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Datasheet for the decision of 13 May 2024

Case Number: T 0166/22 - 3.3.07

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Language of the proceedings: EN

Title of invention:
NON-MEDICAL INCREASE OR MAINTENANCE OF BODY WEIGHT OF A MAMMAL

Patent Proprietor:
N.V. Nutricia

Opponent:
Société des Produits Nestlé S.A.

Headword:
Body weight in the elderly/NUTRICIA

Relevant legal provisions:
EPC Art. 100(b)

Keyword:
Sufficiency of disclosure - (no)

Decisions cited:
G 0002/21

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Case Number: T 0166/22 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 13 May 2024

Appellant: (Opponent)	Société des Produits Nestlé S.A. Entre-deux-Villes 1800 Vevey (CH)
Representative:	Rupp, Christian Mitscherlich PartmbB Patent- und Rechtsanwälte Karlstraße 7 80333 München (DE)
Respondent: (Patent Proprietor)	N.V. Nutricia Eerste Stationsstraat 186 2712 HM Zoetermeer (NL)
Representative:	V.O. P.O. Box 87930 2508 DH Den Haag (NL)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 10 January 2022 rejecting the opposition filed against European patent No. 2658391 pursuant to Article 101(2) EPC**

Composition of the Board:

Chairwoman	L. Basterreix
Members:	J. Molina de Alba
	M. Steendijk

Summary of Facts and Submissions

I. The decision under appeal is the opposition division's decision rejecting the opposition filed against European patent No. 2 658 391.

The patent had been granted with 23 claims. Independent claims 1 and 6 read as follows:

"*1. Non-medical use of at least four components selected from the group of: (i) nucleoside equivalents selected from the group of uridine, deoxyuridine, uridine phosphates (UMP, dUMP, UDP, UTP), nucleobase uracil and acylated uridine, (ii) n-3 polyunsaturated fatty acids selected from the group of DHA, DPA and EPA, (iii) vitamins B selected from the group of vitamin B6, vitamin B9 and vitamin B12 (iv) phospholipids, (v) antioxidants selected from the group of vitamin C, vitamin E and selenium, and (vi) cholines - with the proviso that at least one (i) nucleoside equivalent, at least one (ii) n-3 polyunsaturated fatty acid selected from the group of DHA, DPA and EPA, at least one (iii) vitamin B selected from the group of vitamin B6, vitamin B9 and vitamin B12, and at least one (iv) phospholipid is present - for increasing or maintaining the body weight of a mammal, which mammal is an elderly human above 65 years of age.*"

6. "*A combination of least four components selected from the group of: (i) nucleoside equivalents selected from the group of uridine, deoxyuridine, uridine phosphates (UMP, dUMP, UDP, UTP), nucleobase uracil and acylated uridine, (ii) n-3 polyunsaturated fatty acids*

selected from the group of DHA, DPA and EPA, (iii) vitamins B selected from the group of vitamin B6, vitamin B9 and vitamin B12 (iv) phospholipids, (v) antioxidants selected from the group of vitamin C, vitamin E and selenium, and (vi) cholines - with the proviso that at least one (i) nucleoside equivalent, at least one (ii) n-3 polyunsaturated fatty acid selected from the group of DHA, DPA and EPA, at least one (iii) vitamin B selected from the group of vitamin B6, vitamin B9 and vitamin B12, an [sic] *at least one (iv) phospholipid is present - for use in therapeutically increasing or maintaining the body weight of a mammal, and which mammal is an elderly human above 65 years of age.*"

II. The present decision refers to the following documents:

D18 G.F. Irving et al., JAGS, 57(1), 2009, 11-17

D19 Overview of the mouse strain APP/PS1 retrieved from the website of The Jackson Laboratory in 2021 (https://www.jax.org.strain/005864)

D24 P.J.G.H. Kamphuis et al., The Journal of Nutrition, Health & Aging, 15(8), 2001, 672-676

III. In the decision under appeal, the opposition division held, among other things, that the subject-matter claimed by the patent as granted was sufficiently disclosed.

IV. The opponent (appellant) filed an appeal against the decision. It requested that the decision be set aside and the patent be revoked in its entirety.

V. With its reply to the statement of grounds of appeal, the respondent filed 12 sets of claims as auxiliary requests 1 to 12. Subsequently, with a letter dated

28 February 2023, the respondent replaced auxiliary requests 9 to 12 with new auxiliary requests 9 to 12 and filed additional sets of claims as auxiliary requests 13 to 38.

VI. The board scheduled oral proceedings, in line with the parties' requests, and set out its preliminary opinion on the case.

VII. In response to the board's preliminary opinion, the respondent filed three additional sets of claims as auxiliary requests 39 to 41 and document D24.

VIII. Oral proceedings were held before the board by videoconference. During the oral proceedings, the respondent withdrew all of its auxiliary requests.

At the end of the oral proceedings, the board announced its decision.

