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**Datasheet for the decision  
of 4 May 2012**

**Case Number:** T 0030/09 - 3.3.04

**Application Number:** 00111108.7

**Publication Number:** 1 158 003

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A61K 39/00

**Language of the proceedings:** EN

**Title of invention:**  
Antibodies capable to selectively detect prion PrP<sup>Sc</sup> isoforms

**Patentee:**  
Blood Transfusion Centre of Slovenia

**Opponent:**  
Prionics AG

**Headword:**  
Antibodies to the prior PrP<sup>Sc</sup> isoform/BLOOD TRANSFUSION CENTRE  
SLOVENIA

**Relevant legal provisions:**  
EPC Art. 54, 56

**Keyword:**  
"Main request: all patentability requirements of the EPC  
fulfilled (yes)"



Case Number: T 0030/09 - 3.3.04

**D E C I S I O N**  
of the Technical Board of Appeal 3.3.04  
of 4 May 2012

**Appellant:** Prionics AG  
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**Decision under appeal:** Interlocutory decision of the Opposition  
Division of the European Patent Office posted  
1 September 2008 concerning maintenance of  
European patent No. 1158003 in amended form.

**Composition of the Board:**

**Chairman:** C. Rennie-Smith  
**Members:** G. Alt  
R. Gramaglia

## Summary of facts and submissions

- I. This is an appeal by the opponent (hereinafter "appellant") against the decision of the opposition division expressing its intention to maintain the European Patent No. 1 158 003 in amended form on the basis of the main request. The title of the patent is "Antibodies capable to selectively detect prion PrP<sup>Sc</sup> isoforms".
- II. The main request comprised nine claims. Claim 1 read:
- "1. An antibody binding exclusively to a PrP<sup>Sc</sup> isoform of the prion protein and recognizing the epitope having the three dimensional conformation provided by the protein sequence
- Cys-Ile-Thr-Gln-Tyr-Glu-Arg-Glu-Ser-Gln-Ala-Tyr-Tyr
- of the PrP<sup>Sc</sup> isoform of the prion protein while not binding to the PrP<sup>C</sup> form, obtainable by a method comprising the step of immunising an animal with a peptide consisting of the amino acid sequence
- Cys-Ile-Thr-Gln-Tyr-Glu-Arg-Glu-Ser-Gln-Ala-Tyr-Tyr
- or
- Cys-Ile-Thr-Gln-Tyr-Gln-Arg-Glu-Ser-Gln-Ala-Tyr-Tyr."
- Claims 2 to 4 were dependent on claim 1. The use of the antibody of any of claims 1 to 4 for the preparation of an agent for diagnosis was the subject-matter of claim 5 and their use in a kit for diagnosis that of

claim 7. Claim 6 related to a method of production of the claimed antibodies and claims 8 and 9 to a hybridoma producing antibodies according to any of claims 1 to 4.

III. The following documents are referred to in the present decision:

D1: Nature, vol. 390, 1997, pages 74-77, Korth, C. et al.

D2: Methods in Enzymology, vol. 309, 1999, pages 106-122, Korth, C. et al.

D4: DE 197 41 607.

IV. The patent had been opposed pursuant to Article 100(a) EPC for lack of novelty and lack of inventive step (Articles 54 and 56 EPC).

In the decision under appeal the opposition division considered the subject-matter of all claims to be novel. In particular with regard to claim 1 it reasoned that the process-feature in this claim imparted to the antibody the property that it had to recognise an epitope defined by the peptide used for immunisation, while at the same time excluding that the antibody specifically recognised other epitopes. The monoclonal antibody 15B3, disclosed inter alia in documents D1 and D2, did not destroy the novelty of the subject-matter of claim 1 because it would not be generated when using the peptides in accordance with the process feature in claim 1 for immunisation.

In evaluating the requirements of Article 56 EPC, the opposition division considered document D2 as the closest prior art document as it disclosed that the antibody 15B3 bound at least under certain conditions specifically to the disease form of the prion protein, PrP<sup>Sc</sup>. The problem to be solved was the provision of an alternative monoclonal antibody specific for PrP<sup>Sc</sup> and therefore suitable for the diagnosis of prion-protein - related diseases, such as Bovine Spongiform Encephalitis. The opposition division came to the conclusion that neither document D2 nor document D4 motivated the skilled person to use the peptides according to claim 1 as immunogens in order to generate the now claimed antibodies as a solution to this problem.

