Internal distribution code:

(A) [-] Publication in OJ
(B) [-] To Chairmen and Members
(C) [-] To Chairmen
(D) [X] No distribution

Datasheet for the decision of 22 November 2016

Case Number: T 1120/12 - 3.3.04

Application Number: 00937919.9

Publication Number: 1185298

IPC: A61K39/395, A61K38/17, A61K39/39, A61K39/00, G01N33/68, A61K48/00, A61P25/28

Language of the proceedings: EN

Title of invention:
Prevention and treatment of amyloidogenic disease

Patent Proprietor:
Janssen Alzheimer Immunotherapy

Opponent:
H. Lundbeck A/S

Headword:
Amyloidogenic disease/JANSSEN

Relevant legal provisions:
EPC Art. 56
RPBA Art. 12(2)

Keyword:
"Main request and auxiliary requests 1 to 3 - claim 1 - inventive step (no)"
"Admission of auxiliary request 4 into proceedings (no)"

Decisions cited:

Catchword:
-

Europäisches Patentamt
European Patent Office
Office européen des brevets

Beschwerdekammern
Boards of Appeal
Chambres de recours

European Patent Office
D-80298 MUNICH
GERMANY
Tel. +49 (0) 89 2399-0
Fax +49 (0) 89 2399-4465

Case Number: T 1120/12 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 22 November 2016

Appellant: (Opponent)	H. Lundbeck A/S Ottilavej 9 2500 Valby (DK)
Representative:	Hoffmann Eitle Patent- und Rechtsanwälte PartmbB Arabellastraße 3081925 München (DE)
Respondent: (Patent Proprietor)	Janssen Alzheimer Immunotherapy Little Island Industrial Estate Little Island, County Cork (IE)
Representative:	Goodfellow, Hugh Robin Carpmaels & Ransford LLP One Southampton Row London WC1B 5HA (GB)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 17 February 2012 rejecting the opposition filed against European patent No. 1185298 pursuant to Article 101(2) EPC.**

Composition of the Board:

Chairwoman	G. Alt
Members:	B. Claes
	M. Blasi

Summary of Facts and Submissions

I. The appeal is of the opponent (hereinafter "appellant") against the decision of the opposition division to reject the opposition to European patent No. 1 185 298. The patent is based on European patent application 00 937 919.9, which was filed as an international application published as WO 00/72880 and has the title "*Prevention and treatment of amyloidogenic disease*". The application claims priority from US application No. 09/322,289.

Claim 1 of the patent in suit read:

"1. An Aβ fragment linked to a carrier peptide for use in inducing an immune response against Aβ and thereby preventing or treating a disease associated with amyloid deposits of Aβ in the brain of a patient, wherein the Aβ fragment consists of:

i) Aβ1-7 having the amino acid sequence DAEFRHD
ii) Aβ3-7 having the amino acid sequence EFRHD, or
iii) a multimer of i) or ii)."

II. The following documents are cited in this decision:

D1: WO 99/27944

D4: Declaration by Dr. Wehner dated 21 May 2007

D5: Rammensee (1995), Curr. Opin. Immunol., Vol. 7, No. 1, pages 85-96.

D6: Hoch *et al.* (2003), Neuron, Vol. 38, No. 4, Pages 547-554.

D16: Declaration by Dr Hagen dated 31 October 2011

III. The opposition was based on the grounds for opposition under Article 100(a) EPC, here concerning novelty (Article 54 EPC) and inventive step (Article 56 EPC), and Article 100(b) and Article 100(c) EPC.

IV. In the statement of grounds of appeal the appellant requested that the decision under appeal be set aside and the patent in suit be revoked.

V. With its reply the respondent (patent proprietor) argued, as a main request, that the appeal be dismissed and filed four further requests, *i.e.* auxiliary requests 1 to 4.

Claim 1 of auxiliary request 1 read:

"1. An Aβ fragment, or multimer thereof, linked to a carrier peptide for use in inducing an immune response against Aβ and thereby preventing or treating a disease associated with amyloid deposits of Aβ in the brain of a patient, wherein the Aβ fragment consists of:

i) Aβ1-7 having the amino acid sequence DAEFRHD
ii) Aβ3-7 having the amino acid sequence EFRHD."

