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**Datasheet for the decision
of 16 January 2014**

Case Number: T 1222/10 - 3.3.08

Application Number: 02777127.8

Publication Number: 1430133

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C07K16/28, C12N5/10,
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A61P11/00, A61P17/00

Language of the proceedings: EN

Title of invention:
A SOLUBLE TOLL-LIKE RECEPTOR

Patent Proprietor:
SOCIETE DES PRODUITS NESTLE S.A.

Opponent:
N.V. Nutricia

Headword:
Soluble TLR2 polypeptide breast milk/NESTLE

Relevant legal provisions:
EPC Art. 54, 56
RPBA Art. 13(1)

Keyword:
Admissibility of Main Request and Auxiliary Request 2 (no)
Admissibility of new documentary evidence (yes)
Auxiliary Request 1 - novelty (yes), inventive step (no)

Decisions cited:

G 0009/92, T 0464/97

Catchword:



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Case Number: T 1222/10 - 3.3.08

D E C I S I O N
of Technical Board of Appeal 3.3.08
of 16 January 2014

Appellant:
(Opponent)

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Decision under appeal:

**Interlocutory decision of the Opposition
Division of the European Patent Office posted on
26 March 2010 concerning maintenance of the
European Patent No. 1430133 in amended form.**

Composition of the Board:

Chairman: M. Wieser
Members: P. Julià
J. Geschwind

Summary of Facts and Submissions

I. European patent 1 430 133, based on European patent application No. 02 777 127.8 and published as International patent application WO 03/025015, was granted with nine claims. Claims 1, 5 and 6 read as follows:

"1. A soluble polypeptide obtainable from milk with a molecular weight of about 22, 25, 38, 40, 60, 70, 80 kDa as measured by SDS PAGE analysis and which further has a sequence similarity to the TLR receptor of any of SEQ ID. No. 1 or 2 of at least 90 %."

"5. A consumable product comprising additions of the polypeptide according to any of claims 1 to 3."

"6. A cream, lotion or unguent comprising additions of the polypeptide according to any of claims 1 to 3."

Claims 2 to 4 were directed to preferred embodiments of claim 1. Claims 7 to 9 were directed to several uses of a polypeptide according to any of claims 1 to 3.

II. An opposition against the patent was filed based on grounds under Article 100(a) EPC (lack of novelty and of inventive step, Articles 54 and 56 EPC) and Article 100(b) EPC (insufficiency of disclosure, Article 83 EPC). The opposition division considered the Main Request (claims as granted) and Auxiliary Request 1 not to fulfil the requirements of Article 54 EPC. Auxiliary Request 2 was considered to fulfil all requirements of the EPC and, accordingly, the patent was maintained on the basis of this request. Both Auxiliary Requests 1 and 2 had been filed on 27 November 2009. Except for the deletion of granted claim 5 and the renumbering of

the claims, Auxiliary Request 2 was identical to the granted claims.

- III. An appeal was lodged by the opponent (appellant) against the decision of the opposition division. The appellant maintained the objections raised under Articles 54 and 56 EPC and requested to set aside the decision under appeal and to revoke the patent.
- IV. In reply to the Grounds of Appeal, the patentee (respondent) filed a new Main Request and Auxiliary Requests 1 to 3 and requested to dismiss the appeal.

The Main Request consisted of 16 claims. Claims 1, 9-10, 12 and 14-16 of this request were identical to claims 1-4 and 6-8, respectively, of the request upheld by the opposition division. In addition, the Main Request comprised dependent claims 2-8, each of which was directed to one of the soluble polypeptides of claim 1. Claims 11 and 13 were directed to a nutritional formula and to a skin cream, lotion or unguent, respectively, comprising a polypeptide of any of claims 1-10.

Auxiliary Request 1 read as the Main Request except for the deletion of dependent claims 2-8. Auxiliary Request 2 was identical to Auxiliary Request 1 except for the deletion of claim 11 directed to a nutritional formula. Auxiliary Request 3 was identical to the request upheld by the opposition division.