V. With the response to the appellant's statement of the grounds for appeal, dated 19 May 2009, the patent proprietor (hereinafter "respondent") requested that the appeal be dismissed, i.e. it maintained as a main request the request held allowable by the opposition division, and additionally filed an auxiliary request.

VI. The board informed the parties in a communication annexed to the summons for oral proceedings of its preliminary view that the appeal might be dismissed.

VII. Oral proceedings were held on 4 May 2012. Both parties were represented. The parties' requests at the oral proceedings were as follows:

The appellant requested that the decision under appeal be set aside and that the European patent No. 1 158 003 be revoked.

The respondent requested as a main request that the appeal be dismissed, or as an auxiliary request, that the decision under appeal be set aside and that the patent be maintained on the basis of its auxiliary request filed with its letter of 19 May 2009.

At the end of the oral proceedings the chairman announced the board's decision.

VIII. The appellant's submissions, insofar as they are relevant to the present decision, may be summarized as follows:

Novelty (Article 54 EPC)

Claim 1 did not state that the antibody **only** recognized the epitope with the recited sequence. It was therefore not excluded that the antibodies defined in claim 1 additionally bound to other sequences of the PrP<sup>Sc</sup> protein. This was underpinned by the fact that the respondent had not demonstrated that the claimed antibodies did not bind to further epitopes, although it was very probable that they did. This was so because the peptide used for immunisation included the tyrosine-tyrosine motif which was known in the art to be crucial in the generation of PrP<sup>Sc</sup>-specific antibodies and to be present also in other parts of the prion protein. Therefore, since the antibody 15B3, disclosed for example in document D1, recognized inter alia the epitope recited in claim 1, it was covered by the definition of claim 1 and therefore destroyed the novelty of its subject-matter.

Inventive step (Article 56 EPC)

Document D2 was the closest prior art document. It disclosed the antibody 15B3 and that it specifically bound to PrP<sup>Sc</sup>, i.e. the disease form of the prion protein, but not to PrP<sup>C</sup>, i.e. the normal cellular form of the prion protein. The problem to be solved was the provision of alternative, PrP<sup>Sc</sup>-specific antibodies.

Document D4 disclosed on page 2, lines 37 to 54, nine binding sites of the PrP<sup>Sc</sup> protein by way of the nine Markush formulae a) to i). The document further disclosed on page 5, lines 17 to 20, that synthetic peptides mimicking these binding sites could be used alone for immunisation of non-human animals to generate PrP<sup>Sc</sup>-specific antibodies, i.e. antibodies discriminating between PrP<sup>Sc</sup> and PrP<sup>C</sup>.

The binding sites described by formulae a), b) and c) were the segments of the PrP<sup>Sc</sup> protein to which the antibody 15B3 was known to bind. The skilled person would therefore concentrate on these formulae, test them and would thus arrive at formula c). By consulting Figure 4 of document D4, disclosing the complete sequence of the bovine prion protein, with the threonine-glutamic acid-tyrosine motive present at positions 3 to 5 of the Markush formula c), the skilled person would easily locate the sequence represented by formula c) within the complete prion protein and thus at the same time retrieve a specific peptide sequence encompassed by formula c). The peptide so obtained would be one of the two peptides used for immunisation according to claim 1.

Consequently, the skilled person would arrive at the subject-matter of claim 1 in an obvious manner in the light of the combination of the disclosures in documents D2 and D4.

- IX. The respondent's submissions, insofar as they are relevant to the present decision, may be summarized as follows:

Novelty (Article 54 EPC)

Claim 1 related to antibodies which only bound to the protein sequence mentioned in the claim. Since antibody 15B3 bound to a combined epitope which not only consisted of the segment recited in claim 1, but also encompassed two others, it did not take away the novelty of the subject-matter of claim 1.

Inventive step (Article 56 EPC)

The problem to be solved in view of the closest prior art document D2 was the provision of an antibody which could "really" distinguish between PrP<sup>Sc</sup> and PrP<sup>C</sup>.

Document D4 referred to synthetic peptides from the prion protein, methods of using them for diagnosis and therapy of prion protein-associated disease and, in particular, also for producing antibodies specific for the disease form of the prion protein, PrP<sup>Sc</sup>. The document highlighted nine different generic peptide sequences by way of Markush formulae encompassing a multitude of different peptides. In order to obtain the sequence used according to claim 1 for generating the claimed antibodies the skilled person, starting from



the nine alternative sequences disclosed in document D4, would have to select formula c) and would further have to select, from among the 192 possible peptides covered by this formula, one suitable to carry on. There was no indication in document D4 that would have prompted the skilled person to select in a first step formula c) and in a second step to select the specific sequence identified in claim 1 from among the many alternatives falling under formula c). The subject-matter of claim 1 could not therefore be considered as obvious in view of a combination of the disclosure in documents D2 and D4.