Claim 1 of auxiliary request 2 read:

"1. An Aβ fragment linked to a carrier peptide for use in inducing an immune response against Aβ and thereby preventing or treating a disease associated with

amyloid deposits of Aβ in the brain of a patient, wherein the Aβ fragment consists of:

i) Aβ1-7 having the amino acid sequence DAEFRHD; or
ii) Aβ3-7 having the amino acid sequence EFRHD."

Claim 1 of auxiliary request 3 was identical to claim 1 of the patent as granted (see section I).

Claim 1 of auxiliary request 4 read:

"1. A pharmaceutical composition comprising an Aβ fragment linked to a carrier peptide and a pharmaceutically acceptable adjuvant, for use in inducing an immune response against Aβ and thereby preventing or treating a disease associated with amyloid deposits of Aβ in the brain of a patient, wherein the Aβ fragment consists of:

i) Aβ1-7 having the amino acid sequence DAEFRHD
ii) Aβ3-7 having the amino acid sequence EFRHD, or
iii) a multimer of i) or ii)."

VI. Oral proceedings were held in the absence of the respondent who had informed the board of its non-attendance beforehand in writing. At the end of the oral proceedings the chairwoman announced the decision of the board.

VII. The arguments of the appellant, submitted in writing and at the oral proceedings, in as far as they are relevant for the decision under appeal, can be summarised as follows:

Inventive step (Article 100(a) EPC in combination with Article 56 EPC; Article 56 EPC)

Main request and auxiliary requests 1 to 3 - claim 1

Document D1 disclosed the use of Aβ and fragments thereof for inducing an immune response and preventing or treating a disease associated with amyloid (Aβ) deposits (see examples I to IV). Of the tested antigens, only two were reported to reduce amyloid burden, *i.e.* the full length, aggregated Aβ1-42 and the conjugated Aβ1-5 fragment (document D1, page 53, third full paragraph). Document D1 furthermore disclosed that the Aβ1-5 conjugate was effective at significantly reducing the level of Aβ in the brain (page 56, last line to page 57, line 1) and that a T-cell response was absent (see page 56, lines 25-30).

As compared to the claimed subject-matter relating to the Aβ1-7 fragment the disclosure in document D1 of Aβ1-5 required a minimum of structural modifications and was a suitable starting point for the assessment of inventive step.

The difference between the claimed subject-matter and the disclosure in document D1 was the use of Aβ1-7, rather than of Aβ1-5 fragment.

Paragraph [0040] of the patent acknowledged that document D1 taught the treatment of Alzheimer's disease by Aβ compounds but that the patent however was

directed to "improved" agents and methods, *i.e.* the identification of epitopes within Aβ resulted in agents and methods having increased efficacy, reduced potential for side effects, and/or greater ease of manufacture, formulation and administration. These constituted however general desiderata for every drug development, *i.e.* better efficiency, less side effects and easier manufacturing. Therefore, the patent was silent what the improvement over document Dl was and/or which surprising and unexpected benefit might be provided by Aβl-7 (and Aβ3-7) over Aβl-5 or over the full-length Aβ1-42.

Neither the patent nor document D1 appreciated that T-cell epitopes had to be avoided in the fragments. In fact, exactly the same passages were present in the patent in suit (see paragraphs [0200] and [0201]) and document D1 (see page 56, line 24 to page 57, line 12) on the topic of T-cell epitopes. Furthermore, the patent did not demonstrate that Aβl-7 (and Aβ3-7) was devoid of T-cell epitopes. Support for the argument that Aβl-7 did not contain a T-cell epitope had been filed by the proprietor only later (see document D4).

The patent declared Aβ1-5 as one of the preferred fragments that solved the problem (see paragraph [0048]. Accordingly, document D1 already disclosed a fragment which reportedly solved the purported problem. The problem over D1 could thus be formulated as the provision of alternative fragments of Aβ, as the claimed fragments were not associated with any unexpected benefit.

Providing an Aβ fragment which was slightly longer by two amino acids than Aβl-5 could not be regarded as inventive. Aβl-7 did not solve any problem over the

prior art and was not associated with any unexpected effect. It constituted a mere obvious workshop variant that did not solve any problem over Aβ1-5 of document D1.

