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**Datasheet for the decision
of 15 May 2019**

Case Number: T 0694/16 - 3.3.09

Application Number: 08766831.5

Publication Number: 2170104

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
Nestec S.A.

Headword:
-

Relevant legal provisions:

EPC Art. 54(2), 54(3), 54(5), 100(b)
RPBA Art. 12(4)

Keyword:

Main request: sufficiency of disclosure (no)
Auxiliary request 4: added matter (no), sufficiency of disclosure (yes), novelty (yes), priority right (yes)

Decisions cited:

G 0002/88, G 0001/03, G 0002/08, T 0019/86, T 0893/90,
T 0464/94, T 0233/96, T 0609/02, T 1399/04, T 0734/12,
T 1118/12, T 0895/13

Catchword:

If a claim is directed to a known compound or composition for use in a therapeutic method of treatment or prevention of a disease, and the claim specifies that the subject to be treated displays a clearly defined and detectable marker, which is not displayed by all subjects affected by or likely to develop that disease, then the purposive selection of the patients displaying the marker for the specified treatment is a functional feature characterising the claim.
(Points 5.1-5.21 of the Reasons)



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Case Number: T 0694/16 - 3.3.09

D E C I S I O N
of Technical Board of Appeal 3.3.09
of 15 May 2019

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Decision under appeal:

**Decision of the Opposition Division of the
European Patent Office posted on 26 January 2016
revoking European patent No. 2170104 pursuant to
Article 101(3) (b) EPC.**

Composition of the Board:

Chairman W. Sieber
Members: A. Veronese
 D. Rogers

Summary of Facts and Submissions

- I. The appeal was filed by the proprietor against the decision of the opposition division to revoke European patent No. 2 170 104.
- II. With their notices of opposition, the two opponents had requested revocation of the patent in its entirety on the grounds under Article 100(a) EPC (lack of novelty and lack of inventive step) and Articles 100(b) and 100(c) EPC.
- III. The documents submitted during the opposition proceedings included:
- D1: EP 1 800 675 A1
 - D6: O. Hansson et al., *The Lancet Neurology*, vol. 5, 2006, pp. 228-234
 - D7: D. Praticò et al., *Archives of Neurology*, vol. 59, 2002, pp. 972-976
 - D8: WO 2006/127620 A2
 - D9: R.J. Wurtman et al., *Brain Research*, vol. 1088(1), 2006, pp. 83-92
 - D10: WO 03/041701 A2
 - D11: US 2006/0241077 A1
 - D12: US 2007/0004670 A1
 - D13: WO 2007/073178 A2
 - D20: E. Reynolds, *The Lancet Neurology*, vol. 5, 2006, pp. 949-960
- IV. The decision of the opposition division was based on a main request and auxiliary requests 1 to 4, filed during the oral proceedings, and auxiliary request 5, corresponding to the claims as granted. The opposition division held that none of the claim requests contained

added subject-matter, that the subject-matter of all the requests was sufficiently disclosed, but that the subject-matter of all the requests was not novel over D1 and D13 under Article 54(3) EPC and over D10 under Article 54(2) EPC.

- V. This decision was appealed by the proprietor (appellant), which requested that the decision be set aside and that the patent be maintained on the basis of the main request, or, alternatively, on the basis of one of auxiliary requests 1 to 4, all filed under cover of a letter dated 6 June 2016, or auxiliary request 5 (claims as granted), which were the requests before the opposition division. It also requested that for any discussion on inventive step the case be remitted to the opposition division. A new document was filed with the statement of grounds of appeal:

D29: Public release: 10-MAR-2016, "Nutritional drink can help to conserve memory in case of prodromal Alzheimer's disease" (LipiDiDiet clinical study), Saarland University, 4 pages.

- VI. The only requests relevant for this decision are the main request and auxiliary request 4.

Claim 1 of the main request 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) a methyl donor, 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."

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."*

VII. Respondents 1 and 2 (opponents 1 and 2) requested that the appeal be dismissed. Opponent 2 further requested that the main request and auxiliary requests 1 to 5 not be admitted into the proceedings because they were not convergent. In addition, were the board to acknowledge novelty, opponent 2 requested that the case not be remitted to the opposition division and that a decision on inventive step also be taken.

VIII. In a communication issued in preparation for the oral proceedings, the board drew attention to the points to be discussed during the hearing.

- IX. By letter dated 1 April 2019 the appellant reiterated its request that the case be remitted to the opposition division for any discussion on inventive step. It also filed new documents: D30, D30A, D30B, D30C and D30D.
- X. By letter dated 9 April 2019 opponent 2 requested that the documents filed on 1 April 2019 not be admitted into the proceedings.
- XI. On 15 May 2019 oral proceedings took place before the board. During the hearing, opponent 2 (respondent) withdrew the request that the main request and auxiliary requests 1 to 5 not be admitted into the proceedings and announced that it no longer opposed the remittal of the case to the opposition division for a discussion of inventive step. The appellant withdrew auxiliary requests 1 to 3. At the end of the debate, the chairman announced the decision.
- XII. The appellant's arguments, where relevant for the decision, may be summarised as follows.