## **Reasons for the decision**

### Novelty (Article 54 EPC)

1. Claim 1 relates to antibodies which are inter alia defined by the feature "and recognizing the epitope having the three dimensional conformation provided by the protein sequence Cys-Ile-Thr-Gln-Tyr-Glu-Arg-Glu-Ser-Gln-Ala-Tyr-Tyr of the PrP<sup>Sc</sup> isoform of the protein". There is disagreement between the parties about the meaning of this feature, i.e. whether or not it is to be interpreted as meaning that the claimed antibodies bind exclusively to this epitope.
2. Generally the term "epitope" is used to describe a part of a molecule to which the antigen-binding site of an antibody attaches.
  - 2.1 In the case of a protein, an epitope may be formed by a continuous stretch of amino acids. These epitopes are

sometimes referred to as "linear" epitopes. However, although they are denoted as "linear", these epitopes may also adopt a specific three-dimensional conformation as, for example, the epitope of the PrP<sup>Sc</sup> protein recited in claim 1.

- 2.2 Epitopes may also be formed by amino acids stemming from different parts of a protein, which are however brought into proximity by the folding of the protein into its three dimensional structure. These epitopes are often referred to as "conformational" epitopes.
3. In the case of a conformational epitope, a distinction is made between the denomination of the parts of a protein contributing to the epitope and the epitope as a whole. This is for example apparent from documents D1 and D2 (emphasis added):

"whereas **three distinct peptide sequences** were found to form **the 15B3 epitope**" (document D1, page 75, last two lines of second column); "[t]he **polypeptide segments** of **the 15B3 epitope** ..." (document D1, legend to Figure 2, point b); "[m]apping of **the 15B3 epitope** onto the NMR structure of the C-terminal domain of mouse PrP (ref. 12) reveals close proximity of the **peptide segments 2 and 3**, but a much larger spatial separation of the **segment 1** ..." (document D1, page 76, second column first sentence of first full paragraph); "recognizes **three discontinuous linear polypeptide segments** that are hypothesized to form **a conformational epitope** on the surface of prions" (document D2, legend to Figure 1); "it was assumed that **the epitope** was indeed conformational and that the three polypeptide segments

represented **partial epitopes** thereof" (D2, page 118, in the middle of the second full paragraph).

Hence, if an epitope is formed by distinct parts of a protein, the parts are usually not denoted as "the" epitope.

4. It is also clear from the description of the patent that the epitope recognized by the claimed antibodies is a "linear" epitope (see point 2.1 above) as opposed to a conformational epitope (see point 2.2 above). It is, for example, stated in paragraph [0022]:

"The antibodies are directed to the region comprised by amino acids 190 to 214 of PrP<sup>Sc</sup>, more preferably to the sequence from about 202 to about 214 of PrP<sup>Sc</sup>."

5. The board is therefore satisfied that the skilled person would understand the feature in claim 1 "and recognizing the epitope having the three dimensional conformation provided by the protein sequence Cys-Ile-Thr-Gln-Tyr-Glu-Arg-Glu-Ser-Gln-Ala-Tyr-Tyr of the PrP<sup>Sc</sup> isoform of the protein" to mean that the claimed antibodies bind to a protein segment which is built by the indicated linear sequence and only that sequence.

Hence, by virtue of the first part of claim 1 as just quoted, the claimed antibodies are defined as binding exclusively to "the epitope having the three dimensional conformation provided by the protein sequence Cys-Ile-Thr-Gln-Tyr-Glu-Arg-Glu-Ser-Gln-Ala-Tyr-Tyr of the PrP<sup>Sc</sup> isoform of the protein". In the board's view the process-feature in claim 1 (see

section II above, "obtainable by ....") provides the same definition.

6. The appellant raises the objection that the antibody disclosed in document D1, 15B3, falls under the terms of claim 1.
  
