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Datasheet for the decision of 24 October 2023

Case Number: T 2036/21 - 3.3.09

Application Number: 08766831.5

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IPC: A23L1/29, A23L1/30, A23L1/304, A23L1/305, A61K31/14, A61K31/202, A61K31/7072

Language of the proceedings: EN

Title of invention:
FOOD COMPOSITION FOR PRODROMAL DEMENTIA PATIENTS

Patent Proprietor:
N.V. Nutricia

Opponents:
Fresenius Kabi Deutschland GmbH
Société des Produits Nestlé S.A.

Headword:
Composition for prodromal patients/NUTRITIA

Relevant legal provisions:
EPC Art. 56, 111(2)
RPBA 2020 Art. 12(4), 12(6)

Keyword:
Late-filed document - admitted (yes)
Auxiliary requst 4: inventive step - (yes)
Convincing evidence that the claimed therapeutic effect is achieved - (yes)
Application of the principle of free evaluation of the evidence - (yes)
Binding effect of earlier decision of the Board when the facts are not the same - (no)

Decisions cited:
G 0003/97, G 0001/03, G 0001/12, G 0002/21, T 0694/16, T 2717/17

Catchword:

According to established case law, the principle of the free evaluation of evidence applies universally in proceedings before the EPO when assessing any means of evidence. There is no reason for diverging from this principle when deciding whether a compound or composition induces a therapeutic effect. The EPO deciding body decides on this issue in the light of its conviction, taking into account the evidence available in the proceedings and on the footing that one set of facts is more likely to be true than the other.

This approach does not correspond to that applied in other contexts, where conclusions are only drawn if there is a high grade of statistical confidence. In proceedings before the EPO it is not a prerequisite to perform a statistical analysis of the results and to determine a specific confidence interval, as it is most often required in biomedical research and by health authorities granting marketing authorisations for medicinal products.

(See reasons, points No. 3.25 to 3.29)

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Case Number: T 2036/21 - 3.3.09

D E C I S I O N
of Technical Board of Appeal 3.3.09
of 24 October 2023

Appellant: (Opponent 2)	Société des Produits Nestlé S.A. Entre-deux-Villes 1800 Vevey (CH)
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Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 11 October 2021 concerning maintenance of the European Patent No. 2170104 in amended form.**

Composition of the Board:

Chairman	A. Haderlein
Members:	A. Veronese
	F. Blumer

Summary of Facts and Submissions

I. The appeal was filed by opponent 2 (appellant) against the opposition division's decision posted on 11 October 2021, finding that the European patent as amended according to auxiliary request 4 met the requirements of the EPC. The subject-matter of this request was found to meet the requirements of sufficiency of disclosure and novelty in the earlier decision T 694/16 of the Board of Appeal.

II. The two opponents had originally requested revocation of the patent in its entirety on the grounds pursuant to Article 100(a) EPC (lack of novelty and lack of inventive step) and Article 100(b) and 100(c) EPC.

III. Claim 1 of auxiliary request 4 reads:

"*1. Composition comprising (a) one or more ω-3 fatty acids selected from DHA, DPA and EPA, (b) uridine selected from the group of uridine, deoxyuridine, uridine phosphates, uracil and acylated uridine derivatives, and (c) choline and/or phosphatidylcholine, wherein the composition further includes vitamin B12 and folate, for use in the prevention or delay of the onset of dementia in a person having characteristics of a prodromal dementia patient, wherein said characteristics comprise at least:*

- *a level of more than 350 ng Total-tau per litre cerebrospinal fluid (CSF); and*
- *a weight ratio of abeta-42/Phospho-tau-181 of less than 6.5 in CSF.*"

IV. The documents submitted during the earlier proceedings included:

D6: O. Hansson et al., The Lancet Neurology, vol. 5, 2006, pg. 228-234

D7: D. Praticò et al., Archives of Neurology, vol. 59, 2002, pg. 972-976

D8: WO 2006/127620 A2

D9: R.J. Wurtman et al., Brain Research, vol. 1088(1), 2006, pg. 83-92

D10: WO 03/041701 A2

D20: E. Reynolds, The Lancet Neurology, vol. 5(11), 2006, pg. 949-960

D23: US 2003/0114415

D27: WO 2007/008586

D29: Public release: 10 March 2016, "Nutritional drink can help to conserve memory in case of prodromal Alzheimer's disease" (LipiDiDiet clinical study), Saarland University