The requests on file did not contain added subject-matter. A basis for inserting the wording "for use" into claim 1 was found on page 4, lines 14-17, as filed. A basis for the other amendments could be found on page 13, line 3 (folate and vitamin B12); page 9, lines 28-32 (uridine derivatives); page 11, line 21 (choline and phosphatidylcholine); and claim 2 and page 5, lines 25-29 (the markers). The use of the claimed composition for treating the relevant group of patients was disclosed on page 4, lines 23-24, of the application as filed.

The opposition division's finding on sufficiency of disclosure was correct. The respondents' objections

were unsubstantiated. There were no serious doubts, substantiated by verifiable facts, that the skilled person would not have been able to carry out the invention. The description provided all the technical details for preparing and using the claimed composition for the claimed therapeutic treatment. The beneficial effects of the relevant ingredients in the treatment and prevention of dementia and Alzheimer's disease were known, as shown in the available prior-art documents. Thus, the therapeutic properties of the claimed composition were credible. The relevant markers, as well as their use for identifying prodromal patients, were identified in the patent application, in the patent and in the articles (D6 and D7) cited in these documents. Relying on the teaching of the patent, the documents cited therein, and common general knowledge, the skilled person would have been able to select the patient group identified in the claims. Established methods were available to distinguish patients in a prodromal stage of dementia from those already in the clinical stage of dementia.

The transgenic mouse used to carry out Experiment 4 of the patent was a suitable model of prodromal dementia. The example showed that the tested composition prevented damages typically associated with the onset of Alzheimer's disease. Despite some differences from the claimed composition, the tested composition contained all ingredients necessary to induce the therapeutic effect. The clinical study discussed in D29 confirmed that a representative composition was beneficial in patients affected by Alzheimer's disease. This composition prevented hippocampal and whole-brain atrophy. As far as the main request was concerned, which only mentioned "characteristics" of the disease,

the description contained guidance on identifying markers suitable for carrying out the invention.

The claimed subject-matter enjoyed priority from the earlier application PCT/NL2007/050310. This document was enabling in respect of the claimed subject-matter and represented the first invention for that matter.

The subject-matter of auxiliary request 4 was novel over D1, D10 and D13. None of these documents disclosed the relevant markers. Furthermore, they did not disclose the prevention or the delay of the onset of dementia in the group of subjects defined in the claims. These subjects could be identified and distinguished from those treated according to the prior art using the markers and other established criteria based on cognitive and functional tests. The selection of these patients was not arbitrary. Thus, T 233/96 was not applicable. D1 and D13 did not disclose prevention of dementia either. The abstract of these documents was vague and did not unambiguously disclose this use. The animal model of D1 and D13 was different from that of Example 4 and reproduced, at most, a subject in a clinical stage of Alzheimer's disease.

XIII. The respondents arguments, where relevant for the decision, may be summarised as follows.

The following amendments added subject-matter extending beyond the content of the application as filed:

- The insertion of the wording "for use" into claim 1. This wording was mentioned only on page 4 of the application as filed in a passage which did not mention all the claimed ingredients. This applied in particular to the uridine derivatives

defined in the claims. It further applied to the dependent claims, which were directed to a composition "as such" in the application as filed.

- The omission of a reference to UMP, dUMP, UDP, UTP and of the expression "nucleobase" (uracil) referred to on page 9 as filed.

- As far as auxiliary request 4 was concerned, the reference to a person "having characteristics of a prodromal patient" rather than to a "prodromal patient" as such, and the further limitation of the claims with choline/phosphatidyl choline, vitamin B12 and folate and specific markers.

None of the requests on file fulfilled the requirement of sufficiency of disclosure. The patent application and the patent did not plausibly show that the claimed composition achieved the purposed therapeutic effect. The mouse model used in Experiment 4 was not suitable for demonstrating that the claimed composition delayed or prevented the onset of dementia. The mice were sacrificed too early, before the age when they typically developed dementia. The presence of the relevant markers had not been determined, and the tested composition did not correspond to the claimed one. For similar reasons, the clinical study described in D29 did not make the purported therapeutic effect plausible. Furthermore, no markers were available to distinguish prodromal dementia patients from patients already affected by dementia, especially in early stages. D6 and D7 showed that the preferred markers mentioned in the patent were present not only in prodromal dementia patients, but also in dementia patients and in healthy subjects. A distinction between these subjects being impossible, the claimed

therapeutic method could not be carried out. Furthermore, the claims encompassed compositions comprising minimal amounts of the active agents, which could not be expected to be effective.

For analogous reasons, the priority document was not enabling in respect of the claimed invention. Since the earlier applications D1 and D13 disclosed that invention, the priority document was also not the first application within the meaning of Article 87(4) EPC. Thus, the claimed subject-matter did not validly claim priority.