- V. On 8 August 2013, the board summoned the parties to oral proceedings. In a communication pursuant to Article 15(1) of the Rules of Procedure of the Boards of Appeal (RPBA) annexed to the summons to oral proceedings, the board informed the parties of its

preliminary opinion on the substantive issues of the case. In particular, the board mentioned that the Main Request and Auxiliary Request 1 were considered not to be admissible into the appeal proceedings.

- VI. On 16 December 2013, the respondent replied to the board's communication. With its reply, the respondent filed new documentary evidence (document D7, *infra*) and a new Main Request and Auxiliary Requests 1 and 2.

All claim requests contained claims dependent on claim 1, which were directed to one of the soluble polypeptides of claim 1. None of these requests contained a claim directed to a nutritional formulation and, in all requests, the cream, lotion or unguent was defined as being a skin cream, lotion or unguent. Whereas claim 1 of the Main Request was directed to soluble polypeptides of a molecular weight of about 25, 38, 40, 60, 70, 80 kDa, the soluble polypeptides of 60 and 70 kDa were deleted in claim 1 of Auxiliary Requests 1 and 2.

- VII. Oral proceedings took place on 16 January 2014. In the course of these proceedings, the respondent withdrew all previous claim requests and filed a new Main Request and Auxiliary Requests 1 and 2. None of these requests contained claims dependent on claim 1 and directed to each one of the soluble polypeptides of claim 1. The Main Request was identical to the request upheld by the opposition division except for the limitation of the claim directed to a cream, lotion or unguent to a skin cream, lotion or unguent. Auxiliary Request 1 was identical to the Main Request except for the deletion of the soluble polypeptide of a molecular weight of about 22 kDa in claim 1. Auxiliary Request 2 was identical to Auxiliary Request 1 except

for the deletion of the soluble polypeptides of molecular weights of about 25, 60 and 70 kDa.

VIII. The following documents are cited in the present decision:

D1: T.H. Flo et al., J. Leukoc. Biol., March 2001, Vol. 69, pages 474 to 481;

D2: E. LeBouder et al., J. Immunol., 2003, Vol. 171, pages 6680 to 6689;

D6: WO-A2-00/22945 (publication date: 27 April 2000);

D7: B.M. Henrick et al., PLoS ONE, July 2012, Vol. 7(7), (e40138), pages 1 to 10.

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

Admissibility of the new claim requests

A polypeptide with a molecular weight of about 22 kDa was not present in any of the respondent's claim requests filed in reply to the board's communication pursuant to Article 15(1) RPBA. The reintroduction of this molecular weight into the late-filed Main Request rendered the request inadmissible. Auxiliary Requests 1 and 2 were late filed and they could have been filed at an earlier stage of the proceedings.

Auxiliary request 1

Novelty - Article 100(a) EPC, Article 54 EPC

Claim 1 was directed to soluble TLR2 (sTLR2) polypeptides characterized by sequence similarity,

molecular weight and source. No particular property was conferred by this last feature (obtainable from milk). Milk and plasma were identified in the patent-in-suit as suitable sources and no technical differences were associated to sTLR2 polypeptides obtained from one of these two sources. Claim 3 referred to the polypeptide of claims 1 and 2 obtainable from different mammalian fluids, including milk and plasma. According to document D1, sTLR2 polypeptides were detected in human serum by using TLR2-specific monoclonal antibodies (TL2.1 and TL2.3). As shown in Figure 1 of document D7, these antibodies identified sTLR2 polypeptides with molecular weights identical to those cited in claim 1. These sTLR2 polypeptides were thus anticipated by document D1.