IX. The appellant's arguments relevant to the present decision can be summarised as follows.

The application as filed did not make the effect on elderly humans defined in claims 1 and 6 credible. The mice tested in Examples 3, 4, 9 and 10 were not suitable for modelling weight development in elderly humans since they were at a different stage of life and weight development. The mice were tested between three and six months of age, which meant that they were adults, a stage of life in which body weight continued to increase. Even though the APP/PS1 mice tested in Examples 3 and 4 were aged compared with wild-type mice, they were still adults and were still gaining weight. Signs of ageing in APP/PS1 mice were first detected after six months of age, and a decrease in

body weight was first observed at 14 months of age (D19: page 4, "General Note" and page 8, "growth/size/ body region phenotype"). In contrast, elderliness was a stage of life characterised by a decline in body weight. This was particularly the case for elderly humans having a condition associated with significant weight loss, such as sarcopenia or physiological anorexia of ageing. As the mouse models tested in the application as filed did not have the physiological state of the population they were intended to represent, no conclusions could be drawn. The increase in body weight shown in adult mice in Examples 3, 4, 9 and 10 could not be expected to translate in elderly humans into a weight gain sufficient to fully compensate for the weight loss caused by ageing and associated conditions. Taking D18 into consideration did not change this conclusion.

Post-published evidence in D24 could not be used to remedy the lack of sufficiency of the application as filed (G 2/21).

X. The respondent's arguments relevant to the present decision can be summarised as follows.

The effect in claims 1 and 6 was credible from the application as filed. The tests in Examples 3 and 4 were conducted in APP/PS1 mice, which was an animal model for ageing. They showed that mice fed with a diet enriched with a combination of components according to the invention gained considerably more weight than control mice fed with an isocaloric diet. Examples 9 and 10 confirmed this effect in a normal mouse model. The effect was supported by D18, which showed that elderly humans receiving DHA and EPA as a food supplement for six months gained weight. Elderly

APP/PS1 mice could not be used as a model because they developed symptoms or died. The effect shown in the application as filed was confirmed by the clinical study in post-published document D24.

The appellant had not raised any serious doubts substantiated by verifiable facts as to the ability of the combinations of the invention to compensate for decreasing body weight in elderly humans. Even though the tests in the application were not carried out on elderly mice, it was plausible that the effect shown also arose in elderly humans. The loss of body weight caused by ageing was gradual and slow, and the physiological state of adult and elderly humans was not substantially different. In view of the results in Examples 3, 4, 9 and 10, which showed a significant positive effect on metabolism, it was plausible that the loss of body weight in elderly humans could be fully compensated for by the combination of components according to the invention.

XI. The parties' final requests relevant to the present decision were as follows.

- 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 appeal be dismissed and that the patent be maintained as granted.

Reasons for the Decision

Sufficiency of disclosure (Article 100(b) EPC)

1. Independent claims 1 and 6 as granted are directed to the use of a combination of at least four components for maintaining or increasing body weight in an elderly human above 65 years of age.

2. The parties did not dispute the common general knowledge that, in humans, body weight generally increases with age throughout adulthood, peaking at around 65 years of age, when elderliness begins. During elderliness, body weight remains stable or gradually declines.

The application as filed (page 3, first paragraph) teaches that weight loss in the elderly is associated with decreasing activity and an age-associated decline in basal metabolic rate, neuroendocrine function, immune function and taste and smell perception. Thus, body weight loss in the elderly results from a complex combination of factors specific to elderliness. In addition, involuntary weight loss above 65 years of age is strongly associated with impaired mood and low stamina. The application teaches (page 2, fourth paragraph to page 3, first line) that in part of the elderly human population, body weight loss may occur more quickly or for a longer period of time and reach a critical level. This abnormally large weight loss is in most cases associated with concurrent health problems, such as sarcopenia, and may result in frailty.

3. Examples 3, 4, 9 and 10 of the application as filed contain evidence related to the effect in claims 1 and 6 as granted.

In Examples 3 and 4, three-month-old APP/PS1 mice were fed with a diet enriched with a combination of components according to claims 1 and 6 for three months. Control mice received a non-enriched isocaloric diet. At the end of the tests, the mice that received an enriched diet showed a greater increase in body weight than control mice, namely 20% vs 14% in Example 3 and 25% vs 14% in Example 4.

Examples 9 and 10 disclose the same tests as Examples 3 and 4 but on unspecified mice instead of APP/PS1 mice. At the end of the tests, the mice that received an enriched diet also showed a greater increase in body weight than control mice, namely 17.8% vs 11.5% in Example 9 and 22% vs 11.5% in Example 10.

The parties did not dispute that the mice tested in Examples 3, 4, 9 and 10 were adult mice instead of elderly mice. This is apparent from the fact that the control mice experienced a considerable increase in body weight in all the tests.

4. It was common ground that age-related body weight development is parallel in mice and humans. The matter of dispute between the parties arises from the fact that the application as filed provides evidence of a body weight increase in adult mice while the effect required by claims 1 and 6 is to stop or reverse body weight decline in elderly humans.