Even if Aβ1-42, disclosed in document D1, represented the closest prior art the claimed subject-matter lacked an inventive step. Simply screening a larger fragment for smaller epitopes (as presented in Figures 18 and 19 of the patent) and - as was expected by the skilled person - identifying some fragments which work better and some that work less good than the larger fragment was not inventive, but constituted mere routine screening methodology.

Auxiliary request 4 - admission into the proceedings (Article 12(2),(4) RPBA)

Claim 1 concerned an entirely new aspect of the claimed subject-matter, namely reciting the adjuvant in the pharmaceutical composition comprising the Aβ fragment. Although the amendment may appear in response of problems under Article 83 EPC, no explanation was provided why they were only filed in appeal, whereas sufficiency objections were already submitted with the opposition.

The amendment was based on passages in the description as filed and entirely changed the respondent's case.

The request did also not address certain added subject-matter issues remedied by higher ranking requests, *i.e.* relating to "multimer", and the dependency issue of claim 23, and thus *prima facie* did not solve the existing problems as it was not hierarchical.

Moreover, even though claim 1 of this auxiliary request goes back to granted claims, the respondent provided no arguments how it would overcome the objection of lack of inventive step raised against these claims already in opposition.

VIII. The arguments of the respondent, submitted in writing and in as far as they are relevant for the decision under appeal, can be summarised as follows:

Inventive step (Article 100(a) EPC in combination with Article 56 EPC; Article 56 EPC)

Main request and auxiliary requests 1 to 3 - claim 1

If document D1 constituted the closest prior art, its whole disclosure had to be taken into account, not just one selected part of it. Document D1 not only disclosed the Aβ1-5 fragment and its therapeutic utility, but also many other therapeutically useful fragments of Aβ. The appellant had not explained why the skilled person would select the Aβ1-5 fragment as the fragment to modify in order to solve the problem.

Document D1 did not identify Aβ1-7 (and Aβ3-7) as therapeutically useful fragments. The last sentence of paragraph [0040] of the patent explicitly described the surprising advantage of the claimed Aβ fragments as the reduction of the potential for side-effects that other fragments might cause. In addition, the claimed fragments were able to induce multiple classes of antibodies which were shown in Example XIV to be effective at clearing amyloid deposits.

The reduced possibility of side-effects was provided by the demonstrated lack of T-cell epitopes in the claimed Aβ fragment (see paragraph [0255] of the patent and document D4).

T-cell epitopes were normally 9 amino acids or longer, but could occasionally be shorter in synthetic peptides (see document D5). Later clinical trials demonstrated that in human subjects receiving Aβ 6% of patients experienced inflammatory side-effects due to the generation of a T-cell response against Aβ (see document D6).

Three principle epitopes were shown to be responsible for amyloid deposit clearing, *i.e.* occupying residues 1-5, 3-6 and 3-7 of Aβ and the Aβ1-7 fragment was sufficiently long to include all three (see table 16 of the patent). Aβ1-7 could thus unexpectedly induce three classes of antibodies which were effective in clearing deposits. This made Aβ1-7 particularly useful in treating Alzheimer's disease. Document D16 confirmed that Aβ1-7 (linked to a carrier) raised a significantly higher antibody titer than Aβ1-5. Whereas the antibody titer might not directly correlate to therapeutic efficacy, a fragment that raised more antibodies *in vivo* was more likely to raise antibodies that were particularly useful.

Aβ1-7 was thus able to induce multiple classes of antibodies that were effective in clearing amyloid deposits without at the same time inducing a T-cell response against Aβ, which reduces the possibility of side-effects. Both advantages were described in the application as filed and made the Aβ1-7 fragment particularly useful in treating Alzheimer's disease.

Document D1 did not suggest that the Aβ1-7 fragment would have these combined properties.

The problem to be solved starting from the teaching in document D1 was not therefore merely the provision of alternative peptides for the treatment of diseases associated with Alzheimer's disease, but rather the identification of improved peptides for this purpose.

Although, document D1 observed that Aβ1-5 did not generate a lymphoproliferative (T-cell) response against Aβ, it was however silent whether this absence might be an advantage aspired *i.e.* that generating such a T-cell response was a "risk" that was to be avoided (see paragraphs [0200] and [0201]).

