.1 Claim 1 is a second medical use claim referring to a soluble dietary fibre for use in the treatment or reduction of the incidence of muscle wasting and/or chronic muscle wasting and/or sarcopenia, the dietary fibre comprising at least 30 wt% of oligosaccharides having a chain length of 3 to 10 anhydromonose units.

It was a matter of dispute between the parties whether the claimed therapeutic effect of treating or reducing the incidence of muscle wasting and/or chronic muscle wasting and/or sarcopenia could be obtained with dietary fibres as defined in claim 1.

In its decision, the opposition division reasoned that this issue represented an inventive-step rather than an insufficiency objection (point 3.3 of the decision). In the board's view, this is not correct. If a therapeutic effect is cited in a second medical use claim, this effect constitutes a functional feature of this claim. Consequently, for the invention as defined by the claim to be sufficiently disclosed, the skilled person must be able to put this feature into practice, i.e. to obtain the claimed therapeutic effect. The question as to whether the therapeutic effect as defined in claim 1 is achievable is therefore a matter of sufficiency of disclosure (see, e.g., T 433/05, point 28).

2.2 The first aspect of the opponent's insufficiency objection was the question as to what extent the therapeutic effect was demonstrated in the opposed patent. In this respect, the opponent argued that the only experimental data of the patent were found in example 1. This example compared the respective muscle mass of tumour-bearing mice with tumour-bearing mice fed GOS. However, the overall documentation was poor and the results inconclusive, in particular in view of the subsequently published study D17 (and in the same way D18 and D19), which reached the exact opposite conclusion to example 1. D17 had more probative value than the evidence referred to by the proprietor, namely example 1 of the patent and D24, and therefore, in line with decisions T 219/01 and T 1685/10, sufficiency should be denied.

To decide on the opponent's objection, it is necessary to compare D17 (an analysis of D18 and D19 is not needed since the relevant content thereof is identical to that of D17) with example 1 of the patent and D24 as regards their probative value on the question of whether muscle wasting can be treated or reduced by galactooligosaccharides (which are the oligosaccharides used in example 1 of the patent, D17 to D19 and D24).

2.2.1 The opponent's evidence: D17

D17 is a scientific paper on the effect of various diets on body weight (BW), carcass weight (CW) and muscle weight of tumour-bearing (TB) mice suffering from cachexia. The experiments were divided into experiments A, designed to test the effect of the individual ingredients, and experiments B, designed to test the effect of the complete mixture. Thus, the

experimental diets in experiment A were adapted to contain

- a mixture ("SOM") containing 18 g of the short chain galactooligosaccharide Vivinal® GOS and 2g short chain fructooligosaccharides; or

- 210 g of protein, including casein and leucine ("high protein/leucine" or "HPrleu"); or

- 52.5 g of fat, including fish oil ("FO").

It was common ground between the parties that the galactooligosaccharide-containing mixture SOM corresponds to the dietary fibre referred to in claim 1.

The experimental diet "SNC" in experiment B contained all three components SOM, Hprleu and FO. For TB-SNC mice fed with this diet SNC, a reduction in the loss of skeletal muscle mass was observed (table 2), compared to TB mice fed with a diet not containing those three components.

For TB mice fed with diets containing the individual components, namely SOM, FO or HPrleu, in experiment A, the following qualitative statements are made in D17:

> "The addition of one of the individual nutritional ingredients to the diet did not result in any significant effect on BW or CW compared with animals in the TB group. However, a diet containing the complete mixture of FO, SOM and high protein/leucine improved both BW and CW significantly from 20.1 and 18.0 g, respectively, in the TB group to 21.9 and 20.3,

> respectively, in the TB-SNC group (Table 2), indicating a less cachectic state of the mice. This was emphasised by a positive effect on other cachectic features, such as significant inhibition of weight loss, epididymus fat and skeletal muscles, **which was absent after feeding a diet with the individual nutritional ingredients**" (last full paragraph in the left-hand column on page 2032, emphasis added by the board).
>
> "To evaluate the potential benefits of the specific nutritional interventions on cachexia features and immune function, FO, SOM and high protein/leucine were added to the diet of tumour-bearing mice. **No effect of the individual ingredients was shown on** BW, CW, epididymus fat and weight of **skeletal muscles**, indicating no advances in the poor cachetic state of the mice" (page 2034, right-hand column, third paragraph, emphasis added by the board).