The subject-matter claimed in auxiliary request 4 was not novel in the light of the disclosure of D1, D10 and D13. D1 and D13 (Example 1, Table 2, claims) disclosed a composition comprising all the relevant ingredients and its use for treating Alzheimer's disease. A preventive treatment was also mentioned in Example 1 and in the abstract of these documents. Although D1 and D13 did not explicitly disclose patients carrying the relevant markers, some of the patients already treated had to display those markers, at least based on statistical assumptions. Furthermore, since the markers were unsuitable for properly distinguishing prodromal dementia patients from dementia patients, the treatment of dementia patients described in the prior art fell under the claimed scope. Nor did the claims define a patient group distinguishable from that disclosed in the prior art by its physiological or pathological status. These groups were overlapping, and the selection of the claimed one was arbitrary and did not fulfil the criteria for establishing novelty which were laid down in decision T 233/96. Similar objections were raised on the basis of D10. Reference was made to the compositions described in the claims, in Table 1 and to

other parts of the description mentioning the relevant ingredients and the treatment and prevention of dementia.

Reasons for the Decision

1. *Admissibility of D29*

- 1.1 D29 was filed by the appellant together with the statement setting out the grounds of appeal to support its argument that the invention meets the requirement of sufficiency of disclosure. The document describes the outcome of a clinical study investigating the impact of a composition comprising, like the claimed one, ω -3 fatty acids, choline, uridine monophosphate, phospholipids, antioxidants and B vitamins in people with prodromal Alzheimer's disease.
- 1.2 Since D29 was filed at the earliest possible stage in the appeal and addresses issues relating to the ground of opposition under Article 100(b) EPC that are discussed in the appealed decision and are relevant for the present proceedings, the board sees no reason not to admit this document into the appeal proceedings (Article 12(4) RPBA).

Main request

2. *Sufficiency of disclosure*

- 2.1 Claim 1 of the main request is drafted in accordance with Article 54(5) EPC and 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 "characteristics" of a prodromal dementia patient.

2.2 Dementia is a disease induced by a progressive degeneration of the brain cells affecting, for example, 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. Alzheimer's disease is the most common form of dementia. The pathogenic process of dementia is believed to start long, even decades, before the clinical onset of the disease.

2.3 As explained in the opposed patent, "prodromal (dementia) patients" are subjects who, although not yet suffering from dementia, are bound to develop it. It is the gist of the invention to identify this patient group and to treat it with the claimed composition so that the onset of the disease can be delayed or even prevented (paragraphs [0001], [0007], [0012-0015]). Paragraph [0016] defines "prodromal patients" as persons that display at least one, preferably at least two, of a specific list of criteria. These criteria are listed in paragraphs [0016-0019] of the patent, in dependent claim 2 as granted and on pages 5-6 of the application as filed. They include in particular the presence of specific markers, such as a level of more than 350 ng Total-tau (T-tau) per litre cerebrospinal fluid (CSF) and a weight ratio of abeta-42/Phospho-tau-181 (A β 42/P-tau₁₈₁) of less than 6.5 in CSF. The patent explains that these markers distinguish prodromal patients from other patients presenting symptoms of mild cognitive impairment who will not necessarily develop dementia.

- 2.4 Since claim 1 is drafted under Article 54(5) EPC, attaining the claimed therapeutic effect is a functional technical feature characterising the claim. Thus, the issue of whether the claimed therapeutic method can be carried out and the purported effect achieved is relevant in the context of the assessment of sufficiency of disclosure (G 1/03, see point 2.5.2). As already established in numerous decisions of the boards of appeal, unless this effect is already known to the skilled person at the relevant date, the application must disclose the suitability of the claimed product for the specified therapeutic application (see T 609/02, point 9 and T 895/13, point 5). In the present case, for the therapeutic method to be carried out and the effect to be achieved, the skilled person must, in the first place, be able to identify patients that are in need of treatment and will benefit from the administration of the claimed composition. The selection of this patient group is an essential part of the claimed method. To identify these patients, the skilled person has to rely on the technical information in the patent (and the patent application) and on the common general knowledge available at the date of filing.
- 2.5 As explained above (point 2.3), the patent teaches that prodromal patients are persons who score positively on at least one of a restricted list of criteria. Claim 1, however, does not mention those criteria; rather, it refers to unspecified "characteristics of a prodromal patient".
- 2.6 According to the appellant, in order to identify said "characteristics", the skilled person would turn to the description, and in particular to paragraph [0016]. Relying on the technical teaching presented therein,

the skilled person would be able to identify prodromal patients.