7. Document D1 (and also document D2) reveal that the epitope to which antibody 15B3 binds is a conformational epitope (see point 2.2 above) which is composed of protein stretches from different parts of the human prion protein, i.e. amino acid positions 142-148, 162-170 and 214-226 (see for example document D1, Figure 2). The segment covered by amino acid positions 214-226 in the human prion protein - denoted as 15B3-3 in document D1 - has the same sequence as the epitope recited in the first part of claim 1 (and quoted in point 5 above). However, since this protein segment is a partial epitope in relation to antibody 15B3 and not "the" epitope, and given the interpretation of claim 1 in point 5 above, the antibody 15B3 cannot be considered to fall under the definition in claim 1.
  
8. The party who raises an objection has the burden of proving the facts that it alleges (Case Law of the Boards of Appeal, 6th edition 2010, VI.H.5.2, first sentence). Thus, if its novelty objection is to succeed, it is in the present circumstances the appellant and not, as implied by the appellant's argument (see section VIII above), the respondent who has to provide evidence that, for example, the antibody 15B3 has binding properties matching those stated in claim 1 for the claimed antibodies or that there are other

antibodies having these properties. There is no such evidence before the board.

9. Thus, the novelty of the subject-matter of claim 1, and, since they are dependent or refer to it, also that of claims 2 to 5 and 7 to 9 has to be acknowledged. Novelty of claim 6 was not in issue during these proceedings. Hence, the claims of the main request are considered to fulfil the requirements of Article 54 EPC.

Inventive step (Article 56 EPC)

10. In proceedings before the European Patent Office, the problem-solution-approach is generally applied to assess inventive step. It involves, in a nutshell, the identification of the closest prior art document, the determination of the problem underlying the invention and the assessment of the obviousness or non-obviousness of the claimed solution to this problem (Case Law of the Boards of Appeal, 6th edition 2010, I.D.2, first paragraph).

Closest prior art

11. The primary criterion for the determination of the closest prior art document is that it discloses subject-matter conceived for the same purpose or aiming at the same objective as the claimed invention (Case Law of the Boards of Appeal, 6th edition 2010, I.D.3.1, second paragraph).
12. According to claim 1 the invention disclosed in the present patent consists of antibodies binding exclusively to the PrP<sup>Sc</sup> isoform of the prion protein,

i.e. to its disease form, but that do not bind to the conformationally different PrP<sup>C</sup> form, i.e. its normal cellular form. Due to these binding properties the claimed antibodies are considered as "specific" for the PrP<sup>Sc</sup> form.

13. Both parties, and also the board, consider document D2 as the closest prior art document with regard to the subject-matter of claim 1.

Document D2 discloses the antibody 15B3 which binds to PrP<sup>Sc</sup>. As to the specificity of its binding the following is, for example, stated:

- "This article describes in detail how a monoclonal antibody (MAb) has been raised that specifically recognizes only native, disease-associated PrP<sup>Sc</sup> but not normal PrP<sup>C</sup>." (at the end of the introduction);
- "[m]onoclonal antibody specific against disease-associated PrP<sup>Sc</sup>" (heading on page 118);
- "...led to the identification of a monoclonal antibody named 15B3, that precipitated native PrP<sup>Sc</sup>, but not native PrP<sup>C</sup>, from BSE brain homogenates (Fig. 4)." (page 118, lines 7-9);
- "MAb 15B3, being specific for disease-associated PrP, precipitates PrP only from diseased but not from normal bovine brain, ..." (legend to Fig.4).

Hence, document D2 conveys that the antibody 15B3 is "specific" in the sense of the patent.

14. However, document D2, inter alia, also discloses the results of a Western Blot assay revealing that under the chosen experimental circumstances the antibody 15B3 binds to recombinant native PrP<sup>C</sup>. It is stated on page 118, lines 26-27:

"[...]rbPRP, when overloaded on a SDS-PAGE gel and blotted was stained weakly by MAb 15B3".

15. This result may appear to be at odds with the statements recited above from document D2 that the antibody 15B3 is "specific".

However, the author's explanation for the binding is the high concentration ("when overloaded") of the protein on the Western blot membrane (which is a consequence of its high concentration on the SDS-PAGE gel).

It is generally known that extreme concentrations of proteins, i.e. very high or very low concentrations, may cause an antibody to bind in an unspecific manner.

Hence, seeing this explanation in document D2 and seeing also that the authors of document D2 consider the antibody as "specific", the skilled person would derive from document D2 nothing else than the teaching that the antibody 15B3 specifically binds to PrP<sup>Sc</sup>.

16. Nevertheless the respondent raised doubts as to whether the antibody 15B3 **is** "really" specific (see section IX above).