According to the opponent, it follows from these statements that a composition comprising solely the galactooligosaccharide-containing mixture SOM is not effective in treating or reducing muscle wasting.

However, the qualitative statements in D17 relied upon by the opponent are not supported by any experimental data. In fact, the only data given in D17 for mice fed exclusively with the mixture SOM concern the body weight, tumour weight and carcass weight of the mice (table 1), but no data on skeletal muscle mass are present. Hence, the above statements are not necessarily based on truly measured experimental data. It could equally be that, as argued by the proprietor,

the authors of D17 merely deduced from the fact that the body weight did not change significantly that the same was true for the muscle mass. As will be shown below (point 2.2.2) on the basis of D24, body weight and muscle mass are however not necessarily correlated.

2.2.2 The proprietor's evidence: example 1 of the patent and D24

Example 1 of the patent describes two experiments. In experiment 1, TB mice were fed a composition GOSFOS consisting of galactooligosaccharides "GOS" with a degree of polymerisation of 3 to 8 (corresponding to the dietary fibre as defined in claim 1), fructooligosaccharides "FOS", maltodextrin, lactose and glucose. In experiment 2, the same composition was used except that FOS were replaced by additional GOS. It was found that the galactooligosaccharide compositions GOSFOS and GOS led to a reduction in muscle wasting in TB mice with cancer cachexia (text in the table on page 6). More specifically, the weight of the muscles m. EDL and m. Sol in TB mice fed the mixture GOSFOS was 8.2 and 5.8 respectively compared to 7.7 and 5.5 in the TB mice. Furthermore, the weight of these muscles in mice fed GOS was 8.2 and 6.2, respectively, compared to 7.7 and 5.6 in the TB mice (table on page 6). The data thus show a clear trend towards reduced muscle wasting as a consequence of feeding the galactooligosaccharide-containing compositions GOSFOS and GOS.

The opponent argued that example 1 of the patent did not make it plausible that the claimed therapeutic effect could be obtained, since the diets used in this example consisted of carbohydrates only and thus did not represent a balanced food. The board acknowledges that example 1 indeed states that the food consisted of

various carbohydrates, which, taken literally, implies that no components other than these carbohydrates were present. It belongs however to the skilled person's common general knowledge that in tests such as the one of example 1, balanced foods are used. This was in fact indirectly confirmed by the opponent who stated during the oral proceedings that using carbohydrate-only food would not be a "realistic test". The board therefore shares the proprietor's view that the skilled person reading example 1 would know that the food used in this example must have contained proteins and fats, apart from the cited carbohydrates.

The opponent furthermore argued that example 1 could not prove that the claimed therapeutic effect was obtained, since various pieces of information were missing in the example. In particular, (i) no information was present as regards the number and age of mice, the composition of the control food, or the duration of the experiment, (ii) the body and tumour weight, (iii) the statistical methods used and (iv) the impact of the galactooligosaccharides on muscles different from those tested in example 1. However, as to (i), the opponent has not provided any evidence that the number and age of mice, the composition of the control food or the duration of the experiment are decisive for the question of whether or not the claimed therapeutic effect is obtained; as to (ii), it is not apparent why the fact that no data on body and tumour weight are given in example 1 disqualifies the findings as regards muscle weight, for which data are present; as to (iii), the fact that D17 does not contain any data at all supporting the opponent's allegations takes away much more credibility from D17 than the mere lack of information on the statistical method in example 1, and as to (iv), no proof has been provided that for

muscles different from those tested in example 1 the claimed effect is not achievable.

In fact, the findings in example 1 of the patent are confirmed by the study in D24, which is actually the same study as presented in example 1 of the patent, but finalised after the completion of further measurements:

In experiments 1 and 2 described in D24, the same mice were used as in example 1 of the patent (these mice are denoted cTB in D24). In experiment 1, the mice were fed with a standard chow (available ad libidum) together with a composition containing galactooligosaccharides GOS with a degree of polymerisation of 3 to 8 (corresponding to the dietary fibre as defined in claim 1) applied in admixture with high molecular weight fructooligosaccharides (subjects TB-GF). In experiment 2, these mice were fed with either a composition as in experiment 1 (subjects TB-GF) or a composition containing the galactooligosaccharides GOS alone (subjects TB-GOS).

