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Datasheet for the decision of 23 June 2009

Case Number: T 0188/06 - 3.3.02

Application Number: 99954343.2

Publication Number: 1123093

IPC: A61K 31/23

Language of the proceedings: EN

Title of invention:
Ubiquinone-containing composition suitable for promoting enhanced intramitochondrial transportation of ubiquinones and methods of using same

Patentee:
Sigma-Tau Healthscience S.p.A.

Opponent:
BEIERSDORF AG

Headword:
Ubiquinone-containing composition/SIGMA-TAU

Relevant legal provisions:
EPC Art. 84, 123(2), 54, 56

Relevant legal provisions (EPC 1973):
-

Keyword:
"Main Request - novelty (no): all features of claim 1 anticipated"
"Auxiliary Requests 5, 6, 7, 8, 11, 12 - amendments - added subject-matter (yes)"
"Auxiliary Requests 3, 4, 9, 10 - clarity (no): unclear base of percentage"
"Auxiliary Requests 1, 2, 13 - inventive step (no): provision of obvious alternative"

Decisions cited:
G 0005/83

Catchword:
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Case Number: T 0188/06 - 3.3.02

D E C I S I O N
of the Technical Board of Appeal 3.3.02
of 23 June 2009

Appellant: (Patent Proprietor)	Sigma-Tau Healthscience S.p.A. Via Treviso 4 I-00040 Pomezia (IT)
Representative:	HOFFMANN EITLE Patent- und Rechtsanwälte Arabellastrasse 4 D-81925 München (DE)
Respondent: (Opponent)	BEIERSDORF AG Unnastrasse 48 D-20245 Hamburg (DE)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted 8 December 2005 revoking European patent No. 1123093 pursuant to Article 102(1) EPC 1973.**

Composition of the Board:

Chairman: U. Oswald
Members: H. Kellner
J. Van Moer

Summary of Facts and Submissions

I. European patent No. 1 123 093, based on international patent application PCT/IT99/00331, was granted with three claims.

Claim 1 of this patent reads as follows:

"Use of:
(a) a lipid-soluble benzoquinone selected from the group consisting of Coenzyme Q_{10} (CoQ_{10}), its reduced form, ubiquinol-10 ($CoQ_{10}H_2$) or mixtures thereof, in an amount effective for performing a therapeutical and/or preventive and/or nutritional activity in a human in need thereof, in admixture with
(b) at least one omega-3 polyunsaturated fatty acid or an ester thereof,
for preparing a nutritional/pharmaceutical composition for preventing or treating mitochondriopathies."

II. Opposition was filed against the granted patent under Article 100(a) for lack of novelty and inventive step and under Article 100(b) EPC.

The following documents (all published before the priority date of the patent in suit) were cited inter alia during the proceedings before the opposition division and the board of appeal:

(3) EP-A2-0 023 349

(5) WO-A1-98/35660

(7) Finsterer, J., "Mitochondriopathien", Akt. Neurologie, Vol. 24, 1997, 231-241

(8) Weis, M. et al, "Bioavailability of four oral Coenzyme Q_{10} formulations in healthy volunteers", Molec. Aspects Med., Vol. 15 (supplement), 1994, s273-s280

III. By its decision posted on 8 December 2005, the opposition division revoked the patent under Article 102(1) EPC.

The opposition division held that neither the set of claims of the main request nor the set of claims of the auxiliary request met the requirements of Article 56 EPC.

It first noted that the requirements of Article 83 EPC were fulfilled by the claims of the main request and the auxiliary request, the latter also being originally disclosed (Article 123(2) EPC).

Since claim 1 clearly indicated a "second medical indication" in the meaning of the decision G 5/83 of the Enlarged Board of Appeal, OJ EPO 1985, 64 and since, whereas the symptoms tested in the examples in the patent in suit could have other origins than mitochondriopathy, this had not been demonstrated by the opponent, the patent in suit met the requirements of Articles 100(b) and 83 EPC.

With respect to novelty, the opposition division stated that, despite the term "mitochondriopathy" being broad, it defined a pathological state for which treatment was

not mentioned as such in any of the available prior art documents.

The sets of claims of the main request and of the auxiliary request lacked inventive step in view of document (5) as closest prior art together with document (3) and vice versa. The problem to be defined with respect to document (5) was to provide alternative vehicles for the use of CoQ_{10} against mitochondriopathies. The solution proposed was the use of at least one omega-3 polyunsaturated fatty acid or an ester thereof and auxiliarily vitamin E. Said solution was obvious in view of document (3) which provided a CoQ_{10} formulation comprising omega-3 polyunsaturated fatty acids or esters thereof with increased bioavailability. The addition of vitamin E claimed in the auxiliary request resulted from the general knowledge of the skilled person without any exercise of inventive skill.

IV. The patentee (hereafter appellant) lodged an appeal against said decision and filed grounds of appeal together with a main request to maintain the patent as granted.