17. However, in the present context the board has to determine the relevant disclosure content of the closest prior art document D2 in the framework of the evaluation of inventive step and not the "real" binding properties of the antibody 15B3. The disclosure content of a prior art document is determined from the point of view of the skilled person reading the document at the priority date with his or her common general knowledge. Consequently, knowledge which, for example, arose only after the priority date cannot be taken into account for determining the disclosure content of document D2. There is no evidence before the board that the skilled person at the priority date, on the basis of his or her common general knowledge, was aware that the antibody 15B3 would in fact not be specific and would therefore, or for any other reasons - for which there is no evidence before the board either - after having read document D2 at the priority date, have interpreted its disclosure such that the antibody 15B3 is not specific in the sense that it does not discriminate between PrP<sup>Sc</sup> and PrP<sup>C</sup>.
18. Hence, the board concludes that document D2 teaches that the antibody 15B3 binds to PrP<sup>Sc</sup> in a specific manner.

#### Problem and solution

19. Thus, the problem to be solved by the present invention in relation to the disclosure in the closest prior art document D2 as determined in points 13 to 18 above is the provision of an alternative antibody to the antibody 15B3, i.e. an antibody which binds to the PrP<sup>Sc</sup>



isoform of the prion protein, while not binding to the PrP<sup>C</sup> form.

20. According to claim 1 the solution to this problem is antibodies that recognize the epitope having the three-dimensional conformation provided by the protein sequence Cys-Ile-Thr-Gln-Tyr-Glu-Arg-Glu-Ser-Gln-Ala-Tyr-Tyr of the PrP<sup>SC</sup> isoform of the prion protein and that are obtainable by a method comprising the step of immunising an animal with a peptide consisting of the amino acid sequence Cys-Ile-Thr-Gln-Tyr-Glu-Arg-Glu-Ser-Gln-Ala-Tyr-Tyr or Cys-Ile-Thr-Gln-Tyr-Gln-Arg-Glu-Ser-Gln-Ala-Tyr-Tyr.

#### Obviousness

21. For assessing the obviousness or non-obviousness of claimed subject-matter it has to be determined what the skilled person - who is faced with a particular problem and who does not know the claimed solution, i.e. the invention - would have done in the expectation of solving that particular problem. For determining which particular course of action the skilled person would have pursued, it is not sufficient to show that the elements of the claimed subject-matter are each individually disclosed, for example, in prior art documents. Rather there must be evidence such as, for example, promptings in a prior art document demonstrating that the skilled person would have selected and/or combined the elements (Case Law of the Boards of Appeal, 6th edition 2010, I.D.5; in particular paragraphs 4 and 5).

Since as noted above in point 5, the board considers that the functional feature in the first part of claim 1 and the process-feature in the second part define the same property of the antibody, i.e. that the claimed antibodies are defined as binding exclusively to "the epitope having the three dimensional conformation provided by the protein sequence Cys-Ile-Thr-Gln-Tyr-Glu-Arg-Glu-Ser-Gln-Ala-Tyr-Tyr of the PrP<sup>Sc</sup> isoform of the protein", the question to be answered in the context of the present case is whether or not the skilled person seeking to provide alternative antibodies to the 15B3 antibody (see points 18 and 19 above) would be motivated to provide antibodies as a solution defined as recognizing exclusively "the epitope having the three dimensional conformation provided by the protein sequence Cys-Ile-Thr-Gln-Tyr-Glu-Arg-Glu-Ser-Gln-Ala-Tyr-Tyr of the PrP<sup>Sc</sup> isoform of the protein".

22. The appellant argues that the claimed subject-matter is obvious in view of a combination of the disclosure in the closest prior art document D2 with the disclosure in document D4.
23. Document D4 is a patent application. It discloses synthetic peptides regarded as mimicking binding sites of the PrP<sup>Sc</sup> protein and their use in prophylaxis, diagnosis, therapy and also for generating PrP<sup>Sc</sup>-specific antibodies.
24. According to the appellant's argument document D4 discloses that these synthetic peptides could be used individually (as opposed to "in combination") for the immunisation of non-human animals in order to generate

PrP<sup>Sc</sup>-specific antibodies. The appellant's argument thus implies that document D4 teaches that antibodies may be PrP<sup>Sc</sup>-specific when they bind to linear epitopes of the PrP<sup>Sc</sup> protein.