In experiment 1 the weight of three out of four investigated muscles, namely of the muscles m. EDL, m. TA and m. Sol, was higher in the TB-GF mice than in the cTB mice, which had not received the galactooligosaccharide composition. In experiment 2, the weight of all muscles m. EDL, m. TA, m. Gas and m. Sol was higher in the TB-GF and TB-GOS mice, compared to the cTB mice (table 3a, b).

The board acknowledges that in experiment 1 of D24, TB-GF subjects showed a more pronounced rather than a reduced loss in the weight of m. Gas and that m. Gas is the muscle with the biggest muscle mass. However, firstly, overall there was still a weight gain due to

the feeding of the galactooligosaccharide composition GF in experiment 1. More specifically, the weight of m. EDL, m. TA and m. Sol increased in experiment 1 by 2.3 while that of m. Gas decreased only by 1.3. Secondly, at least in experiment 2, also the weight of m. Gas increased, namely by 2.5 for composition GF and even by 3.6 for composition GOS, compared to the mice being fed standard chow only (cTB). Therefore, when the muscle-weight data in D24 are considered in their entirety, they support the finding in example 1 of the patent that galactooligosaccharide compositions reduce muscle wasting and thus provide the claimed therapeutic effect.

The opponent argued that the increase in muscle weight observed in experiments 1 and 2 of D24 was statistically irrelevant. However, as set out above, except for the muscle weight reduction for m. Gas in experiment 1 of D24, the weight of all muscles in both experiments increased when the galactooligosaccharide compositions GF and GOS were fed. There is thus at the very least a clear trend towards an increase in muscle weight and thus a reduction in muscle wasting due to the feeding of these compositions.

The opponent furthermore argued that the feeding of the galactooligosaccharide compositions GF and GOS led to a reduction in lean body mass, as evidenced by table 2 of D24, and that a reduction in lean body mass equated according to page 2, lines 10 to 13 of the patent to an increase in muscle wasting. In the opponent's opinion, the claimed therapeutic effect was therefore not obtained in view of the lean body mass data in D24.

The passage on page 2 of the patent, referred to by the opponent, reads as follows:

> "Severe weight loss and in particular muscle wasting is a serious phenomenon that occurs on a broad scale in patients suffering from diseases, disorders and trauma. Muscle wasting (abbreviated as MW) in chronic disease is defined as an involuntary loss of body weight of more than 5% within one month. If loss of lean body mass (abbreviated as LBM) occurs at a more gradual rate but during a longer period, the inventors refer to chronic muscle wasting."

The first sentence in this passage makes it clear that muscle wasting is a specific form of weight loss in patients suffering from diseases, disorders or trauma. In view of this introductory sentence, the reference to a loss of body weight or lean body mass in the next two sentences would be read by the skilled reader as referring to a loss of body weight or lean body mass as a result of a loss of muscle weight. Hence, also in view of this passage, not all lean body mass losses equal muscle wasting, but only those which are due to loss of muscle weight. This is confirmed by the experimental section of the patent where exclusively the weight of muscles is recorded. Therefore, the fact that the lean body mass is reduced in D24 by feeding the galactooligosaccharide compositions GF and GOS does not necessarily mean that muscle weight is reduced as well. In fact, as set out above, the data given for muscle weight in D24 clearly indicate the opposite.

2.2.3 In view of the above, the board considers it more credible than not that galactooligosaccharides as covered by the definition of dietary fibres in claim 1

lead to the claimed therapeutic effect of a reduction or treatment of muscle wasting. The opponent's first insufficiency argument must thus fail.

2.3 According to the opponent's second insufficiency argument, and in line with the decision of the opposition division, it was not plausible that the therapeutic effect of claim 1 was obtained for oligosaccharides other than galactooligosaccharides, even if one accepted the therapeutic effect in view of example 1 and D24.