With its letter of 22 May 2009, it submitted nine further sets of claims as first to ninth auxiliary requests together with further documents, inter alia document (7) defining mitochondriopathies and document (8), being the closest prior art in the view of the appellant.

V. On 23 June 2009, oral proceedings took place before the board. The appellant submitted four further sets of

claims as auxiliary requests and, after renumbering, presented a complete set of his requests as main request and first to thirteenth auxiliary request.

Claim 1 of the set of claims of the first auxiliary request reads:

"Use of:
(a) a lipid-soluble benzoquinone selected from the group consisting of Coenzyme Q_{10} (CoQ_{10}), its reduced form, ubiquinol-10 ($CoQ_{10}H_2$) or mixtures thereof, in an amount effective for performing a therapeutical and/or preventive and/or nutritional activity in a human in need thereof, in admixture with
(b) at least one omega-3 polyunsaturated fatty acid **selected from the group consisting of eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA) and mixtures thereof,** or esters thereof,
for preparing a nutritional/pharmaceutical composition for preventing or treating mitochondriopathies."
(Differences with respect to claim 1 as granted highlighted in bold)

Claim 1 of the second auxiliary request differs from claim 1 of the first auxiliary request in the addition of the wording
"wherein the nutritional/pharmaceutical composition further comprises a non omega-3 polyunsaturated fatty acid selected from the group consisting of a saturated, monounsaturated, omega-6, omega-9 fatty acid and a mixture thereof" at the end of the claim.

The same insertion constitutes the difference between the fourth auxiliary request with respect to the third.

In the set of claims of the third auxiliary request, the difference with respect to claim 1 as granted is another definition of component (b):

"(b) at least one omega-3 polyunsaturated fatty acid or an ester thereof, **comprising eicosapentaenoic acid (EPA) and/or docosahexaenoic acid (DHA) and/or esters thereof in an amount exceeding 65% by weight**" (differences as inserted with respect to claim 1 as granted highlighted in bold).

Claim 1 of the fifth auxiliary request differs from claim 1 of the third auxiliary request in the addition of "**of the overall mixture of omega-3 polyunsaturated fatty acids"** to the definition of component (b) after the term "in an amount exceeding 65% by weight" just as is the case for the sixth, eleventh and twelfth auxiliary request with respect to the fourth, ninth and tenth auxiliary request respectively.

In Claims 1 of the seventh to the twelfth auxiliary requests, the nutritional/pharmaceutical composition additionally is defined by the following wording at the end of the claim:

"wherein the nutritional/pharmaceutical composition consists of:
the above component (a),
the above component (b),
optionally a non omega-3 fatty acid selected from the group consisting of a saturated, monounsaturated, omega-6, omega-9 fatty acid and a mixture thereof,
optionally Vitamin E,

optionally proteins, and
optionally carbohydrates."

This additional definition is inserted to claim 1 as granted and thus the seventh auxiliary request is constructed. In the same way, claim 1 of the ninth auxiliary request differs from third auxiliary request, the eleventh auxiliary request from the fifth and the twelfth auxiliary request from the eighth auxiliary request. With respect to the final version of this eighth auxiliary request itself, the following is to be mentioned:

In claims 1 of the eighth and the tenth auxiliary request the reduced form of CoQ_{10} is omitted and linolenic acid (LNA) is introduced as one of the omega-3 polyunsaturated fatty acids; the wording of these claims is:

eighth auxiliary request:

"Use of:
(a) Coenzyme Q_{10} (CoQ_{10}) in an amount effective for performing a therapeutical and/or preventive and/or nutritional activity in a human in need thereof, in admixture with
(b) at least one omega-3 polyunsaturated fatty acid selected from the group consisting of eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), linolenic acid (LNA) and mixtures thereof, or esters thereof,

for preparing a nutritional/pharmaceutical composition for preventing or treating mitochondriopathies,

wherein the nutritional/pharmaceutical composition consists of:
the above component (a),
the above component (b),
optionally a non omega-3 fatty acid selected from the group consisting of a saturated, monounsaturated, omega-6, omega-9 fatty acid and a mixture thereof,
optionally Vitamin E,
optionally proteins, and
optionally carbohydrates."

tenth auxiliary request (with the additional 65% definition of DHA and EPA):

"Use of:
(a) Coenzyme Q_{10} (CoQ_{10}) in an amount effective for performing a therapeutical and/or preventive and/or nutritional activity in a human in need thereof, in admixture with
(b) at least one omega-3 polyunsaturated fatty acid selected from the group consisting of eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), linolenic acid (LNA) and mixtures thereof, or esters thereof,

comprising eicosapentaenoic acid (EPA) and/or docosahexaenoic acid (DHA) and/or esters thereof in an amount exceeding 65% by weight,

for preparing a nutritional/pharmaceutical composition for preventing or treating mitochondriopathies,

wherein the nutritional/pharmaceutical composition consists of:
the above component (a),

the above component (b),
optionally a non omega-3 fatty acid selected from the group consisting of a saturated, monounsaturated, omega-6, omega-9 fatty acid and a mixture thereof,
optionally Vitamin E,
optionally proteins, and
optionally carbohydrates."