25. However, document D4 also discloses that the peptides may be used in combination for immunisation. It is, for example, stated on page 5, lines 17 to 19:

"Schliesslich betrifft die Erfindung auch noch ein Verfahren zur Herstellung von PrP<sup>Sc</sup>-spezifischen Antikörpern. Zur Immunisierung wird nicht menschlichen Säugetieren **mindestens** eins der erfindungsgemässen Polypeptide .... verabreicht ...."

26. Thus, in order to arrive at the invention - which relates to antibodies recognizing a linear epitope of PrP<sup>Sc</sup> having a particular three-dimensional conformation - the skilled person would initially be required to take a first decision in view of the disclosure in document D4, i.e. he or she would have to decide to generate antibodies reacting with linear epitopes on PrP<sup>Sc</sup>.

However, in the board's view the skilled person neither gets a hint from the disclosure in document D4 that linear epitopes are preferred for generating PrP<sup>Sc</sup>-specific antibodies, nor can such a pointer be considered as being given by the common general knowledge because, according to the documents available in these proceedings, the only antibody known to be specific at the priority date of the patent, i.e. the antibody 15B3, recognizes a conformational epitope

formed by three different, spaced apart protein segments.

Thus, the board concludes that the skilled person had no motivation to prefer individual peptides as antigens over the combination of peptides when wanting to provide PrP<sup>Sc</sup> specific antibodies.

27. Document D4 discloses the synthetic peptides referred to therein by way of nine different Markush formulae representing different binding sites of the PrP<sup>Sc</sup> protein, denoted as formulae a) to i). Formula c) encompasses a peptide having the sequences recited in claim 1, in particular that of the epitope according to the first part of claim 1.
28. Even if it was assumed that the skilled person had a reason for preferring to generate PrP<sup>Sc</sup>-specific antibodies based on linear epitopes (see point 26 above), a further question arising in view of the disclosure in document D4 is whether or not he or she would be motivated to select, out of the nine binding regions disclosed in document D4, the region described by Markush formula c) which, as noted above, encompasses a peptide with the sequence of the epitope according to claim 1.
29. According to the appellant's argument (see section VIII above) the skilled person would have selected formula c) because he or she would have, in the first place, focussed on formulae a), b) and c) since he or she would have recognized that these formulae are general ways of describing the three regions taking part in the binding of the antibody 15B3 to the PrP<sup>Sc</sup> protein. He or

- she would then have "tested" and thus found that the region represented by formulae c) provides for a PrP<sup>Sc</sup>-specific linear epitope.
30. The board notes that it is not explicitly disclosed in document D4 that formulae a), b) and c) represent the sequences of the three partial 15B3 binding regions. However, the sequences of the partial epitopes were known at the priority date (see for example documents D1 and D2) and it is therefore assumed for the sake of the argument that the skilled person would have recognized that formulae a), b) and c) represent in fact the three partial epitopes of the antibody 15B3.
31. In the board's view, the common general knowledge about being a partial epitope of the complete antibody 15B3 binding site would rather have prevented than encouraged the skilled person to consider regions a), b) and c) as candidates for protein stretches that could form linear epitopes. It is not prima facie evident that a part of a protein which mediates specific binding of an antibody only in concert with two other parts of that protein would provide for specific binding also as an individual part. Moreover, the fact that the skilled person is seeking an **alternative** to the antibody 15B3 (see point 19 above) would also rather speak against focussing on the regions represented by formulae a), b) and c).
32. Thus, the board is not convinced of the reason given by the appellant as to why the skilled person would have selected the regions represented by the Markush formula a), b) and c) when looking for PrP<sup>Sc</sup>-specific antibodies. It is concluded therefore that the skilled person would

not have had the motivation to consider formulae a), b) and c) and, in particular, to select the formula c).

33. Since the skilled person would not have selected formula c), it is not necessary to consider the next step of the appellant's argument, i.e. that the skilled person, departing from the Markush formula c), would have easily arrived at one of specific peptides used according to claim 1 for immunisation by consulting Figure 4 of document D4 (see section VIII above).
34. Hence, the board comes to the conclusion that, starting from the disclosure in document D2, the disclosure in document D4 would not have led the skilled person to the subject-matter of claim 1.
35. Thus, the subject-matter of claim 1 cannot be considered as obvious in view of a combination of documents D2 and D4. This conclusion also applies to the subject-matter of claims 2 to 9 because they are either dependent on claim 1 or refer to it. The requirements of Article 56 EPC are fulfilled.

**Order**

**For these reasons it is decided that:**

The appeal is dismissed.

The Registrar:

The Chairman:

B. Atienza Vivancos

C. Rennie-Smith