D31: H. Soininen et al., The Lancet Neurology, vol. 16, 2017, pg. 965-975

D31a: Supplementary Annex to D31

D43: H.C. Diener, Fortschritte der Medizin, Fortbildung, Kritisch Gelesen, 2018, vol. 8(160), pg. 31

D44: J. Cummings et al., Journal of Alzheimer's Disease, vol. 55, 2017, pg. 1131-1139

D47: Soininen et al., Alzheimer's Dementia, 2020, pg. 1-12

D48: Expert declaration by L.M. Broersen, filed by the respondent with its reply to the statement setting out the grounds of appeal

V. In the decision under appeal, the opposition division found that the claimed subject-matter involved an inventive step, arguing *inter alia* that:

- D31, D31a and D47 were relevant to the discussion of inventive step and were to be admitted into the opposition proceedings

- D27 was the closest prior art; the claimed subject-matter differed from the teaching of this document in the specific composition claimed and in the specific target group

- example 4 of the patent and the studies in D29, D31 and D47 showed that the claimed treatment was effective

- starting from D27, the underlying problem was the provision of a composition for delaying the onset of dementia in the prodromal dementia patient defined in claim 1

- neither D27 nor the other cited documents provided a pointer to the claimed solution; the same conclusion was drawn starting from D10 or D23

VI. With its reply to the statement setting out the grounds of appeal, the proprietor (respondent) filed D48, a declaration from a technical expert describing additional experiments.

VII. The opponent's/appellant's arguments which are relevant to the decision can be summarised as follows.

- D48 should not be admitted.

- The opposition division had correctly admitted D31, D31a and D47 but did not take proper account of their teaching.

- When assessing inventive step and formulating the technical problem, it had to be established whether the purported effect was achieved and whether the problem was solved across the whole range claimed. This did not require the issue of lack of sufficiency to be reopened.

- D29, D31 and D47 stated explicitly that the claimed treatment was not effective for preventing or delaying the onset of dementia; there were no differences between the active and the control group, in particular in the incidence and time of onset of clinical dementia; the positive results mentioned in these documents did not relate to delaying or preventing the onset of dementia.

- D10 was the closest prior art; the claimed subject-matter differed from the teaching of this document in that the composition contained uridine and in that a patient group identified by certain markers was treated; in view of these differences there were two separate problems: 1) providing an alternative composition and 2) finding an alternative patient group; the solutions to these problems were obvious in view, e.g. of D9 and D6.

- The same reasoning applied starting from D8, D23 or D27 as closest prior art, and combining the teaching of these documents with that of e.g. D6, D7, D10, D20 and D33.

VIII. The proprietor's/respondent's arguments which are relevant to the decision may be summarised as follows.

- The issue of whether the claimed effect was achieved had already been decided by the board in its previous decision T 694/16, when dealing with sufficiency of disclosure. Reopening this issue when discussing inventive step inevitably resulted in reopening the issue of sufficiency of disclosure, which was already settled by the board. This should not be allowed. If this issue was reopened the case had to be remitted.

- The appellant had misinterpreted the teaching of D29, D31, and D47, picking out passages which did not truly represent the outcome of the clinical trial described therein; these documents made it credible that the claimed therapeutic effect was achieved; this was confirmed by D44 and D48.

- D6 or D7, which focused on prodromal patients identified by relevant biomarkers were the closest prior art; starting from D6 or D7, which did not disclose any therapeutic treatment, the problem was the provision of a personalised treatment for prodromal patients; the claimed solution was not obvious because the skilled person would not have reasonably expected the claimed composition to be effective in these patients.

- The same conclusion could be drawn starting from D8, D10, D23 or D27 as the closest prior art; in particular, starting from D27, the claimed subject-matter differed both in terms of the claimed ingredients and the target group; only by applying

hindsight could the claimed subject-matter be considered obvious.