With respect to this tenth auxiliary request, the twelfth auxiliary request contains the 65% definition of DHA and EPA including the reference to the "overall mixture of omega-3 polyunsaturated fatty acids".

The wording of the thirteenth auxiliary request is (with respect to claim 1 as granted, parts of claim 2 as granted are incorporated):

"Use of:
(a) a lipid-soluble benzoquinone selected from the group consisting of Coenzyme Q_{10} (CoQ_{10}), its reduced form, ubiquinol-10 ($CoQ_{10}H_2$) or mixtures thereof, in an amount effective for performing a therapeutical and/or preventive and/or nutritional activity in a human in need thereof, in admixture with
(b) at least one omega-3 polyunsaturated fatty acid or an ester thereof,

for preparing a nutritional/pharmaceutical composition for preventing or treating mitochondriopathies

wherein the mitochondriopathy is selected from
CPEO (Chronic Progressive External Ophthalmoplegia Syndrome);
ARMD (Age-Related Macular Degeneration) and

NARP (Neuropathy, Ataxia and Retinis pigmentosa)."

VI. The arguments of the appellant during the proceedings may be summarised as follows:

(a) The teaching of the patent in suit was new. In particular, the subject-matter of document (8) was not anticipating because it did not concern mitochondriopathies. Simple supplementation of CoQ_{10} could be envisaged for many reasons, most of them having nothing to do with mitochondriopathies, and the mention of "Co-enzyme Q_{10} deficiency" under the diseases in claim 2 of the patent in suit could not be taken to define "supplementation" as treatment of a mitochondriopathy.

In addition, the teaching of this document stopped at CoQ_{10} levels in the blood-serum and it was not demonstrated that cellular or mitochondrial membranes were crossed, as was the case in the patent in suit. There, it was clearly demonstrated by the conduct of the Macular Photostress Test that CoQ_{10}, in combination with omega-3 polyunsaturated fatty acids, reached mitochondrial structures.

Finally, in addition to the reported influence of the sex of the patients tested on the results (with smoking as the probable cause), the result demonstrated in document (8) that further addition of other components neutralised the effect caused by soy bean oil, and the admission that it would be of importance to develop a formulation for i.v. use, showed that in the end no conclusion at all

could be derived from that document, especially not the teaching of the patent in suit.

(b) With respect to inventive step, the conclusions of the opposition division were not correct, since the problem to be solved in view of document (5) was the provision of a CoQ_{10}-containing composition having an improved effect in preventing or treating mitochondriopathies and not the provision of alternative vehicles for the use of CoQ_{10} against mitochondriopathies, which did not take account of the improvement and, in addition, contained already a pointer to the teaching of the patent in suit.

The improvement could be seen from the percentages resulting from clinical trials as set out in the tables in the description of the patent in suit, where the percentages meant persons with a positive reaction in relation to all persons tested.

In addition, when taking into account documents (5) and (3) per se, the improvement could be inferred on the grounds of plausibility alone, since document (5) was not aware of any amelioration of CoQ_{10}-containing compositions in their affinity to mitochondriae but only in improved penetration through external skin and mucosa to reach CoQ_{10}-deficient tissue.

Thus, in the absence of particular emphasis on the treatment of mitochondriae, the person skilled in the art, when reading document (5), would not have

consulted a secondary document, particularly not one that did not mention mitochondriopathies.

Furthermore, document (3), taken into account by the opposition division, was restricted in its teaching to absorptivity of CoQ_{10} through the lymphatic duct, which had nothing to do with crossing cellular membranes and finally even those of the mitochondriae.

Therefore, there was no discernible reason for a skilled reader of document (5) to combine that reference with document (3) or document (8) when faced with the objective problem to be solved by the invention.

(c) The additional features in the claims of the auxiliary requests were thought to produce more distance between the requested subject-matter and the state of the art under discussion. In particular EPA and DHA were not used in the teachings of the documents introduced into the proceedings.

(d) Concerning the issue of clarity with respect to the third, fourth, ninth and tenth auxiliary requests as submitted during the oral proceedings, the appellant argued that it was clear from the context within the claim that the 65%-value referred to "at least one omega-3 polyunsaturated fatty acid" as being 100%.

(e) Original disclosure of the subject-matter of these claims, as well as that of the fifth, sixth,

eleventh, and twelfth auxiliary requests was to be found in the original claims concerning the use of CoQ_{10} and omega-3 polyunsaturated fatty acid in combination with the description. Original disclosure of the seventh and eighth auxiliary requests resulted inter alia from the examples.

VII. The respondent's arguments, apart from contradicting the appellant's arguments in general, may be summarised as follows:

The auxiliary requests introduced during the oral proceedings resulted in singling out the only condition of the minimum amount of 65%, omitting the upper value of 95% and disregarding the "if" clause constituting the first half of the sentence where the percentages were disclosed in the description as originally filed. In addition, there was a contradiction with regard to the same subject-matter, as represented in the original claims.