Document D1 did not motivate the skilled person to modify the Aβ1-5 fragment and expect the specific Aβ1-7 fragment (and AP3-7 fragment) to be advantageous.

Examples XIV and XVI of the patent demonstrated the utility of the claimed Aβ1-7 fragment. Example XIV, in particular Table 16, showed that antibodies binding to epitopes within Aβ1-7 both bind and clear amyloid deposits. Other tested epitopes in the same region (Aβ4-10 and Aβ5-10) were shown not to induce phagocytosis. Example XVI of the patent demonstrated furthermore that the Aβ1-7 fragment linked to a tetanus toxoid carrier, in MAP configuration, showed a significant lowering of cortical Aβ levels in a mouse model of Alzheimer's disease which allowed the conclusion that the immunogen was effective in inducing a sufficient immune response significantly to retard Aβ deposition in the cortex (see paragraph [0270]).

Auxiliary request 4 - admission into the proceedings (Article 12(2),(4) RPBA)

The claims of this request were limited to recite a pharmaceutical composition comprising an adjuvant, for which basis could be found in the application as filed.

IX. The appellant requested that the decision under appeal be set aside and the patent be revoked. It requested to not admit into the proceedings auxiliary request 4, filed by the respondent with the reply to appellant's statement of grounds of appeal.

The respondent requested in writing that the appeal be dismissed (main request), or alternatively, that, whilst setting aside the decision under appeal, the patent be maintained in amended form on the basis of one of the sets of claims filed as auxiliary requests 1 to 4 with the reply to the statement of grounds of appeal (see section V).

Reasons for the Decision

1. The appeal is admissible.

2. Oral proceedings were held and the appeal proceedings continued in the absence of the duly summoned respondent in accordance with Rule 115(2) EPC and Article 15(3) RPBA. In accordance with the latter provision, the respondent was treated as relying on its written case, *i.e.* on the content of the reply to the statement of grounds of appeal being the sole substantive submission filed by the respondent. By not attending the oral proceedings, the respondent availed

itself of the opportunity to present any comments on the issues addressed at the oral proceedings.

Validity of the claimed priority

3. The opposition division held that the subject-matter of claim 1 of the patent as granted could not be accorded the priority date because the fragments Aβ1-7 and Aβ3-7 were not disclosed in the application from which priority was claimed (see section I). Accordingly, document D1 was considered state of the art in accordance with Article 54(2) EPC.

4. The respondent has not argued differently and the board also concurs with finding of the opposition division in this respect. Accordingly, the effective date for the claimed subject-matter in patent in suit is the filing date.

Inventive step (Article 100(a) EPC in combination with Article 56 EPC; Article 56 EPC)

Main request and auxiliary request 3 - claim 1

5. The claimed invention relates to fragments of a peptide termed Aβ or β-amyloid peptide being the principle constituent of amyloid deposits, so-called senile plaques, formed in the brain of patients with Alzheimer's disease. Aβ peptide is an internal fragment of 39 to 43 amino acids of a precursor protein called amyloid precursor protein (APP). Mutations in APP are thought to promote generation of Aβ and the deposition thereof and thereby to cause Alzheimer's disease.

6. Claim 1 (see sections I and V) is *inter alia* for fragment 1-7 or 3-7 of Aβ (*i.e.* Aβ1-7 and Aβ3-7) linked to a carrier peptide for use in inducing an immune response against Aβ thereby preventing or treating a disease associated with amyloid deposits of Aβ in the brain of a patient.

7. During the oral proceedings the board decided that the the subject-matter of claim 1 in the aspects relating to fragment Aβ1-7 lacked an inventive step. In view of the following reasoned negative judgement in this respect a decision of the board on the aspects of the claim relating to Aβ3-7 is not required.

The closest prior art

8. In order to assess whether or not a claimed invention meets the requirements of Article 56 EPC, the boards of appeal apply the "problem and solution" approach, which requires as a first step the identification of the closest prior art. In accordance with the established case law of the boards of appeal, the closest prior art is a teaching in a document conceived for the same purpose or aiming at the same objective as the claimed invention (Case Law of the Boards of Appeal of the European Patent Office, 8th edition 2016, I.D.3.1).