The requests

IX. Opponent 2 (appellant) requested that the decision under appeal be set aside and that the patent be revoked.

X. The patent proprietor (respondent) requested that the appeal be dismissed or, alternatively, that the patent be maintained on the basis of auxiliary request 5 as filed during the opposition proceedings, by letter dated 11 September 2020.

Reasons for the Decision

1. *Admittance of D48*

The appellant requested that D48 not be admitted into the appeal proceedings, on the grounds that it was filed late and was not *prima facie* relevant. The board does not agree, because:

- D48 was filed at the very first stage of the appeal proceedings, namely with the reply to the appellant's statement of grounds of appeal

- D48 addresses the objection of lack of inventive step starting from D27 as closest prior art

- numerous documents were filed as "potential" closest prior art documents during the opposition proceedings, and only at a late stage did the discussion crystallise around D27

- new facts, e.g. D31, were submitted at a late stage, after remittal, throwing doubt on whether the therapeutic effect could be achieved

- the tests in D48 complement those described in the opposed patent and are *prima facie* relevant, because they show the importance of combining ω-3 fatty acids with the other claimed agents

- the filing of D48 is not detrimental to the economy of the proceedings

For these reasons, the board considers that D48 has to be admitted into the appeal proceedings (Articles 12(4) and 12(6) RPBA 2020).

Auxiliary request 4

2. Auxiliary request 4 is the only relevant request.

3. *Inventive step*

The claimed invention

3.1 Claim 1 of auxiliary request 4 is drafted in accordance with Article 54(5) EPC. It relates to a composition comprising ω-3 fatty acids, uridine derivatives, a methyl donor and other ingredients, for use in the prevention or delay of the onset of dementia in a person having specific "characteristics" of a prodromal dementia patient. These characteristics, hereinafter "biomarkers", include at least: more than 350 ng/l Total-tau and a weight ratio of abeta-42/Phospho-tau-181 of less than 6.5 in the cerebrospinal fluid.

3.2 Dementia is a disease induced by a progressive degeneration of the brain cells affecting, *inter alia*, the hippocampus. The disease is accompanied by a gradual decrease in the ability to think and remember to such an extent that it interferes with a person's daily functioning. The pathogenic process of dementia is believed to start long, even decades, before the clinical onset of the disease. Alzheimer's disease is the most common form of dementia.

3.3 As explained in the opposed patent, "prodromal (dementia) patients" are subjects who, although not yet suffering from clinical dementia, are on the way towards developing it. The invention aims at identifying these patients and at treating them with the claimed composition, so that the clinical onset of the disease can be delayed or even prevented: paragraphs [0001], [0007], and [0012] to [0015].

3.4 Paragraphs [0016] to [0018] teach that "prodromal patients" display specific biomarkers, and in particular the two indicated in claim 1. These biomarkers allow a distinction between prodromal patients and other patients presenting symptoms of mild cognitive impairment who are not prodromal and will not necessarily develop dementia.

3.5 The gist of the invention is to provide a "personalised treatment" targeting prodromal patients identified by the biomarkers specified in claim 1, who are more likely to benefit from the treatment, while sparing those that would not benefit from it.

Closest prior art

3.6 The opposition division found that D27 was the closest prior art, because it disclosed compositions comprising ω-3 polyunsaturated fatty acids (PUFAs) for delaying the onset of dementia, and markers for identifying subjects likely to respond to PUFA supplementation.

3.7 The appellant primarily considered D10 to be the closest prior art and in the alternative D8, D23 or D27. The respondent considered D6 or in the alternative D7 to be the closest prior art.

3.8 The board is of the opinion that, as decided by the opposition division, D27 is the closest prior art for assessing inventive step. D27 focuses specifically on the treatment and prevention of dementia and pre-dementia and discloses, in particular:

- compositions comprising ω-3 PUFAs, such as DHA and EPA and their use for treating and preventing dementia and pre-dementia and for delaying the onset of dementia in an individual (page 1, lines 5 to 7, page 4, lines 3 to 22, claims 1, 49 and 63)

- methods for identifying and targeting subjects susceptible to dementia and pre-dementia, which include measuring biomarkers including, *inter alia*, tau protein and phosphorylated tau protein (page 4, lines 10 to 16, page 20, lines 24 to 30, page 23, lines 1 to 26, pages 47 and 48, claims 8 and 21)

3.9 D27 is the only document, among those proposed as the starting point by the parties, which mentions a therapy aimed at preventing dementia and pre-dementia in a group of subjects identified using biomarkers.