- 2.7 The board does not agree. The expression "characteristics" encompasses the criteria enumerated in the description and in granted claim 2 but is not limited thereto. The patent does not provide any pointer as to how further criteria, other than those that are explicitly mentioned, could be identified. Furthermore, no evidence has been provided that this could be done by relying on the common general knowledge at the relevant date. The difficulty in identifying further "characteristics" is highlighted by the fact that the patent acknowledges that other manifestations, such as "mild cognitive impairment" which can be observed before the onset of Alzheimer's disease, are not sufficient to consider a person to be a "prodromal patient" (see paragraphs [0005], [0007]). Thus, an entire research programme would have to be conducted in order to identify further criteria beyond those explicitly identified in paragraphs [0016-0019]. This would put an undue burden on the skilled person wishing to carry out the invention over the entire scope of claim 1. Thus, the invention identified in the main request does not meet the requirement of sufficiency of disclosure (Articles 83 and 100(b) EPC).

Auxiliary request 4

3. *Added subject-matter*

- 3.1 At the oral proceedings before the opposition division, the chairman pointed out that the expression "*for the prevention or delay of the onset of dementia in a person having characteristics of a prodromal dementia patient*" in claim 1 as granted did not limit the claim

to a therapeutic use within the meaning of Article 54(5) EPC, because it did not contain the wording "for use". The proprietor then filed an auxiliary request 4 (identical to auxiliary request 4 in these appeal proceedings) in which the objected expression in claim 1 read: "*for **use in** the prevention or delay of the onset of dementia in a person having characteristics of a prodromal dementia patient*".

- 3.2 The insertion of "for use" was objected to on appeal on the ground that it added subject-matter. However, page 4, lines 14-17, explicitly refers to a composition for use in the prevention or delay of the onset of dementia in a person having characteristics of a prodromal dementia patient. The board concedes that this passage does not define all the ingredients characterising the composition of claim 1. Nevertheless, when reading the application as filed as a whole, it would be clear to the person skilled in the art that the invention relates to the preparation of a composition for use in the therapeutic method identified in the claim and that all the compositions disclosed in the application as filed are intended for use in that therapeutic method. Furthermore, claim 1 as filed refers to: "Use of a composition ... for the prevention or delay of the onset of dementia in a person having characteristics of a prodromal dementia patient". Such wording is of course not allowable under the EPC but normally serves as the basis for the reformulation of the subject-matter as a second medical use claim in line with Article 54(5) EPC. Thus, the rewording of the aforementioned expression does not result in any change in the technical teaching. This equally applies to the same amendment in the dependent claims.

- 3.3 According to the respondents the feature "in a person having characteristics of a prodromal dementia patient", wherein said characteristics comprise a given T-tau level and a given ratio of A β 42/P-tau₁₈₁, also had no basis in the application as filed. The relevant passage identifying those markers (page 5, lines 26-28) referred to "prodromal patients" but not to "a person having characteristics of a prodromal dementia patient".
- 3.4 The board disagrees. From the application as filed as a whole, it is readily apparent to the skilled reader that the persons displaying the markers are subjected to the claimed treatment and are "prodromal patients" (see e.g pages 4 and 5). Thus, claim 1 does not contain added subject-matter.
- 3.5 The ingredients and the markers included in claim 1 to further characterise the claimed subject-matter are mentioned on page 9, lines 28-32 (uridine derivatives), on page 11, line 21 (choline and phosphatidylcholine) and on page 13, line 3 (folate and vitamin B12). Claim 2 and page 5, lines 25-29, disclose the two relevant markers. It is also clear from these passages that these ingredients, as well as the two markers, are the preferred ones in the application as filed.
- 3.6 The respondents argued that page 9, lines 28-32, was not a proper basis for the definition of component (b) in claim 1. This passage refers to "uridine or an equivalent thereof selected from the group consisting of uridine (i.e. ribosyl uracil), deoxyuridine (deoxyribosyl uracil), uridine phosphates (UMP, dUMP, UDP, UTP), nucleobase uracil and acylated uridine derivatives". The board accepts that the wording in claim 1 "(b) uridine selected from uridine ...", which

was already in granted claim 1, is at first glance rather odd. However, it is clear that component (b) of the claimed composition has to be selected from the given list of compounds. The omission from claim 1 of a reference to the specific compounds UMP, dUMP, UDP, UTP does not add any new subject-matter. These agents are in fact listed in the application as filed only as possible examples of uridine phosphates. The fact that claim 1 simply refers to uracil and not to "nucleobase uracil" does not result in added subject-matter either, because uracil is a nucleobase.

3.7 For these reasons auxiliary request 4 does not contain subject-matter extending beyond the content of the application as filed (Articles 100(c) and 123(2) EPC).

4. Sufficiency of disclosure

4.1 Claim 1 of auxiliary request 4 has been limited so as to require that the person having the characteristics of a prodromal patient displays at least the following CSF markers:

- a level of more than 350 ng Total-tau per litre CSF, and
- a weight ratio of A β 42/P-tau₁₈₁ of less than 6.5 in CSF.

4.2 These CSF markers, which are the preferred ones according to paragraph [0017] of the opposed patent and page 5, lines 25-29, of the patent application as filed, correspond to those described in D6, a scientific article mentioned in paragraph [0017] of the patent and on page 5 of the patent application as filed.