Inventive step - Article 100(a) EPC, Article 56 EPC

If, starting from the closest prior art document D1, the technical problem was the provision of bioactive sTLR2 polypeptides, the problem was not solved over the whole scope of claim 1. There was no evidence in the patent-in-suit showing that all the sTLR2 polypeptides of claim 1 were bioactive. Such evidence was also not derivable from documents D2 and D7. Claim 1 comprised sTLR2 polypeptides for which no activity had ever been demonstrated. Thus, starting from document D1, the technical problem to be solved had to be formulated only in minimalist terms, namely, as being the provision of sTLR2 polypeptides irrespective of their activity.

The relevance of sTLR2 polypeptides was evident from document D1 itself which explicitly referred to the development of a specific ELISA assay for carrying out further studies. No hindsight was thus required to

consider sTLR2 polypeptides as being of relevance. Moreover, document D1 provided the skilled person with the specific means (anti-TLR2 antibodies) for identifying and isolating these sTLR2 polypeptides. When doing so, document D7 showed that a skilled person, using routine techniques and standard experimental protocols, would have inevitably obtained several sTLR2 polypeptides falling within the scope of claim 1.

Furthermore, in view of the results shown in the prior art and in the patent itself, the feature in claim 1 referring to the source of the polypeptides (obtainable from milk) could not be taken into account for inventive step. It did not confer any technical characteristic or property that could distinguish a sTLR2 polypeptide obtained from milk from the same polypeptide when obtained from another source (serum).

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

Admissibility of the new claim requests

None of the claim requests contained the board's objected claims dependent on claim 1. The requests were thus a direct reply to the objection raised by the board. The presence of a soluble polypeptide of a molecular weight of about 22 kDa in the Main Request could not surprise the appellant since this subject-matter was in the proceedings from the beginning. Moreover, comments on this subject-matter were made by the board in its communication and no submissions were filed by the appellant in reply thereto. Except for the deletion of claims dependent on claim 1, no other amendments were introduced in

Auxiliary Request 1. Auxiliary Request 2 was identical to Auxiliary Request 1 except for the deletion of the molecular weights of about 25, 60 and 70 kDa.

Auxiliary Request 1

Novelty - Article 100(a) EPC, Article 54 EPC

There was no disclosure of any sTLR2 polypeptide in document D1, let alone of any of the specific molecular weights cited in claim 1. Document D1 referred to preliminary data only. The anti-TLR2 antibodies (TL2.1 and TL2.3) used in document D1 were different from the antibodies used in the patent-in-suit and in document D2. These antibodies had different specificity and the results obtained with them could not be compared, as shown by Figure 7 of document D7 (N-17 and TL2.1/TL2.3). A comparison of this Figure 7 with Figures 1-2 of the patent-in-suit showed also that different anti-TLR2 antibodies identified different sTLR2 polypeptides. Thus, document D1 did not anticipate the sTLR2 polypeptides of claim 1.

Inventive step - Article 100(a) EPC, Article 56 EPC

The closest prior art document D1 was concerned with full-length TLR2. It did not disclose any sTLR2 polypeptide but merely contained a reference to preliminary data with no indication of any possible function. Moreover, all data in document D1 were obtained from human serum and there was no reference to human breast milk. Document D6 was the sole document on file in which a bioactive (immunomodulatory) soluble (sCD14) form of a membrane-bound (CD14) receptor was identified in human breast milk.

Starting from any of these two documents, the technical problem to be solved was the provision of bioactive sTLR2 polypeptides from breast milk. The problem was solved by the claimed subject-matter as shown by Examples 4 (sTLR2 polypeptides of MW 38/40 and 80) and 6-7 (all sTLR2 polypeptides) of the patent-in-suit and by documents D2 and D7 (sTLR2 polypeptides of high and low MW, respectively).