3.10 Concerning the other documents cited by the parties as starting points to assess inventive step, it is noted that:

- D6 describes biomarkers, including those mentioned in claim 1, for identifying patients who are at an early stage of Alzheimer's disease. However, D6 does not mention any specific composition for treating these patients, let alone the one defined in claim 1; D7 identifies different biomarkers, and its teaching does not go beyond that of D6.

- D10 discloses a composition which differs from the claimed one in that uridine is not included (table 1). The composition is used to increase the sensitivity of receptors and to treat and prevent a variety of diseases including epilepsy, ADHD, sleep disorders, schizophrenia, Parkinson's disease, trauma, stroke and dementia (page 1, lines 4 and 5, page 10, lines 13 to 17). However, D10 mentions neither prodromal dementia nor biomarkers for identifying dementia patients needing treatment.

- D8 discloses a composition comprising an ω-3 PUFA such as DHA, which may also contain uridine or a choline, and its use for increasing the production of phospholipids (claims 1, 3, 5 and 6). The composition can be used to treat memory impairment, memory loss and Alzheimer's disease, possibly at an early stage (claims 13 and 14, paragraphs [0079] and [0080]); however, D8 does not mention vitamin B12 and folate; prodromal dementia and biomarkers for identifying dementia patients needing treatment are not mentioned either.

- D23 discloses a composition comprising citicoline and, possibly, also DHA and choline, for treating Alzheimer's disease and mild cognitive impairment (paragraphs [0027], [0028], [0063], claims 1, 3, 7 and 9); however D23 does not mention folate and vitamin B12 is only mentioned in a section relating to the prior art; prodromal dementia and biomarkers for identifying dementia patients needing treatment are not mentioned either.

3.11 Since D27 is the only document which describes, like the opposed patent, a therapy for preventing dementia and pre-dementia in subjects identified using biomarkers and the composition used for the treatment includes, like that claimed, ω-3 PUFAs, this document is the closest prior art.

Distinguishing features

3.12 The claimed subject-matter differs from the teaching of D27 in that:

- the claimed ω-3 PUFAs are combined with a uridine compound, choline or phosphatidylcholine, folate and vitamin B12; D27 does not disclose any composition comprising these agents, in addition to the ω-3 PUFAs

- specific biomarkers are identified, which are not disclosed in D27: this document refers generically to tau and phosphorylated tau protein, but not in the cerebrospinal fluid (CSF), let alone in the claimed amounts; the specific phosphorylation site in the tau protein is not mentioned either

Technical effect; discussion on the basis of new facts of issues settled by the board in earlier decision

3.13 The present appeal was filed against the opposition division's decision ensuing after remittal of the case by the board in decision T 694/16. The appellant argued that D31 and D47, filed after that remittal, provided evidence that the claimed composition neither prevented nor delayed the onset of dementia at the prodromal stage. No therapeutic effect was achieved in prodromal patients. In its opinion, this was relevant to formulating the technical problem underlying the invention and for assessing inventive step.

3.14 The respondent countered that in its earlier decision the board had already decided that the claimed composition was suitable for inducing the claimed effect and that the requirement of sufficiency of disclosure was fulfilled. According to G 1/03, point 2.5.2, the issue of whether an effect specified in a claim was achieved was relevant to assessing sufficiency of disclosure, rather than inventive step. Therefore, the appellant's arguments reopened issues which had already been settled by the board. The objections based on D31 and D47 should thus not be admitted.

3.15 The board does not agree with the respondent. In its earlier decision T 694/16, after dealing with the issues of sufficiency of disclosure and novelty, the board remitted the case to the opposition division for further prosecution on the basis of current auxiliary request 4.

3.16 The European Patent Convention, and in particular Article 111(2) EPC, does not preclude the opposition

division from taking into account facts which were not at the disposal of the board remitting a case for further prosecution. Furthermore, although the issue of whether an effect specified in the claim is achieved is relevant to assessing sufficiency of disclosure, in the present case it may also have an impact on how the problem is formulated when assessing inventive step. The appellant's arguments based on D31 and D47 have thus to be taken into account in the context of its objection of lack of inventive step.