In addition, the subject-matter of the patent as granted was not new with respect to document (8).

VIII. The appellant (patentee) requested that the decision under appeal be set aside and that the patent be maintained on the basis of the main request or any of the auxiliary requests 1 to 13 submitted during the oral proceedings.

The respondent (opponent) requested that the appeal be dismissed.

Reasons for the Decision

1. The appeal is admissible.

2. *Fifth, sixth, eleventh and twelfth auxiliary request; admissibility and original disclosure*

2.1 The sets of claims which the appellant for the first time introduced during the oral proceedings were admitted into the proceedings, since by their wording a simple and clear-cut amendment was introduced in direct response to the objections of the respondent.

2.2 *Subject of the amendment*

In each of the claims 1 of these requests, the text indicated in bold by the board is added with respect to claim 1 as granted and as a consequence, component (b) uniformly is defined as

"at least one omega-3 polyunsaturated fatty acid or an ester thereof, **comprising eicosapentaenoic acid (EPA) and/or docosahexaenoic acid (DHA) and/or esters thereof in an amount exceeding 65% by weight of the overall mixture of omega-3 polyunsaturated fatty acids**",

which clearly means that the sum of weights of all present omega-3 polyunsaturated fatty acids or esters is to be taken as 100% and at least one of DHA, EPA and their esters have to amount to at least 65% of it.

2.3 *The amendment and its context in the application as filed*

2.3.1 The amendment relates to preferred omega-3 polyunsaturated fatty acids and their relative quantity in the composition.

2.3.2 The preferred omega-3 polyunsaturated fatty acids are disclosed in the application as originally filed, claim 2 and description, page 5, last but one paragraph, as EPA, DHA and linolenic acid (LNA) and at least by reference as the esters thereof; in the description, EPA and DHA additionally are mentioned as particularly preferred.

2.3.3 In the text following these indications as well in the original claims as in the description (claims 4 and 5; paragraph bridging pages 5 and 6), the optional presence of **non** omega-3 polyunsaturated fatty acids is introduced.

2.3.4 As preferred embodiment in this respect, in the original claims 6 and 7, the percentage of omega-3 fatty acids as part "of the overall mixture of omega-3 and non omega-3 fatty acids" is defined as exceeding 65% and as being lower than 95% respectively.

In parallel to this subject-matter of the claims, it is stated in the description (first paragraph on page 6):

"If one or more of these non omega-3 fatty acids are present, the amount of the aforesaid omega-3 fatty acids, particularly EPA and/or DHA, preferably exceeds

65% and is lower than 95% by weight of the overall mixture of omega-3 fatty acids."

The term "aforesaid omega-3 fatty acids" clearly refers at least to EPA, DHA and LNA, with EPA and DHA in particular, mentioned in the paragraph before this statement, if not to all omega-3 polyunsaturated fatty acids constituting component (b) as set out in the middle of page 5. Therefore, the 100%-value belonging to the percentage of 65 is and has to be "the overall mixture of omega-3 **and non omega-3 fatty acids**" (bold letters by the board) as is laid down in original claims 6 and 7 and the wording in the description has to be classified as to "and non omega-3" being omitted by typographical error.

Thus, from the consistent meaning of the original application (claims and description) the value of 65% is related to all omega-3 (polyunsaturated) fatty acids constituting component (b), as preferred embodiment to EPA, DHA and LNA and as preferred in particular to EPA and DHA as part of all fatty acids being present in the composition. But it never automatically relates to both EPA and DHA specifically as part of the overall mixture of omega-3 polyunsaturated fatty acids.

2.4 *Original disclosure of the amendment with respect to the wording in the application as filed; consequence (Article 123(2) EPC)*

For three reasons, the definition of component (b) being claimed in the fifth, sixth, eleventh and twelfth auxiliary requests is not originally disclosed:

2.4.1 The adjective "polyunsaturated" before the term "fatty acids" at the end of this definition, being the basis of the 100%-reference, is disclosed neither in the description nor in the claims of the application as originally filed and tries to introduce a meaning of the 100%-reference that is not derivable from this disclosure.

2.4.2 The sole passage referring only to 65% - without mentioning 95% in the same context - is claim 6 as originally filed. As already set out above, in this claim, however, it is totally clear that the 100%-value related to it means "the overall mixture of omega-3 and non omega-3 fatty acids" and not "of the overall mixture of omega-3 polyunsaturated fatty acids" as the appellant tries to claim.

2.4.3 Finally, in the requests under examination the appellant tried to isolate a part of a sentence containing an obvious typographical error to claim a subject-matter that is not derivable from the application as originally filed in its overall context and therefore has no basis in the meaning of Article 123(2) EPC.

2.5 Thus, the subject of claims 1 of the fifth, sixth, eleventh and twelfth auxiliary request contains subject-matter which extends beyond the content of the application as filed (Article 123(2) EPC).