9. Like the opposition division in the decision under appeal, the appellant considered document D1 to represent the closest prior art. Document D1 is an earlier patent application by the same applicant as the proprietor of the patent in the field of the prevention and treatment of amyloidogenic disease, such as Alzheimer's disease (AD). The disclosures of document D1 and the patent overlap to a large extent. Both

documents also have examples I to X and a large portion of example XI in common.

10. The common disclosure of the two documents, which therefore constitutes a teaching comprised in the prior art, relates in its most pertinent parts *inter alia* to the immunisation of so-called PDAPP mice with Aβ or with non-conjugated and conjugated smaller fragments thereof originating from different parts of Aβ. Joint example III discloses that the immunisation of PDAPP mice with the human aggregated long form of Aβ, *i.e.* Aβ1-42, results in the prevention of Aβ plaque formation and reduction of amyloid plaque deposits already established in the brain. Joint example IV discloses the screening of four specific human Aβ fragments conjugates, *i.e.* linked to a carrier peptide (see patent [0185]) in the immunisation of PDAPP mice to determine which epitopes convey the response reported on in example III. A reduction of established amyloid plaques, including a reduction in total Aβ in the brain of PDAPP mice, was achieved by immunisation with a conjugated Aβ1-5 fragment being derived from the N-terminus of human Aβ. Immunisation of PDAPP mice with conjugates of the three other human Aβ fragments which were screened, *i.e.* sheep anti-mouse IgG-conjugated Aβ1-12, Aβ13-28 and Aβ33-42 fragment conjugates, as well as an aggregated Aβ25-35 fragment, did not significantly reduce either the amount of established amyloid plaques or the total amount of Aβ in the brain of PDAPP mice (see document D1, page 52, lines 15 to 23 and page 53, lines 23 to 28 and the patent paragraphs [0189] and [0193]).

11. Although the respondent has not contested the appropriateness of document D1 to represent the closest prior art, it was however argued that the entire

content of document D1 ought to be considered and not merely the Aβ1-5 fragment conjugate disclosed therein.

12. The board can concur with the respondent, that rather than solely the disclosure of the Aβ1-5 fragment, the whole teaching in document D1 represents the closest prior art for the skilled person. Hence and in this context, the relevant insights disclosed in document D1 are that, whereas immunisation with conjugates of the human Aβ1-12, Aβ13-28 and Aβ33-42 fragments (and an aggregated human Aβ25-35 fragment of Aβ), *i.e.* four fragments spanning the whole of the Aβ1-42 form of Aβ, did not lead to a reduction of established amyloid plaques, including a reduction in total Aβ in the brain of PDAPP mice, as could be observed for immunisation with the aggregated Aβ1-42, this effect *was* however achieved by immunisation with the conjugated human Aβ1-5 fragment. Of particular note in this context is that, whereas the conjugate of the human Aβ1-5 fragment is able to achieve the desired technical effect, the larger human Aβ1-12 fragment conjugate, comprising the Aβ1-5 fragment, failed to do so.

The technical problem and its solution

13. According to established case law of the boards of Appeal the technical problem is formulated by taking into account those features distinguishing the claimed invention from the disclosure of the closest prior art and the technical effects caused thereby.

14. The subject matter of claim 1 relates to the human Aβ1-7 fragment conjugate as therapeutically useful in inducing an immune response against Aβ and thereby preventing or treating a disease associated with amyloid deposits of Aβ in the brain of a patient.

15. As to features distinguishing this human Aβ1-7 fragment from the fragments disclosed in the closest prior art, the Aβ1-7 fragment is two amino acids longer than the Aβ1-5 fragment, but 5 amino acids shorter than the Aβ1-12 fragment. As to the effect caused by this difference the board is satisfied that for the purpose of the present assessment examples IX and XI of the patent can be accepted to demonstrate the same technical effect for the Aβ1-7 fragment conjugate as for the Aβ1-5 fragment conjugate disclosed in document D1 in terms of a reduction of established amyloid plaques, including a reduction in total Aβ in the brain of PDAPP mice.

16. The respondent has submitted however, that there was a further feature distinguishing the claimed compounds from those of the closest prior art. It was argued that in particular the last sentence of paragraph [0040] of the patent explicitly described the surprising advantage of the claimed Aβ fragment as the reduction of the potential for side-effects that other fragments might cause. This reduction of the potential for side-effects was provided by the absence of T-cell epitopes in the Aβ1-7 fragment (see paragraph [0255] of the patent and document D4) this absence accordingly being a further distinguishing feature.