The LipiDiDiet trial described in D31 and D47

3.17 D31 and D47 relate to the clinical trial "LipiDiDiet". The trial investigated the effects of Fortasyn Connect (Souvenaid), a composition according to claim 1, on patients affected by prodromal Alzheimer's disease expressing the biomarkers of claim 1.

3.18 The appellant drew attention to the following passages of D31 and D47:

- "*During the 24-month trial period 59 (37%) participants in the control group and 62 (41%) in the active group were diagnosed with dementia (p=0.642, Fisher's exact test)*" (D31, page 971, left-hand column)

- "*No significant difference was found between groups for the NTB primary endpoint in the mITT analysis or on conversion to dementia*" (D31, page 972, right-hand column)

- "*During the trial, no overall difference was observed between active and control groups in the number of participants diagnosed with dementia*

over 36 months (66 [43.1%] and 70 [44.3%], respectively) or in the time to dementia using Kaplan-Meier analysis (Figure S2B)" (D47, page 5, passage bridging left- and right-hand columns)

- "*Despite the clear cognitive, functional, and structural benefits observed, neither the cumulative incidence of dementia nor the mean time to dementia diagnosis were different between groups over 36 months*" (D47, page 9, left-hand column)

3.19 In its opinion, these passages explicitly taught that the tested composition neither prevented nor delayed the onset of dementia in the treated group of prodromal patients. Therefore, D31 and D47 provided clear-cut evidence that the claimed composition was not suitable for inducing the claimed therapeutic effects.

3.20 These arguments are not convincing because the message which the appellant conveys focusing on the cited passages is not a true representation of the teaching of D31 and D47. The entire content of these documents must be taken into account to understand the meaning and significance of these passages.

3.21 As already mentioned before, the "LipiDiDiet" study described in D31 and D47 was a placebo controlled clinical trial investigating the effects of Fortasyn Connect, a composition according to the invention, on cognition and other factors in prodromal Alzheimer's disease patients displaying the biomarkers of claim 1. D31 relates to the effects observed during the first 24 months, D47 over a period of 36 months.

3.22 The primary endpoint of the clinical trial was the "Neuropsychological Test Battery" (NTB). Secondary

endpoints included dementia diagnosis, "Clinical Dementia Rating-Sum of Boxes" (CDR-SB), ventricular and total brain atrophy (D47, page 3, left-hand column, section "Outcomes").

3.23 The passages of D31 and D47 cited by the appellant state that neither the cumulative incidence of dementia nor the time to dementia were significantly different between the treated group and the placebo group during the study. However, D31 and D47 also explicitly state that the LipiDiDiet study was not designed to allow conclusions to be drawn on these discrete endpoints (D31, page 973, last paragraph and D47, page 9, left-hand column, last paragraph). D47 also explains that the cognitive decline in the control group was much lower than expected, rendering the primary endpoint inadequately powered (D47, page 2, left-hand column, last paragraph and page 8, right-hand column, first paragraph). D47 furthermore explains that the tests to diagnose dementia were only clustered at major study visits (D31, page 973, first paragraph of the left-hand column). For these reasons, the time of onset of dementia could not be accurately determined in the trial.

3.24 This means that D31 and D47 do not convey to the skilled person the message that "the tested composition is unsuitable for preventing or delaying the onset of dementia in a prodromal patient", but rather that "this effect was not detected, possibly because the clinical trial was not designed and adequately powered to do so".

Standard rendering a technical effect credible

3.25 The crucial point which has to be decided is whether further evidence is available which makes it credible that the claimed composition is suitable for preventing or delaying the onset of dementia in a prodromal patient.

3.26 It is observed that, even if the tests aimed at assessing an endpoint of a clinical trial do not yield a statistically significant outcome, other results may still be taken into account to evaluate the efficacy of a treatment. In some cases, these may provide valuable information in relation to the endpoint for which no significant results were observed.