3. *Third, fourth, ninth and tenth auxiliary requests; Article 84 EPC*

Since each claim 1 of these auxiliary requests identically contains the feature "65% by weight" without any explicit reference to the entity representing 100%, and since there are at least two possibilities, namely

– "at least one omega-3 polyunsaturated fatty acid"

– or the whole composition

that can constitute the entity representing 100%, these requests are unclear in the meaning of Article 84 EPC.

4. *Seventh and eighth auxiliary requests; Article 84 and Article 123(2) EPC*

4.1 Claims 1 of these two requests contain the following identical passage at the end of the claim:

"wherein the nutritional/pharmaceutical composition consists of:
the above component (a),
the above component (b),
optionally a non omega-3 fatty acid selected from the group consisting of a saturated, monounsaturated, omega-6, omega-9 fatty acid and a mixture thereof,
optionally Vitamin E,
optionally proteins, and
optionally carbohydrates"

4.2 Apart from the fact that deficiencies of clarity are raised with respect to the components to be present "optionally" in these claims 1,

– because "composition consisting of …" does not by itself mean "consisting at maximum of" and
– because, therefore, each of the specified components absolutely must be present in the composition,

there are also deficiencies with respect to the original disclosure:

4.3 Source of original disclosure can only be found in the two examples of compositions on page 13 of the application as originally filed (PCT/IT99/00331) that both contain proteins as well as carbohydrates.

The wording cited above under point 4.1 which was chosen by the appellant, however, comprises compositions containing either proteins alone or carbohydrates alone, which was not the subject-matter of the examples of compositions in the application as filed.

Therefore, claims 1 of the seventh and eighth auxiliary requests do not fulfil the provisions of Article 123(2) EPC.

5. *First, second and thirteenth auxiliary requests; Articles 123(2) and (3); Article 84 EPC*

The additional features set out in these requests are to be found in the application as filed (see the text beginning on page 5, last but one paragraph and ending on page 6, first paragraph) in the context they refer to in the amended claims.

The subject-matter of the thirteenth auxiliary request constitutes a restriction with respect to the claims as granted; its claim 1 contains the features of granted claims 1 and 2 together.

Therefore, the subject-matter as granted is amended in such a way as not to exceed beyond the content of the application as originally filed and as not to extend the protection the patent in suit conferred (Articles 123(2) and (3) EPC).

The amended claims in addition clearly define the subject-matter to be protected and they are supported by the description.

6. *Main request, first, second and thirteenth auxiliary requests; Article 83 EPC*

The board has nothing to add to the argumentation of the opposition division with respect to sufficient disclosure of the invention (claims as granted; main request); the same is applicable in analogy with respect to the teaching of the amended claims of the auxiliary requests in connection with the description.

7. *Main request; Article 54 EPC*

Optional features omitted, the teaching of claim 1 of the patent in suit relates to the

– use of Coenzyme Q_{10} (CoQ_{10}),

- in an amount effective for performing a therapeutical and/or preventive and/or nutritional activity in a human in need thereof,
- in admixture with at least one omega-3 polyunsaturated fatty acid or an ester thereof,
- for preparing a pharmaceutical composition for preventing or treating mitochondriopathies.

As a preferred embodiment in defining the subject-matter of the patent in suit, from the teaching of claim 2 as granted, a disease "Co-enzyme Q_{10} deficiency" is mentioned, which therefore must be included within the meaning of the term "mitochondriopathies".

The teaching of document (8) is that Bioquinon®, 100 mg CoQ_{10} in soy bean oil, is commercially available in Denmark (see first paragraph of the introduction on page s273) and is used for supplementation, meaning the removal of deficiencies of CoQ_{10} in humans (see first two full paragraphs on page s278). Bioquinon® showed the highest bioavailability of CoQ_{10} with regard to the samples under examination in the study (see last two sentences of the abstract on page s273).

Thus, document (8) relates to the

- use of Coenzyme Q_{10} (CoQ_{10}) (see first two paragraphs of the introduction on page s273),
- in an amount effective for performing a therapeutical and/or preventive and/or nutritional activity in a human in need thereof (see first two full paragraphs on page s278, mentioning "p.o. supplementation"),

– in admixture with at least one omega-3 polyunsaturated fatty acid or an ester thereof (see first paragraph of the introduction on page s273, while soy bean oil is known to contain linolenic acid, an omega-3 polyunsaturated fatty acid),
– for preparing a pharmaceutical composition for preventing or treating mitochondriopathies (see first two full paragraphs on page s278, mentioning "p.o. supplementation").

As can be seen from this analysis, all features of claim 1 of the patent in suit are disclosed in document (8), therefore its teaching is fully anticipated (Article 54 EPC).

8. *First and second auxiliary requests; Articles 54 and 56 EPC*

8.1 Claims 1 of the first and second auxiliary requests are restricted to the use of one or both of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) as omega-3 polyunsaturated fatty acids which are not contained in soy bean oil.

Their subject-matter is therefore new with respect to document (8).