However, the burden of proof to show that oligosaccharides other than galactooligosaccharides do not provide the claimed therapeutic effect is on the opponent. In the absence of any experimental evidence, the opponent's argument is nothing more than an unsubstantiated allegation, and as such cannot lead to a finding of insufficiency of disclosure.

2.4 According to the opponent's third insufficiency argument, and again in line with the opposition division's decision, it is not plausible that the therapeutic effect on muscle wasting in cancer is likewise observed in sarcopenia, since the latter has a very different biochemical mechanism.

2.4.1 The opponent argued in particular that according to D9, galactooligosaccharides led to a protective effect against the development of certain types of tumours in rats and that by way of this mechanism the galactooligosaccharides indirectly led to a reduction in muscle loss in cancer cachexia. The same could not apply to the non-cancer related muscle wasting in sarcopenia.

The board accepts that less development of tumours, as observed in D9, may indirectly reduce muscle loss. This does not however exclude the possibility that treatment with galactooligosaccharides in addition directly reduces muscle loss in patients with cancer cachexia and that the same also occurs in patients suffering from sarcopenia. In this respect, the board does not share the opposition division's view that D15 confirms that muscle wasting in cancer cachexia and sarcopenia is based on distinct physiological phenomena. In fact, D15 (penultimate and last paragraph of the left-hand column of page 907) rather points to the contrary by stating that all atrophic conditions including muscle wasting associated with cancer and muscle wasting associated with sarcopenia **share the commonality** of an imbalance in the protein system, resulting in reduced protein synthesis and increased protein breakdown/ proteolysis, which in turn results in reduced muscle mass and muscle fibre size.

2.4.2 Therefore, no insufficiency arises for the different types of muscle wasting covered by claim 1.

3. Novelty

3.1 According to the opponent's only novelty attack, the subject-matter of claim 1 lacks novelty over D12.

3.2 D12 discloses the use of a composition for preventing muscle loss, the composition comprising (i) a protein source which includes at least about 50 wt% of whey protein, (ii) a lipid source having an omega 3:6 fatty acid ratio of about 5:1 to about 10:1, (iii) a carbohydrate source and (iv) a balanced macronutrient profile comprising at least vitamin E and vitamin C (page 2, line 25 to page 3, line 10).

The prevention of muscle loss is attributed in D12 to the whey protein present in this composition (page 3, lines 16 to 21 and page 4, line 28 to page 5, line 4).

Dietary fibres as defined in claim 1 are disclosed in D12 only as one of various optional further components. Specifically, on page 9, lines 19 to 30 of D12, prebiotic fibres such as Raftilose®, a fructooligosaccharide with a degree of polymerisation of 3 to 7, are mentioned. However, D12 does not disclose the Raftilose in the context of the prevention of muscle loss. On the contrary, all that is disclosed in D12 is the following:

> "A prebiotic fiber is a fiber which beneficially affects the host by stimulating growth and/or activity of bacteria in the colon which have the potential to improve host health" (page 9, lines 20 to 22).
>
> "The soluble, prebiotic fibres are reported to promote the growth of Bifidobacteria in the gastrointestinal tract and, in certain circumstances prevent or decrease the growth of pathogens such as Chostridiae. Further, promoting the growth of Bifidobacteria is reported to have various other beneficial effects. Also, during fermentation of the fibres in the colon, short chain fatty acids are produced. These fatty acids are a fuel for intestinal cells" (page 9, line 31 to page 10, line 4).

Hence, the subject-matter of claim 1 (and by the same token of claims 2 to 11) is novel over D12.

3.3 Incidentally, it is noted that nowhere does D12 disclose the compositions of claims 12 to 15, in particular the type and amount of further components as required by these claims. Therefore, also the subject-matter of these claims is novel over D12.

4. Inventive step

4.1 The opponent argued that the subject-matter of claim 1 lacked inventive step in view of D12 as the closest prior art.

4.1.1 Like the patent, D12 aims at reducing the incidence of muscle wasting. Consequently, this document can be considered to represent the closest prior art.

4.1.2 As set out above, the composition to be used according to claim 1 differs from the composition disclosed on page 2, line 25 to page 3, line 10 of D12, in that it contains a dietary fibre comprising at least 30 wt% of oligosaccharides having a chain length of 3 to 10 anhydromonose units.