- 4.3 The respondents considered that the invention defined in auxiliary request 4 was not sufficiently disclosed because, even by relying on these markers, the skilled person would not be able to distinguish prodromal dementia patients from patients who have already developed dementia, in particular at an early stage. Furthermore, according to D6 these markers could also be found in dementia patients.
- 4.4 This argument cannot be accepted. D6 discusses the results of a study investigating the correlation between the relevant CSF markers and the development of Alzheimer's disease in patients affected by mild cognitive impairment (MCI). The combination of T-tau and A β 42/P-tau₁₈₁ ratio was used in D6 to assess the potential for conversion from MCI to Alzheimer's disease and other forms of dementia. The patients recruited for the study were selected from among a patient population that fulfilled established criteria for MCI, but not criteria for dementia. These criteria, mentioned on page 229, are not based on markers, but rather on cognitive and functional tests. The recruited patients were then monitored by experienced physicians until they developed dementia or until they had been cognitively stable for more than four years. The diagnosis for dementia was performed according to the aforementioned criteria. The expression of the CSF markers was monitored for four years and their presence was correlated to the probability of the onset of dementia. The results show that the relative risk of progression to dementia was substantially increased in the patients presenting higher concentrations of T-tau and A β 42 at baseline. The correlation was much stronger than, and independent of, other established risk factors relating to age, sex, education, genotype and

plasma homocysteine. The cut-off values used in the study correspond to those indicated in claim 1 (D6, abstract, page 231, right-hand column and page 232, left-hand column).

- 4.5 Considering how the clinical study was planned and carried out, it is evident that at the publication date of D6 (i.e. before the priority date), criteria not involving the use of the markers were available for detecting the onset of dementia and for distinguishing subjects already affected by dementia from prodromal dementia patients and other subjects, affected for example by MCI. This is in line with the teaching of paragraphs [0004] and [0021] of the opposed patent.
- 4.6 The respondents also pointed to a passage of D6 (on page 232, right-hand column, second full paragraph from the bottom) which appears to indicate that some healthy patients can also display the markers. However, despite this finding, the authors consider the observed degree of specificity of the method acceptable and conclude, on page 233, right-hand column: "Taken together, our results show that CSF analysis of T-tau, P-tau and A β 42 are strong and independent risk markers for development of clinical Alzheimer's disease in patients with MCI". In this context it is noted that, for the treatment now claimed to be clinically useful, what counts is that a substantial proportion of the treated population will benefit from the treatment and that the majority of the subjects that would not benefit from it are not unnecessarily treated. This concept is outlined in D6, page 233, left-hand side, last paragraph, stating that by pre-selecting patients using the CSF markers, a substantial number of patients who would not benefit and would even incur the risks of side-effects can be spared the treatment.

- 4.7 For these reasons it is concluded that using the markers indicated in claim 1 and other criteria that were already established at the filing date, the skilled person would be able to identify a group of prodromal patients not yet affected by dementia but bound to develop it, and to distinguish them from patients already affected by dementia or by other disorders, such as MCI.
- 4.8 The respondents further contended that no evidence rendering it credible that the claimed composition was suitable for preventing or delaying the onset of dementia in a person as defined in claim 1 was available.
- 4.9 The board notes that the description of the opposed patent contains detailed information on choosing the relevant ingredients and formulating them into a composition suitable for use in therapy. Furthermore, as pointed out by the appellant, the individual ingredients making up the claimed composition had already been used before the priority date for treating and preventing dementia, including Alzheimer's disease and other disturbances associated with cognitive impairment. This was not contested by the respondents and is confirmed by several documents mentioned in the proceedings (e.g. D8, D9, D10, D11, D12 and D20). In particular, compositions comprising ω -3 fatty acids (e.g. DHA), uridine and/or choline were considered particularly beneficial (D8, D9, D11, D12). Accordingly, and in the absence of any concrete evidence to the contrary, the board sees no reason why at the filing date a skilled person might have considered the claimed composition unsuitable for inducing these same therapeutic effects in prodromal

patients. On the contrary, D6 states that prodromal patients are those who are likely to benefit most from existing drug therapies (page 228, right-hand column).

4.10 Experiment 4, described in paragraph [0059] of the patent and on page 17 of the application as filed, provides additional evidence that the claimed composition is effective in prodromal patients. The experiment involved the use of APP/PS1 transgenic mice, which serve as a model of Alzheimer's disease and typically start to manifest behavioural and cognitive disturbances at an age of ten months. The mice and their wild type littermate controls were fed either Diet A (control chow) or Diet C, comprising all the ingredients indicated in the claims. Three months after the start of the dietary intervention and after reaching an age of six months, the mice were sacrificed and the brains were collected and analysed to visualise and quantify the neurodegeneration in sections of the brain. As shown in Figure 1, before the onset of behavioural or cognitive changes, Diet C induced a significant decrease in neurodegeneration in the neocortex of the APP/PS1 transgenic mice.