The only document introduced into the proceedings which relates to mitochondriopathies in its broad sense is document (5). There, one of the diseases to be treated by CoQ_{10} preparations is "Mitochondriale Krankheiten" which is to be translated as "mitochondriopathies" (see

document (5), claim 1 together with claim 4 and description, page 1, lines 1 and 2).

Just as in document (8), EPA and DHA are not mentioned in document (5) and therefore, also with regard to this document, novelty is to be recognised for the subject-matter of the first and second auxiliary request.

8.2 With respect to the inventive step requirements, the following is to be considered:

8.2.1 Document (5) constitutes the closest prior art. During the oral proceedings, both parties did not introduce any submissions to the contrary.

This document relates to the use of CoQ_{10} in admixture with the pulmonary surfactant for preparing a pharmaceutical composition for preventing or treating mitochondriopathies (claim 1 of document (5) together with claim 4). Pulmonary surfactant is added in order to support the transport of CoQ_{10} to tissue suffering from a lack of this coenzyme (see document (5), page 2, last but one paragraph).

8.2.2 Neither the description of the patent in suit nor the parties' submissions provide any evidence as to a valid comparison of the claimed subject-matter with the subject-matter taught by document (5), the use of CoQ_{10} in admixture with the pulmonary surfactant.

8.2.3 Accordingly, the problem underlying the patent in suit can only be seen in the provision of an alternative in the use of CoQ_{10} for preparing a pharmaceutical

composition for preventing or treating mitochondriopathies.

8.2.4 This problem, according to claim 1 of the first or the second auxiliary request, is solved by admixing EPA and/or DHA to CoQ_{10} (together with additional non omega 3 fatty acid as claimed in the second auxiliary request).

8.2.5 Having regard to the common general knowledge of the person skilled in the art and to the worked examples of the patent in suit with respect to the treatment of photophobia and age-related macular degeneration (ARMD), the board is convinced that the composition as set out in point 8.2.4 above can be used to treat mitochondriopathies und thus the problem has been plausibly solved.

8.2.6 Document (3) is a publication in the same field as that of document (5), namely the problem of absorptivity of CoQ_{10} as active in the treatment of diseases, in particular the remedy of coronary functions (see page 3, lines 16 to 18 together with page 1, lines 1 and 2). Such diseases are also the subject-matter of the teaching in document (5) (see claim 4, "Krankheiten des Herz-Kreislaufs") und thus provide an additional link between these two documents. In this respect, document (3) refers in particular to compositions of CoQ_{10} including a higher fatty acid or a monoglyceride of higher fatty acid (see claim 1). The addition of this fatty acid or esters thereof is said to improve absorptivity of CoQ_{10}, demonstrated by the level of CoQ_{10} measured in the lymph of the treated animals (see

page 8, lines 33 to 35 together with table 1 on page 10).

Since the skilled person, trying to solve the problem related to the patent in suit - which just refers to an alternative - thus knows document (3) and its teaching, and since it is the common general knowledge of the skilled person that fish oil containing EPA and DHA is a common mixture of fatty acids to be introduced in nutritional and pharmaceutical compositions, the board can only conclude that the subject-matter of claims 1 of the first and second auxiliary requests does not involve an inventive step.

8.2.7 This is true, even if claim 1 of the second auxiliary request contains as a further feature the presence of "non omega-3 polyunsaturated fatty acid selected from the group consisting of a saturated, monounsaturated, omega-6, omega-9 fatty acid and a mixture thereof" at the end of the claim. The so-called "selection" expressed in this claim contains all relevant non omega-3 polyunsaturated fatty acids in terms of usual fatty acids to be used in nutritional and pharmaceutical compositions and thus finally amounts to just a synonym for "non omega-3 polyunsaturated fatty acids".

Such fatty acids are bound to accompany the use of EPA and DHA at any time because normally these are not added in totally isolated and purified form but as a component of natural oils like fish oil.

9. *Thirteenth auxiliary request; Articles 54 and 56 EPC*

9.1 Claim 1 of the thirteenth auxiliary request is restricted to the use of omega-3 polyunsaturated fatty acid in admixture with CoQ_{10} for preparing a nutritional/pharmaceutical composition for preventing or treating mitochondriopathies wherein the mitochondriopathy is selected from
CPEO (Chronic Progressive External Ophthalmoplegia Syndrome);
ARMD (Age Related Macular Degeneration) and
NARP (Neuropathy, Ataxia and Retinis pigmentosa).

9.2 Its subject-matter is therefore new with respect to document (8) and document (5) which do not mention omega-3 polyunsaturated fatty acids in the treatment of these particular mitochondriopathies.

9.3 With respect to the inventive step requirements, the following is to be considered:

9.3.1 For the same reasons as set out under point 8.1, document (5) constitutes the closest prior art.

9.3.2 Neither the description of the patent in suit nor the parties' submissions provide any evidence as to a valid comparison of the claimed subject-matter with the subject-matter taught by document (5).