4.1.3 As furthermore set out above when discussing sufficiency of disclosure, it is credible that the dietary fibres to be used according to claim 1 lead to the claimed therapeutic effect, i.e. the treatment or reduction of the incidence of muscle wasting and/or chronic muscle wasting and/or sarcopenia. The same effect is achieved in D12 by the whey protein (page 3, lines 16 to 21 and page 4, line 28 to page 5, line 4). The objective technical problem is therefore the provision of the claimed therapeutic effect by a different means.

4.1.4 There is no indication at all in D12 that this therapeutic effect can be achieved by the use of a dietary fibre as defined in claim 1. On the contrary, D12 discloses that it is the whey protein rather than the optional dietary fibres disclosed therein that is responsible for obtaining this effect (see the above-quoted passages on pages 3 to 5 of D12). Therefore, if anything, D12 teaches away from the claimed alternative. The subject-matter of claim 1 (and by the same token of claims 2 to 11) is thus inventive in view of D12.

4.1.5 The opponent argued that the objective technical problem was the provision of an alternative composition. The composition of D12 was known to prevent muscle wasting. In the absence of any particular effect, no motivation was needed to select the optional dietary fibres disclosed in D12 to arrive at the subject-matter of claim 1.

The board acknowledges that the objective technical problem might indeed be the provision of an alternative composition if claim 1 was a "normal" product claim directed to a substance or composition. However, claim 1 is formulated as a further medical use claim directed to a substance or composition for use in a therapeutic application. As set out in G 2/08 (point 5.10.9), non-obviousness of such a claim "is not derived from the substance or composition as such" (in the present case the oligosaccharide-containing soluble dietary fibre) "but from the purpose the claimed substance or composition is related to, namely from its intended therapeutic use" (in the present case the treatment or reduction of the incidence of muscle wasting and/or chronic muscle wasting and/or sarcopenia). In analogy to non-medical use claims, it

is the causal relationship between the substance or composition on the one hand and the effect achieved therewith on the other hand that constitutes a functional feature of the claim (see G 2/88, point 10.3). This causal relationship constitutes the claim's contribution over the prior art. Accordingly, the inventive step of such a claim hinges on the question as to whether this causal relationship, and not just the substance or composition as defined in the claim, is obvious. Hence, in the present case, the objective technical problem is not just the addition of a further arbitrary substance (fibre) to the composition of D12, which already provides the therapeutic effect due to the presence of whey protein. On the contrary, the objective technical problem is the provision of this causal relationship, i.e. the achievement of the claimed therapeutic effect with a different means, namely the specified fibres of claim 1. It is this problem that has been used in the problem-and-solution approach above (see point 4.1.3).

4.2 In an alternative approach, the opponent used D15 as the closest prior art to attack the subject-matter of claim 1 under inventive step.

4.2.1 D15 is a review article on molecular mechanisms of muscle atrophy. It is thus in the same technical area as the opposed patent and therefore, as argued by the opponent, can be considered to represent the closest prior art.

D15 discloses that the transcription factor NF-κB induces muscle atrophy (last paragraph on the left-hand column of page 908), that salicylate can be used to treat NF-κB induced muscle atrophy and that high doses

of salicylate are not well tolerated in humans (last paragraph of D15).

4.2.2 The subject-matter of claim 1 differs from D15 in that instead of salicylate, oligosaccharides having a chain length of 3 to 10 anhydromonose units are used to obtain the claimed therapeutic effect.

4.2.3 In the same way as for D12, the objective technical problem is the provision of an alternative means to obtain the claimed therapeutic effect.

4.2.4 There is no indication at all in D15 that this can be achieved by the dietary fibres as defined in claim 1.

The opponent argued in this respect that the use of dietary fibres as defined in claim 1 was obvious in view of D22. The opponent in particular explained that the skilled person learning from D15 that NF-κB induces muscle atrophy and that this could be treated by salicylate, of which high doses were not well tolerated by humans, would look for an alternative means to reduce the NF-κB level. From D22 (first paragraph on the left-hand column of page 799), the skilled person would be taught that butyrate inhibits the activity of NF-κB, and that butyrate levels in the gut could be influenced by dietary fibres (last paragraph of D22). Since it was known from e.g. D9 or D23 that oligosaccharides such as galactooligosaccharides led to an increased intestinal production of butyrate, it would have been obvious to use these galactooligosaccharides instead of the salicylate in D15 to treat NF-κB induced muscle atrophy.