17. The board notes in this context however that both document D1 (see page 56, line 24 to page 57, line 3) and the patent in suit (see paragraph [0200]) equally disclose: "*These results show that AN 1792 and AN 1528 stimulate strong T cell responses, most likely of the $CD4^+$ phenotype. The absence of an Aβ-specific T cell response in animals immunized with Aβ1-5 is not surprising since peptide epitopes recognized by $CD4^+$ T cells are usually about 15 amino acids in length,*

although shorter peptides can sometimes function with less efficiency. Thus the majority of helper T cell epitopes for the four conjugate peptides are likely to reside in the IgG conjugate partner, not in the Aβ region. This hypothesis is supported by the very low incidence of proliferative responses for animals in each of these treatment groups. Since the Aβ1-5 conjugate was effective at significantly reducing the level of Aβ in the brain, in the apparent absence of Aβ-specific T cells, the key effector immune response induced by immunization with this peptide appears to be antibody."

18. Accordingly, the board is of the opinion that rather than being a feature distinguishing the claimed Aβ1-7 conjugate from the Aβ1-5 conjugate disclosed in the closest prior art, the reported lack of T-cell epitopes in the Aβ1-7 conjugate constitutes a feature in common between the claimed subject-matter and the Aβ1-5 conjugate disclosed in the prior art.

19. The board can concur with the appellant that, as such, there is no explicit disclosure in document D1 that a T-cell response against Aβ was undesirable and an advantage aspired. The board considers however that the skilled person would infer from the disclosure in document D1 that the presence of T-cell epitopes is not required for successfully formulating Aβ fragment conjugates having the required therapeutic utility.

20. In view of these considerations the board can agree with the respondent and the opposition division that the problem to be solved, starting from the disclosure in document D1, was not therefore merely the provision of alternative peptides for the treatment of diseases

associated with amyloid deposits Aβ in the brain, such as Alzheimer's disease, as was argued by the appellant.

21. The board judges that, rather, the technical problem to be solved is the identification of further conjugates of peptides derived from Aβ for the treatment of diseases associated amyloid deposits Aβ in the brain, such as with Alzheimer's disease, which do not generate a T-cell response against Aβ. The solution to this problem are, *inter alia*, conjugates with Aβ1-7.

Obviousness

22. Document D1 teaches already a fragment of Aβ1-42 which reportedly solves the technical problem underlying the present invention, *i.e.* the Aβ1-5 conjugate. Furthermore, the skilled person was taught in document D1 (see point 15 above) that peptide epitopes recognised by $CD4^+$ T cells are usually about 15 amino acids in length and also the respondent has submitted that T-cell epitopes are normally 9 amino acids or longer, but could occasionally be shorter in synthetic peptides (see document D5). Accordingly, the skilled person would not expect to generate T-cell epitopes by adding one or a few further amino acids of the N-terminal part of the Aβ1-42 to the Aβ1-5 conjugate.

23. On the other hand, the skilled person was taught in document D1 that the human Aβ1-5 conjugate fragment was able to achieve the desired technical effect whereas the slightly larger human Aβ1-12 fragment conjugate, comprising the Aβ1-5 fragment, failed to do so.

24. The board judges that the above considerations would incite the skilled person having the desire of formulating further conjugates of peptides derived from

Aβ for the treatment of diseases associated with Alzheimer's disease, which do not generate a T-cell response against Aβ, *i.e.* conjugates other than the Aβ1-5 fragment, to formulate slightly extended versions of the Aβ1-5 conjugate, such as Aβ1-6, Aβ1-7 and Aβ1-8 in the firm believe of a reasonable expectation that these fragments successfully solve the objective technical problem.