9.3.3 Accordingly, the problem underlying the patent in suit can only be seen in the provision of an alternative in the use of CoQ_{10} for preparing a pharmaceutical composition for preventing or treating mitochondriopathies.

9.3.4 This problem, according to claim 1 of the thirteenth auxiliary request, is solved by admixing omega-3 polyunsaturated fatty acids to CoQ_{10} in the preparation of a nutritional/pharmaceutical composition for preventing or treating mitochondriopathies wherein the mitochondriopathy is selected from CPEO (Chronic Progressive External Ophthalmoplegia Syndrome); ARMD (Age Related Macular Degeneration) and NARP (Neuropathy, Ataxia and Retinis pigmentosa).

9.3.5 Having regard to the common general knowledge of the person skilled in the art and to the worked examples of the patent in suit with respect to the treatment of photophobia and age-related macular degeneration (ARMD), the board is convinced that the composition as set out in point 9.3.4 above can be used to treat mitochondriopathies in general and thus the problem has been plausibly solved.

9.3.6 As already set out under point 8.2.6, the skilled person knows document (3) and document (5), which both relate to the use of CoQ_{10}. Document (3) refers in particular to compositions of CoQ_{10} including linolenic acid or a monoglyceride of linolenic acid as higher fatty acid or monoglyceride of higher fatty acid (see claim 1 of document (3) in connection with page 3, lines 21 to 23 and worked example "specimen 2" on page 6). The addition of this fatty acid or esters thereof is said to improve absorptivity of CoQ_{10}, demonstrated by the level of CoQ_{10} measured in the lymph of treated animals.

Since the skilled person, trying to solve the problem related to the patent in suit, thus knows document (3) and its teaching, he is ready to use the composition of "specimen 2" and, since it is his common general knowledge that CPEO and NARP are mitochondriopathies, the board can only conclude that he will use it for preparing a CoQ_{10}-containing composition for preventing or treating one of these diseases.

Therefore, the subject-matter of claim 1 of the thirteenth auxiliary request does not involve an inventive step either.

10. In the circumstances of the case, the arguments of the appellant cannot succeed:

10.1 Concerning the issue of clarity, the appellant argued that it was clear from the context within the relevant claims that the 65%-value referred to "at least one omega-3 polyunsaturated fatty acid" as being 100%, since both terms appeared in the paragraph defining component (b).

Assuming that there is more than one single possibility, in principle, the mere optical positioning of a percentage within a paragraph - without another clear and unambiguous indication - is not enough to define that the percentage relates to the entity set out in the same paragraph as representing 100% and nothing else.

As an example, in claim 15 of the application as originally filed by the appellant himself and in the patent as granted, the term "… for preparing a

nutritional/pharmaceutical composition …" was also contained in the paragraph defining component (b) and despite this, it was not meant to relate to component (b) only. In reality, it was meant to relate to the use of the whole composition, as can be seen from the optical appearance of the corresponding claim of the main request as filed during the appeal proceedings.

10.2 *Main request; novelty*

In this respect, the appellant argued that the teaching of document (8) finally wouldn't work with respect to the treatment of mitochondriopathies
because the details mentioned were not streamlined in this direction,
because only serum levels of CoQ_{10} were measured and because, finally, the need to develop an intravenous (i.v.) composition was expressed.

Disclosure of document (8), however, starts from the statement, that Bioquinon®, containing CoQ_{10} in soy bean oil, is the reference composition in the market for supplementation of CoQ_{10} (see page s273, last two paragraphs together with page s278, first two full paragraphs). Its teaching is that the authors failed to find a composition exhibiting better bioavailability with respect to serum levels of this active. Maybe they described no full scientific explanation of all the phenomena observed in the disclosed studies, but at least the basic statement is unaffected by this, and in addition it is also in full conformity with the teaching of the patent in suit. Finally, the appellant himself confirms that omega-3 polyunsaturated fatty

acid, in particular also LNA contained in soy bean oil, helps CoQ_{10} to reach the mitochondriae.

In addition, the measurement of serum levels of CoQ_{10} gives no hint that mitochondriae as the target of action would not be reached or membranes not be crossed. On the contrary, high serum level of the active, taken orally, is to be seen as an important prerequisite for reaching cellular structures like mitochondriae at all.

With respect to the suggestion by the authors of document (8) for the development of an i.v. formulation, it has to be stated that this suggestion is only for scientific research designed to "determine the absolute bioavailability of p.o. CoQ_{10} formulations" (see page s279, paragraph 2) which has nothing to do with Bioquinon® and its successful use.

10.3 *First and second auxiliary requests; inventive step*

As far as inventive step is concerned, the appellant argued that the skilled person would not have taken into account document (3) as secondary state of the art together with document (5), because the examination of lymphatic levels of CoQ_{10} had nothing to do with mitochondriae.

In the same way as with respect to the serum levels reported in document (8), however, the lymphatic levels of CoQ_{10} have to be seen rather as a support than a hindrance with regard to effects for treating mitochondriopathies.