Considering the differences in body weight development between adult and elderly humans and the age-related

factors that produce these differences, it may be asked whether an adult mouse model is suitable for showing whether a composition can stop or reverse the weight loss typical of healthy elderly humans (claim 1) or elderly humans with an undesirably low body weight or at risk of an having undesirably low body weight (claim 6). For the reasons set out below, the board has serious doubts that this is the case.

4.1 It is a basic principle of animal modelling that the animal should have the essential characteristics of the humans they are modelling, which in this case is the gradual decline of body weight typical of elderly humans. As explained above, this principle was not satisfied by the mice tested in Examples 3, 4, 9 and 10, which were at a stage of life in which their body weight was increasing. There is also no evidence on file that, on the priority date, the mice tested in Examples 3, 4, 9 and 10 constituted established or generally recognised models for body weight development in elderly humans.

4.2 In this respect, the respondent referred to D19, which is an extract from the website of a laboratory that supplies APP/PS1 mice. D19 was retrieved in 2021 and therefore does not belong to the prior art. However, the parties did not dispute that the content of D19 was known on the priority date of the application. The board saw no reason to decide otherwise.

The first page of D19 states that APP/PS1 mice contain two mutations associated with early-onset Alzheimer's disease and that they may be useful in studying neurological disorders of the brain, specifically Alzheimer's disease, amyloid plaque formation and ageing. According to the respondent, APP/PS1 mice are a

model for ageing because they are aged compared with wild-type mice of the same age. Therefore, the evidence on APP/PS1 mice in Examples 3 and 4 of the application was transposable to elderly humans.

This argument is not convincing. The APP/PS1 mice tested in Examples 3 and 4 were at a stage of life in which their body weight was increasing. Even though they were physiologically more aged than wild-type mice of the same age, their body weight development was still that of an adult rather than an elderly mouse. At the end of the tests in Examples 3 and 4, the mice were six months old. As noted by the appellant, D19 teaches that APP/PS1 mice start developing signs of ageing by six or seven months of age, with decreased body weight being observed at 14 months (page 4, entry "General Note"; page 8, section "growth/size/body region phenotype"). Therefore, even if APP/PS1 mice could be an accepted model for certain aspects of ageing, the board has doubts about their suitability for mimicking the extent of body weight changes in elderly humans.

4.3 The respondent also argued that increasing or maintaining body weight was a process that may occur at any age, so it could be detected in any mice independently of their age; there were substantially no physiological differences between adult and elderly humans. Furthermore, as the increase in body weight observed in Examples 3, 4, 9 and 10 for the treated mice was 30 to 50% greater than for the control mice, it was credible that the metabolic response in the elderly would be sufficient to fully counter their weight loss.

The board does not dispute that body weight is managed at all ages and that Examples 3, 4, 9 and 10

demonstrate a significant metabolic effect of the combination of components in claims 1 and 6 as granted. However, body weight is not managed in the same way in adult and elderly humans. As taught in the application as filed (see point 2 above), body weight loss in the elderly results from a complex combination of factors that are specific to elderliness. These factors include an age-associated decline in basal metabolic rate and neuroendocrine function. Therefore, an elderly human cannot be expected to respond to the combination of components of the invention in the same way and to the same extent as an adult.

It may be plausible that the combination of components of the invention produces some positive metabolic effect in the elderly. However, claims 1 and 6 require not only that there is some effect but also that this effect is quantitatively sufficient to fully counter and even reverse the age-related tendency of the elderly to lose weight. In the board's view, the skilled person would not assume that such an effect was credible from the evidence in the application as filed. This is even truer for elderly humans having a condition associated with significant weight loss, such as sarcopenia or physiological anorexia of ageing.

4.4 The respondent also referred to D18, which allegedly showed that elderly Alzheimer's patients who received a diet supplemented with DHA and EPA for six months gained weight. As DHA and EPA belong to component (ii) of claims 1 and 6, the skilled person would conclude that the combination of components in claims 1 and 6 generally increased body weight in the elderly.

It is established case law that the application must be sufficiently disclosed on the date of filing, on the

basis of application as a whole and taking into account the common general knowledge of the skilled person. D18 does not constitute common general knowledge, nor was it cited in the application as filed. Therefore, the content of D18 would not affect the skilled person's assessment of whether the claimed subject-matter was sufficiently disclosed on the filing date.

5. The board therefore concludes that there exist serious doubts substantiated by verifiable facts as to whether the combination of components in claims 1 and 6 is generally suitable for maintaining or increasing the body weight of an elderly human above 65 years of age.

In accordance with the finding of the Enlarged Board of Appeal in decision G 2/21, Reasons 77, the proof of the effect recited in claims 1 and 6 had to be provided in the application as filed. A deficiency in this respect cannot be remedied by post-published evidence. Therefore, the evidence in D24 cannot be taken into consideration.

6. As a consequence, the ground for opposition of Article 100(b) EPC prejudices the maintenance of the patent as granted.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The patent is revoked.

The Registrar: The Chairwoman:

A. Vottner L. Basterreix

Decision electronically authenticated