3.27 In this context, attention is drawn to the fact that proceedings before the EPO are conducted with application of the principle of free evaluation of evidence. According to this principle, the competent EPO body decides in the light of its conviction arrived at freely, taking into account the evidence available in the proceedings and on the footing that one set of facts is more likely to be true than the other (Case Law of the Boards of Appeal, 10th edition, 2022, sections III.G.4.1 and III.G.4.3 and decisions G 3/97, Reasons 5, G 1/12, Reasons 31 and G 2/21, Reasons 55).

3.28 There are no reasons not to apply this principle when deciding whether it is credible that a compound or composition induces a therapeutic effect.

3.29 It is also noted that this approach does not correspond to that applied in other contexts, where conclusions are only drawn if there is a high degree of statistical confidence. In proceedings before the EPO it is not a

prerequisite to perform a statistical analysis of the results and to determine a specific confidence interval, as is most often required in biomedical research and by health authorities granting marketing authorisations for medicinal products. As held in G 3/97, Reasons 5 "the principle of free evaluation would be contradicted by laying down firm rules of evidence defining the extent to which certain types of evidence were, or were not, convincing" (see also decision T 2717/17, Reasons 4.3.5).

Technical effects evidenced by D31 and D47

3.30 D47 teaches that the LipiDiDiet trial was primarily designed for the analysis of changes on continuous scales, such as NTB and CDR-SB and on brain atrophy, which reflect cognitive deterioration, disease status and trajectory, rather than discrete outcomes, such as the onset of dementia (D47 page 9, right-hand column last paragraph and page 8 right-hand column).

3.31 The outcome of this analysis shows that after 36 months the administration of Fortasyn Connect to prodromal dementia patients induces a significant improvement of:

- the NTB 5-item and the NTB memory domain scores, which reflect a slower deterioration in cognitive abilities (D47, discussion, page 7, passage bridging left- and right-hand columns, page 8, right-hand column and figures 2A and 2B)

- the scores of CDR-SB, which is considered to reflect real-life performance, providing a sensitive and meaningful primary clinical outcome assessment in prodromal/early Alzheimer's disease trials and an indication of disease status and

trajectory (D47, page 7, passage bridging left- and right-hand columns, page 8, right-hand column, first paragraph, figures 2C and 2D)

- a reduction of brain atrophy (D47, page 7, passage bridging left- and right-hand columns, page 8, right-hand column)

3.32 Furthermore, while acknowledging that the LipiDiDiet trial was not designed to detect changes in the incidence of dementia, the authors of D47 suggest that from the CDR-SB analysis "a stronger effect would be expected in participants at earlier stages of prodromal AD". In their opinion the CDR-SB analysis across the spectrum of MMSE values and the fewer dementia cases during the third year in the active group corroborate this hypothesis (page 9, left-hand column).

3.33 Taking into account the results of the clinical study, the authors of D47 conclude the article stating that:

"*In conclusion, the present study provides evidence for potentially altered disease trajectories supporting the positive effects of long-term multinutrient intervention in prodromal AD. Over 3 years, significant benefits were observed on cognition, function, and brain atrophy, with clinically relevant effect sizes demonstrated. Prolonged intervention resulted in a broader range of endpoints showing statistically significant differences than reported before. Such sustainable benefits lasting for 3 or more years have not been reported before for an intervention in prodromal AD. The totality of our results highlights that the benefits might be increased with early and long-term intervention.*" (page 10, right-hand column, emphasis added by the board)

3.34 The results presented in D47 and the conclusions drawn by its authors leave no doubt that Fortasyn Connect, a composition according to the invention, induces a beneficial and unprecedented effect in prodromal Alzheimer's disease patients.

3.35 As already mentioned above, Alzheimer's disease, the most common form of dementia, is induced by progressive degeneration of the brain cells causing a gradual decrease in cognitive functions. Therefore, it is credible that, as argued by the respondent, by slowing down this progressive degeneration, the onset of dementia will be delayed or even prevented in prodromal dementia patients as defined in claim 1.