As a further argument, the appellant claimed an improvement with respect to the state of the art, in particular document (5).

Since the teaching of the main request is not new with respect to document (8), this argumentation is to be seen in the light of the particular features in claim 1 of the first and second auxiliary requests respectively, the use of EPA and/or DHA or their esters:

10.3.1 Evidence for improvement by way of clinical trials

In addition to the fact that there is no evidence supporting the effect of improvement with respect to the closest prior art, namely document (5) disclosing CoQ_{10} compositions in admixture with pulmonary surfactant, even the reports of clinical trials on file do not provide evidence of any advantage of compositions containing EPA or DHA or their esters as additives.

The only compositions used in the disclosed clinical trials and evidently containing DHA or EPA or their esters are those containing fish oil. Compositions containing "omega 3(>65%)" are not identified as containing DHA or EPA or their esters, as is set out under point 2.3.4 of this decision. Such a content cannot be derived from the indication of the percentage of 65% alone.

With respect to compositions containing fish oil, there is no evidence of any advantage of these compositions in the description of the clinical trials, either by way of describing effects in words or by presenting any

comprehensive numbers. The percentages contained in the tables give no meaningful information since they are not defined in any way and no reasonable meaning can be deduced from the text accompanying these tables.

The two examples specifically mentioned by the appellant, represented by the last two lines in table III of the patent in suit, suffer from both problems described above:

First, there is no evidence that "omega-3(>65%)" contains DHA or EPA or their esters and thus the data from the second trial does not disclose anything in favour of the use of these fatty acids.

The second problem is that the appellant submitted that, despite the absence of an explicit definition in the description of the patent in suit, the percentages in tables I to III should be read as "persons reacting to the mixture of CoQ_{10} and omega-3 fatty acid / persons in trial" with respect to the "Macular Photo Stress Test".

But in the absence of an explicit definition of figures, for instance percentages, presented in a patent, the arguments in favour of a particular meaning of these figures must be convincing.

The structure of the values of the percentages delivered in the patent in suit, however, does not support the appellant's definition; on the contrary, it renders the explanation as good as impossible:

On the one hand, if 16 persons are being treated within the trial documented in table II (see page 5 of the

patent, line 3), one person relates to 6.3%. Thus, the figures in table II representing persons reacting to the treatment should vary in steps of 6.3%, or at least in steps of 3.15% to enable the inventor to count half persons in situations where he was unable to determine whether a reaction was given or not, as the appellant submitted. But values of 7.3%, -1.2% or -2.3% are not in accordance with such a pattern.

On the other hand, the values for use of "858 mg omega-3" are intended to represent successful treatment. However, if the submission of the appellant was correct, the last line of table II represented 3 persons of 16 and the last line of table III represented 15.1% of 43 persons, that is 6.5 persons, neither figure supporting real success in the treatment of diseases.

Thus, the skilled person finds himself prevented from deducing any advantage for the compositions used in accordance with the teaching of claims 1 of the first and the second auxiliary requests.

10.3.2 Evidence for improvement by way of plausibility

The appellant tried to make clear that the skilled person would be sure from reading document (5) together with his common general knowledge that CoQ_{10}, admixed with pulmonary surfactant, per se was not able to reach the mitochondriae and therefore, treatment of mitochondriopathies as alleged in claim 4 of document (5) would not work. Thus, the teaching of the patent in suit was in any case superior to that of document (5). In particular, the well-known effect of pulmonary surfactant in wetting the surfaces of the

lung because of the bipolar nature of surfactants would cast doubt on the assertion that CoQ_{10} was enabled by pulmonary surfactant to cross mitochondrial membranes, as opposed to the omega-3 polyunsaturated fatty acids used in the teaching of the patent in suit.

In document (5), however, pulmonary surfactant is set out to be a complex of phospholipids, neutral lipids and surfactant proteins. Thus, the submission of the appellant does not give all the details necessary to estimate credibility of effects of pulmonary surfactant or the credibility of the teaching of this document. In addition, it is the very heart of the claimed invention of document (5) that pulmonary surfactant surprisingly is able to enter the outer skin and the mucous membranes of the gastro-intestinal region, the mouth and the vagina and that, therefore, compositions containing CoQ_{10} can be made more effective (see page 2, paragraph 2 and page 1, last paragraph, lines 1 to 3).

Thus, there is no evidence of a prejudice on the part of the person skilled in the art that the teaching of document (5) would not work and that the teaching of the patent in suit was therefore automatically at an advantage over this state of the art.

11. Thus, the subject-matter of the fifth to eighth and of the eleventh and twelfth auxiliary requests does not meet the requirements of Article 123(2) EPC, the subject-matter of the third, fourth, ninth and tenth auxiliary requests is not in line with the provisions of Article 84 EPC, the subject-matter of the main request is not new (Article 54 EPC) and the subject-matter of the first, second and thirteenth auxiliary

requests does not meet the requirements of Article 56 EPC.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

N. Maslin U. Oswald