4.11 The respondents argued that the claimed composition did not correspond to Diet C used for the test. However, as noted by the appellant, Diet C contains all the claimed ingredients: two ω -3 fatty acids (DHA and EPA), uridine monophosphate (UMP), choline, lecithin (a phospholipid mixture comprising phosphatidylcholine as major component), folate and vitamin B12. These ingredients, together, make up the major fraction of Diet C. Furthermore, ω -3 fatty acids, UMP and choline, which are known to induce beneficial effects in the treatment and prevention of Alzheimer's disease, are present in higher amounts. Thus, without any evidence to the

contrary, the board considers that Diet C is sufficiently representative of the claimed composition and also suitable for making its beneficial effects credible.

- 4.12 The respondents also complained that claim 1 was very broad and encompassed compositions comprising minimal amounts of the claimed ingredients which might not result in the therapeutic effect. However, the board considers that a skilled person would not contemplate embodiments that were clearly outside the scope of practical application.
- 4.13 Neither the fact that the mice were sacrificed at six months, i.e. before the onset of behavioural changes, nor the fact that the presence of the claimed markers was not assessed in these mice deprives Experiment 4 of its significance. Dementia is a disease induced by a progressive degeneration of the brain cells. Thus, the neurodegenerative process observed in young APP/PS1 mice is suitable for reproducing the processes accompanying the development of dementia in prodromal patients. Furthermore, since the markers specified in the claims are used to identify patients affected by prodromal dementia, and the young APP/PS1 mice can be considered a model for prodromal patients, the observed results are suitable for substantiating an effect in the patient population defined in the claims. The finding that Diet C prevents neurodegeneration in the control mice too does not detract from these conclusions.
- 4.14 In addition, the results described in the post-published document D29 cannot be disregarded. This document describes the results of a two-year clinical study aimed at assessing the benefits of a nutritional

composition comprising, like the claimed one, ω -3 fatty acids, choline, uridine monophosphate, phospholipids, antioxidants, and B vitamins in prodromal patients. Although no significant differences were noted for the cognitive composite score in the observed patients, a significant reduction in the hippocampal and whole-brain atrophy - key factors in the development of dementia - were observed in the treated prodromal patients (page 2 third paragraph from the bottom). Taking the results into account the authors state that they have "found something that can help slow down some of the most distressing symptoms in prodromal AD, especially in those who started the intervention early. Indeed these patients who have lost the least cognitive function, have the most to gain" (page 2, last paragraph).

- 4.15 Although the composition described in D29 does not contain all the ingredients listed in claim 1, and no reference is made to the claimed CSF markers, the results provide additional substantiation of the therapeutic utility of the claimed composition for the same reasons as discussed in the context of Example 4 (points 4.11-4.12).
- 4.16 On the basis of these facts, and in the absence of any concrete evidence to the contrary, the board considers it credible that the claimed composition is suitable for inducing the purported therapeutic effect in the patient identified in the claim.
- 4.17 Accordingly, the invention defined in auxiliary request 4 fulfils the requirement of sufficiency of disclosure (Articles 83 and 100(b) EPC).

5. Novelty

5.1 The respondents objected to the novelty of the claimed subject-matter having regard to the disclosure of D1 and D13 under Article 54(3) EPC and of D10 under Article 54(2) EPC.

5.2 Claim 1 is drafted under Article 54(5) EPC and is directed to:

- a composition comprising ω -3 fatty acids selected from DHA, DPA and EPA, uridine or a certain derivative thereof, choline and/or phosphatidylcholine, vitamin B12 and folate,
- said composition being intended for use in the prevention or delay of the onset of dementia,
- in a person having characteristics of a prodromal dementia patient, those characteristics comprising at least the two CSF markers indicated in claim 1.

Documents D1 and D13

5.3 It was undisputed by the parties that D1 and D13 disclose a composition comprising all the ingredients enumerated in claim 1 and their use for treating Alzheimer's disease (D1: page 14, "Diet B", claims 9 and 16; and D13: pages 36-38, claims 8 and 15). It was also undisputed that these documents do not mention any CSF markers.

5.4 The respondents' novelty objection was based, in the first place, on the assumption that the definition of the patient given in claim 1 was unsuitable for distinguishing prodromal dementia patients from

dementia patients because the specified CSF markers were expressed in both patient groups. A distinction between the claimed preventive treatment and the treatment disclosed in D1 and D13 was therefore impossible, and novelty had to be denied.

5.5 This assumption is incorrect. As already established above (points 4.4-4.7), the skilled person can distinguish prodromal patients from dementia patients using established criteria based on cognitive and functional tests. From the wording of claim 1, it is clear that the patients who are to be treated express the specified CSF markers but are still in a stage preceding the onset of dementia. A distinction between the aforementioned patients being possible, claim 1 cannot be considered to encompass the treatment of patients already affected by dementia.