3.36 The results shown in figure 2D of D47 which display the variations in the CDR-SB scores across the spectrum of MMSE values make it also credible that, as argued by the respondent, patients at the earliest stage of prodromal disease benefit the most from the treatment. The strongest difference between the treated group and the placebo groups is in fact observed in the patients scoring the highest MMSE values. These are those having the least signs of cognitive impairment. Further support for this is found in figure 1 of D44, which summarises the results of clinical studies conducted in patients suffering from dementia at different stages.

3.37 The appellant drew attention to D43, a short article commenting on the results shown in D31, and drawing negative conclusion on the outcome of the LipiDiDiet trial. However, D43 only relates to the results observed after 24 months of trial and almost two years before the publication of D47. Thus, D43 does not take

account of the results of the complete 36 month trial which are discussed above.

3.38 For these reasons, the board concludes that the results described in D47 make it credible that the claimed composition prevents or delays the onset of dementia in the patient identified in claim 1. Furthermore, that patients at the earliest stage of prodromal disease benefit the most from the treatment. These conclusions confirm the earlier finding in decision T 694/16, which was based *inter alia* on example 4 of the opposed patent and on D29.

Technical effects evidenced by D48

3.39 The board also agrees with the respondent that the tests carried out in the APP/PS1 mouse described in D48 make it credible that ω-3 fatty acids are not, alone, as effective in preventing degenerative processes associated with dementia as the claimed composition. These tests confirm the statement on page 2 of public release D29, that the single ingredients of the claimed composition are not powerful enough to translate into an effective intervention.

3.40 The appellant criticized the tests in D48, arguing that only incremental effects on neurodegeneration were measured, not the onset of dementia. Furthermore, that the mice were sacrificed at six months, although memory deficit typically only appears at ten months.

3.41 These arguments are not convincing. Dementia is a disease induced by a progressive degeneration of the brain cells. Thus, the neurodegenerative process which is already observed in young APP/PS1 mice at six months

is suitable for reproducing the processes accompanying the development of dementia in prodromal patients.

3.42 For these reasons, it is credible that a composition combining the specifically claimed ingredients is more suitable for preventing or delaying dementia in the patients defined in claim 1 than a composition comprising only ω-3 fatty acids.

Technical problem

3.43 Starting from D27 as the closest prior art, and taking into account the aforementioned technical effects, the underlying technical problem is formulated, as proposed by the respondent, as "how to provide a personalized treatment and prevent or delay the onset of dementia in the prodromal dementia group who benefit the most from intervention".

Non-obviousness of the claimed solution

3.44 The appellant considered that, starting from D27, the claimed subject-matter would have been obvious considering the teaching of D6, D7, D8, D10 and D23.

3.45 The board does not agree. The appellant's argument is based, firstly, on the assumption that the claimed composition does not induce the technical effect discussed above and furthermore that, starting from D27, two separate and unrelated technical problems underlie the claimed invention, namely: identifying an alternative patient group and providing an alternative composition. However, as already established above, these assumptions are not true.

3.46 Furthermore, neither D27, nor the other cited prior art documents suggest to the skilled person confronted with the underlying technical problem to administer the claimed composition to a patient population identified using the biomarkers specified in claim 1. In particular, none of these documents suggests maximising the therapeutic benefits of the intervention by targeting patients at the earliest stage of dementia identified by the claimed markers. Moreover, none of them suggests modifying the compositions of D27 by including the other agents listed in claim 1.

3.47 D6 and D7 describe relevant markers of Alzheimer's disease expressed in the prodromal stage. However, as far as a treatment of patients identified using these markers is concerned, these documents do not go beyond speculation. In particular, there is nothing to prompt a composition as defined in claim 1.

3.48 D8, D10 and D23 disclose compositions comprising some of the ingredients making up the claimed composition. However, these documents are completely silent with regard to the identification of a patient population using biomarkers. Furthermore, none of them discloses a composition as defined in claim 1. Thus, even if the skilled person were to have considered replacing the composition described in D27 with one of those described in these documents, they would not have arrived at the composition defined in claim 1.

3.49 For these reasons, it is concluded that the skilled person would have arrived at the claimed invention only with the benefit of hindsight. Accordingly, the subject-matter of claim 1, as well as that of the dependent claims, which is more limited in scope, involves an inventive step (Article 56 EPC).

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

H. Jenney A. Haderlein

Decision electronically authenticated