25. The respondent has argued additionally that the data in table 16 on page 46 of the patent demonstrated that at least three epitopes were responsible for amyloid deposit clearing, *i.e.* occupying residues 1-5, 3-6 and 3-7 of Aβ. These three fragments were able to induce three different classes of antibodies, *i.e.* IgG2b, IgG1and IgG2a, respectively. The claimed Aβ1-7 fragment was sufficiently long to include all three of these epitopes and thus unexpectedly able to induce three classes of antibodies which were effective in clearing deposits. Accordingly, Aβ1-7 conjugates were thus characterised by a further advantageous property, *i.e.* the ability to induce multiple classes of antibodies that were effective in clearing amyloid deposits in the absence of a T-cell response against Aβ, which reduces the possibility of side-effects. This was not obvious in the light of the prior art.

26. However, the board notes that the respondent has provided no arguments whether, and in how far, the alleged advantageous structural particulars of Aβ1-7 related to the presence of multiple epitopes also advantageously contributed to the technical effect aimed to be achieved by the invention, namely the treatment of diseases associated with amyloid deposits Aβ in the brain, such as Alzheimer's disease by means of a reduction of established amyloid plaques,

including reduction of total Aβ in the brain of patients. In fact, it has been acknowledged by the respondent that there is no direct correlation between antibody titer and therapeutic efficiency. In the absence of such correlation these structural particulars referred to by the respondent can, in the opinion of the board, not contribute to the non-obviousness of the subject-matter of claim 1.

27. In view of these considerations the subject-matter of claim 1 of the main request and auxiliary request 3 lacks an inventive step.

Auxiliary requests 1 and 2 - claims 1

28. Claim 1 of both auxiliary request 1 and 2 (see section V) relate to the same subject-matter as for which the board came to a negative conclusion on inventive step. Accordingly, the above findings apply *mutatis mutandis* to these claims.

29. The subject-matter of claim 1 of auxiliary requests 1 and 2 thus lacks an inventive step.

Auxiliary request 4 - admission into the proceedings (Article 12(2), (4) RPBA)

30. According to Article 12(4) RPBA, everything presented by the parties under Article 12(1) RPBA, in particular in the reply to the grounds of appeal (*cf.* Article 12(1)(b) RPBA), shall be taken into account by the board if and to the extent it relates to the case under appeal and meets the requirements of Article 12(2) RPBA, the board having the power to hold inadmissible facts, evidence or requests which could have been presented or were not admitted in the first

instance proceedings. Article 12(2) RPBA *inter alia* provides that the reply to the statement of grounds of appeal shall contain a party's complete case, set out clearly and concisely why it is requested that the decision under appeal be upheld and should specify expressly all the facts, arguments and evidence relied on.

31. Claim 1 of auxiliary request is for a pharmaceutical composition comprising the Aβ1-7 fragment conjugate and an adjuvant. The request, in relation to which the appellant had requested that it not be admitted into the proceedings, was filed with the reply to the appellant's statement of grounds of appeal.

32. The board considers the appellant's argument that no reasons were given why this claim request was only filed in appeal, which alludes to the aspect that this auxiliary request not only could, but also should have already been filed during opposition proceedings, of little weight in the circumstances of the present case. Following a preliminary opinion of the opposition division that the patent as granted fulfilled the requirements of the EPC, the opposition had been rejected during the oral proceedings before the opposition division without any new aspects arising. Therefore, the board cannot identify a situation during the opposition proceedings in which the filing of an auxiliary request by the respondent was procedurally required to such extent that this omission should be detrimental to the respondent at the appeal stage. The respondent's presentation of this auxiliary request at the appeal stage only is therefore not procedurally objectionable.

33. However, when filing this claim request together with the reply to the statement of grounds of appeal, the respondent has not explained how this request would remedy all issues addressed by the appellant in relation to the patent as granted. In particular, claim 1 of auxiliary request 4 is based on granted claims 13 and 15 and the latter claims had been objected to by the appellant in the notice of opposition for lack of inventive step. In such a situation, the mere information in the respondent's reply to the statement of grounds of appeal as to where in the application as filed the basis for the claimed subject-matter can be found, and addressing the topic of sufficiency of disclosure, but omitting any explanation as to why the claimed subject-matter of this auxiliary claim request involved an inventive step did not, in the board's view, represent a sufficient substantiation of this claim request within the meaning of Article 12(2) RPBA.

34. In view of these considerations the board did not admit auxiliary request 4 into the proceedings in accordance with Article 12(4) RPBA.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The patent is revoked.

The Registrar: The Chairwoman:

P. Cremona G. Alt

Decision electronically authenticated