5.6 The novelty objection was based, in the second place, on a literal interpretation of claim 1, taking the wording "person having characteristics" at face value when construing the claim and comparing it with the prior art. According to the respondents, when the treatment disclosed in D1 and D13 was carried out, some patients "having" the relevant characteristics, i.e. displaying the relevant CSF markers, had necessarily been subjected to the claimed treatment. This was inevitable at least based on statistical assumptions. In this context the respondents also argued that D1 and D13 disclosed not only the treatment but also the prevention of dementia. Thus, subjects not yet affected by clinical dementia but displaying the relevant CSF markers had necessarily been treated. Reference was made to the abstract and to Example 1 of D1 and D13, and to page 5, line 28, and claim 13 of D13.

- 5.7 The decisive issue for deciding novelty in the present case is how claim 1 has to be construed, in particular as to the feature "for use in the prevention or delay of dementia in a person having characteristic of a prodromal dementia patient, wherein said characteristics comprise...".
- 5.8 Claim 1 is a "purpose-limited product claim" defining a composition intended for use in the treatment of a patient expressing specific markers in the CSF. It stems from the very nature of a "purpose-limited product claim" that said claim must be interpreted taking into account the purpose of the therapeutic invention and how the invention is to be carried out. The perspective of the skilled person who works in the relevant field and understands that purpose must also be considered.
- 5.9 In the present case this is a person working in the field of personalised medicine. Their goal is to move away from the "one-size-fits-all approach" of traditional medicine and to provide a treatment tailored to specific groups of patients who best profit from the treatment. The articles D6 and D7 cited in the opposed patent illustrate how personalised therapies are developed in this field. Typically this involves:
- The identification of a group of patients that is distinguished from a larger patient population by a particular physiological and pathological status and that possibly responds better to a certain treatment.
 - The identification of detectable biomarkers characterising the members of the group (for

example by conducting clinical studies as described in D6 and D7).

- The screening of a population of subjects to identify patients displaying the relevant markers and the selective targeting of these patients with that treatment.

5.10 When reading claim 1 in a technically sensible and constructive manner, the skilled person would promptly understand that the purpose of the treatment is to target selectively prodromal patients identified by the CSF markers, rather than other subjects that do not display the markers. This implies that there is a functional relationship between the markers that characterise the patients and the therapeutic effect which is sought. The presence of this functional relationship confirms that the purposive selection of patients is an essential technical feature qualifying claim 1. This has to be taken into account when assessing novelty.

5.11 The claimed treatment is one in which, as stated in decision G 2/08 (point 5.10.9), the notional novelty is derived from the purpose for which the claimed composition is intended. Thus, the crucial issue is whether this purposive treatment has been made available to the public within the meaning of Article 54(2) EPC.

5.12 When deciding on the novelty of claims directed to a new use of a known compound, the Enlarged Board of Appeal has already considered that "...a line must be drawn between what is in fact made available and what remains hidden or otherwise has not been made available...". Thus, the relevant issue is what has

been made available, and not "...what may have been inherent in what was made available..." (G 2/88, points 10-10.1).

5.13 The board in the present composition is of the opinion that this principle applies also to claims drafted under Article 54(5) EPC. The relevance of G 2/88 to claims directed to the treatment of new patient groups has already been endorsed in T 1118/12 (point 7). It is also supported by the statement in G 2/88 that "... the question of "inherency" does not arise under Article 54 EPC" (i.e. in relation to all aspects relating to novelty).

5.14 For this reason, the issue of whether patients displaying the markers of claim 1 were present among a population of previously treated patients and were already "inevitably" or "inherently" treated is irrelevant for assessing novelty in the present case. The only thing which counts is that D1 and D3 do not disclose a method whereby a patient or a group of patients displaying the relevant CSF markers but not affected by dementia was purposively and selectively targeted for carrying out the preventive treatment defined in claim 1.

5.15 The claimed method can be seen as one which aims at hitting a target which is hidden behind a screen, but the screen reveals a spot which allows the position of the target to be actively aimed at. This allows hitting the target precisely while reducing the risk of hitting other objects present behind that screen. No such a method is disclosed in D1 and D13.

5.16 For these reasons the respondents' argument that merely because of statistical considerations novelty has to be

denied must fail. It is noted that in numerous decisions the boards have already decided that the assessment of what has been disclosed cannot be made on the basis of probability or statistical considerations (T 1118/12, points 6-8; T 734/12, point 28; T 1399/04, point 31; T 464/94, point 16).

5.17 The respondents' novelty objection was based, lastly, on the ground that, applying the principles set out in decision T 233/96, the claimed subject-matter did not represent a novel therapeutic application. The board in T 233/96 (point 8.7), interpreted the earlier decisions T 19/86 and T 893/90 such that the conclusion reached in these decisions, namely that the treatment or diagnosis of the same disease could represent a novel therapeutic application provided it is carried out on a new group of subjects, does not apply,

- if the group overlaps with the group previously treated or

- if the choice of the novel group is arbitrary in that there is no functional relationship between the particular physiological or pathological status of this group of subjects and the therapeutic or pharmacological effect achieved.