The board does not agree. Firstly, the skilled person starting from D15 and looking for an alternative means

to provide the claimed therapeutic effect would not have considered D22, since this document is not related at all to muscle wasting but focuses on drugs preventing excess inflammation in the gut (see e.g. the introductory paragraph on page 798). Secondly, even combining D15 with D22, the skilled person would not arrive at the claimed subject-matter since the dietary fibres in D22 are not as defined in claim 1. An additional step would be needed, namely to look into the further documents D9 or D23 and to select the fibres disclosed therein. These documents are however in a field completely different from muscle wasting, namely the effect of galactooligosaccharides on specific forms of cancer (D9) and the stimulation and growth of bifidobacteria in the colon (D23). There is no motivation at all in the two documents D9 and D23 to use the dietary fibres disclosed therein in order to obtain the claimed therapeutic effect. Therefore, arguing that the skilled person would combine the various aspects of D15, D22 and D9 or D23 in such a way as to arrive at the subject-matter of claim 1 is based on hindsight. The subject-matter of this claim is therefore inventive in view of D15 as the closest prior art.

4.3 The opponent furthermore argued that the subject-matter of claims 12 and 13 was not inventive in view of D12.

4.3.1 The food supplement and carbohydrate composition of these claims differ from the composition disclosed on pages 2 and 3 of D12 *inter alia* by the same feature as claim 1, namely the specific dietary fibres. Therefore, in the same way as for claim 1, the objective technical problem is the provision of an alternative means to achieve the claimed therapeutic effect and, for the reasons given above, the claimed alternative is not

obvious. Therefore, the subject-matter of claims 12 and 13 is inventive in view of D12.

4.4 In the written proceedings, the opponent argued that the subject-matter of claims 12 and 13 was obvious in view of D9 as the closest prior art. As set out above, D9 is however in a technical area entirely different from that of the patent. Therefore, D9 cannot be considered to represent the closest prior art.

4.5 The opponent argued lastly that the subject-matter of claims 14 and 15 was obvious in view of D6 as the closest prior art

4.5.1 Like the opposed patent, D6 concerns nutritional compositions for the prevention and treatment of cachexia in cancer patients (page 1, lines 1 to 2 and page 7, lines 1 to 2). It stresses specifically the issue of muscle wasting (page 2, lines 1 to 3). Therefore, in line with the opponent's argument, D6 can be considered to represent the closest prior art.

D6 teaches the use of a composition comprising an oil blend containing ω-6 and ω-3 fatty acids, branched chain amino acids and an antioxidant component to prevent or treat cachexia and the muscle wasting associated therewith (page 4, lines 14 to 23 and claim 1 in conjunction with page 2, lines 1 to 3).

The supplement and composition of claims 14 and 15 differ from those of D6 *inter alia* in that dietary fibres of a specific chain length are present.

In the same way as for D12 and D15, the objective technical problem is the provision of an alternative means to provide the claimed therapeutic effect.

This problem is solved by the use of a dietary fibre as defined in claims 14 and 15 (by way of back-reference to claims 1 to 4).

The only place where a dietary fibre is disclosed in D6 is example IV (fructooligosaccharides FOS). However, there is no information in D6 why these fructooligosaccharides have been included in the composition of this example. In fact, what is disclosed in D6 to be effective to treat cachexia (and the muscle wasting linked to it) is the combination of the fatty acid blend, the nitrogen source and the antioxidant (see page 4, lines 14 to 23 and claim 1 of D6).

The skilled person looking for an alternative means to obtain the claimed therapeutic effect would thus not have had any motivation to use the fructooligosaccharides disclosed in D6, let alone fructooligosaccharides as covered by the definition of the dietary fibres in claims 14 and 15. Therefore, the subject-matter of these claims is inventive in view of D6.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The patent is maintained unamended.

The Registrar: The Chairman:

D. Hampe W. Sieber

Decision electronically authenticated