5.18 According to the respondents, claim 1 defined a patient group that was encompassed by and thus overlapped with the group of patients subjected to a preventive treatment described in D1 and D13. The choice of the patient group defined in claim 1 was also arbitrary. Hence, applying T 233/96 novelty was to be denied.

5.19 The present board concurs with the conclusions already reached by another board (see T 1399/04, point 35) that

decision T 233/96 related to a special case, namely one where the patient selected for treatment was characterised by the feature that the patient, "... is unable to exercise adequately", which was considered vague, unsuitable for properly defining the claimed subject-matter, and not related to the purported therapeutic effect. The present board also concurs with that board that the interpretation of T 19/86 and T 893/90 given in T 233/96 has no basis in the relevant parts of those decisions (points 5-8 of T 18/96 and points 4.2-4.6 of T 893/90).

5.20 The conclusions drawn in T 233/96 thus cannot be applied to the present case, where the treated patients are identified by clearly testable criteria. Accordingly, novelty may not be denied on the ground that the claimed patient group is embedded and necessarily overlaps with a larger population of previously treated patients and the first condition in T 233/96 is not satisfied. The argument that the selection of the patient group defined by claim 1 was arbitrary is not convincing either. As already concluded above (point 4.6), by selecting patients displaying the markers specified in claim 1 a group of prodromal patients who can profit from the therapy is subjected to the treatment, whereas non-prodromal subjects are spared an unnecessary intervention and from the risks of side-effects. The selection of these patients is thus purposive and not arbitrary.

5.21 For the reasons set out above, even assuming, in the respondents' favour, that D1 and D13 disclosed the prevention of dementia, the claimed subject-matter would not be anticipated by these prior-art documents.

Document D10

5.22 D10 discloses compositions comprising ω -3 fatty acids (preferably DHA), vitamin B12, folic acid and, possibly, one or more of the other ingredients specified in the claims (see e.g. claims 1, 4-6 and Table 1). It also discloses the use of these compositions for treating or preventing dementia (see claim 12). However, like D1 and D13, document D10 does not mention a method for identifying and selecting patients using the relevant CSF markers. Accordingly, for the reasons already discussed above, D10 also does not disclose a treatment delaying or preventing the onset of dementia in a patient as defined in claim 1. Furthermore, although all the relevant ingredients of the claimed composition are mentioned in D10, their combination is not directly and unambiguously disclosed. Uridine in particular is mentioned on page 9, line 22, but is not present in either the composition of Table 1, or in any other part of the application disclosing combinations of the other relevant agents. A composition as defined in claim 1 of auxiliary request 4 is therefore not disclosed in D10.

5.23 For these reasons the board concludes that the subject-matter of claim 1 of auxiliary request 4, as well as of the dependent claims, which are more limited in scope, is novel over D1, D10 and D13 (Article 54 EPC).

6. *Priority right*

6.1 The respondents argued that the subject-matter of auxiliary request 4 did not validly enjoy priority from the earlier application PCT/NL2007/050310, because this document was not "enabling" with regard to the therapeutic application claimed in the opposed patent.

6.2 The priority document differs from the application as filed and the patent in that it does not contain Example 4. The technical teaching of the other parts of the disclosure and the references to the prior art (e.g. to D6 and D7) are the same. The board has already set out above that the teaching of the application as filed, together with the knowledge available before the priority date, renders the purported therapeutic effect credible. Example 4 confirmed but was not essential for this finding. Accordingly, there are no reasons to consider the priority document to be non-enabling with regard to the claimed invention.

6.3 The respondents also argued that the earlier application PCT/NL2007/050310 is not the first application within the meaning of Article 87(4) EPC in view of the disclosure of D1 and D13. Since, however, D1 and D13 do not anticipate the claimed subject-matter as set out above, this objection cannot succeed.

6.4 For these reasons, the subject-matter of auxiliary request 4 validly claims priority.

7. *Remittal*

8. The appealed decision did not address the issue of inventive step. The appellant requested that for any discussion relating to this ground of opposition the case be remitted to the opposition division. The respondents did not object to this request. In this situation, and taking into account the complexity of the issues to be discussed, the board considers it appropriate to remit the case to the opposition division for further prosecution.

9. *Admissibility of D30, D30A, D30B, D30C and D30D*

10. Documents D30, D30A, D30B, D30C and D30D were filed by the proprietor in relation to inventive step. Since the appeal proceedings do not deal with this issue, the board does not need to decide on their admissibility.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.
2. The case is remitted to the opposition division for further prosecution upon the basis of auxiliary request 4 filed under cover of a letter dated 6 June 2016.

The Registrar:

The Chairman:



M. Canueto Carbajo

W. Sieber

Decision electronically authenticated