There was no reference in document D6 to TLR2 let alone to sTLR2 polypeptides. There was no reason for a skilled person to combine documents D6 and D1, since they related to different technical fields, namely human breast milk and human serum, respectively. Hindsight knowledge of the patent was required for such a combination. Likewise, hindsight was also required to consider the putative sTLR2 polypeptides referred to in document D1 to be of any relevance. From the whole content of document D1, it was not obvious to focus on these putative sTLR2 polypeptides. Even if the skilled person nevertheless had considered them, it was still necessary to develop a suitable technique for identifying and isolating these sTLR2 polypeptides. Document D2 showed that several anti-TLR2 antibodies were available to the skilled person to achieve this goal. Accordingly, for identifying the sTLR2 polypeptides referred to in document D1, it was necessary in a first step to select an anti-TLR2 antibody. However, as shown in document D7, different antibodies identified different sTLR2 polypeptides. Thus, it was not obvious that a skilled person would identify any of the sTLR2 polypeptides of claim 1. The less so, since a high variability and important differences were found among the sTLR2 polypeptides identified in document D7, which resulted from the

genetic background and the conditions of the sample used.

- XI. The appellant (opponent) requested that the decision under appeal be set aside and the patent revoked.
- XII. The respondent (patentee) requested that the decision under appeal be set aside and that the patent be maintained on the basis of the Main Request or, alternatively, on the basis of Auxiliary Requests 1 or 2, all filed on 16 January 2014 at the oral proceedings before the board.

Reasons for the Decision

Admissibility of new requests and documentary evidence

1. At the beginning of the oral proceedings before the board, all claim requests on file contained claims dependent on claim 1 and each of these claims were directed to one of the sTLR2 polypeptides of claim 1 (cf. point VI *supra*). These claims were neither present in the granted claims nor in the set of claims upheld by the opposition division in the opposition proceedings (cf. points I and II *supra*). As stated by the board in its communication pursuant to Article 15(1) RPBA (cf. point V *supra*), the introduction of these dependent claims was not made in reply to any ground of opposition and, since the patentee/respondent did not appeal the decision of the opposition division, their introduction was not in line with the case law established by the Boards of Appeal (cf. G 9/92, OJ EPO 1994, page 875). Therefore, none of these requests was considered to be admissible into the appeal proceedings. Only after being informed at the oral proceedings that the board saw no reason to change its

- opinion on this issue, the respondent decided to withdraw these requests and to file a new Main Request and Auxiliary Requests 1 and 2 to replace its previous requests (cf. point VII *supra*).
2. The filing of the Main Request is not considered to be a direct reply to the objections raised against the admissibility of previous claims requests. The changes in the Main Request are not restricted to a mere deletion of the objected dependent claims but comprise further the reintroduction of a sTLR2 polypeptide having a molecular weight of about 22 kDa (cf. points VI and VII *supra*), i.e. subject-matter that had already been withdrawn in earlier stages of the proceedings and that was not present in any of the claim requests on file at the beginning of the oral proceedings before the board.
 3. Likewise, the amendments in Auxiliary Request 2 are not exclusively directed to overcome the objections raised against the admissibility of the previous claim requests but go beyond this purpose. Rather Auxiliary Request 2 comprises a substantive amendment, namely the deletion of sTLR2 polypeptides of molecular weights of about 25, 60 and 70 kDa. This amendment, which does not directly arise from the objections to the non-admissible dependent claims, comes as a surprise because especially the deleted polypeptide having a molecular weight of 25 kDa was present in all requests that have been on file so far, in particular, in all requests on file at the beginning of the oral proceedings before the board. Moreover, no reasons have been given to explain the deletion of this subject-matter at this late stage of the appeal proceedings and why this amendment could not have been made at an earlier stage of the proceedings.

4. The filing of Auxiliary Request 1 is a direct reply to the objections raised against the admissibility of previous claim requests since, in comparison to these requests, the sole amendment introduced in Auxiliary Request 1 is the deletion of the objected dependent claims (cf. points VI and VII *supra*). Auxiliary Request 1 is identical to the request upheld by the opposition division except for the introduction of the term "skin" to define the claimed cream, lotion or unguent (claim 5). This amendment had already been introduced in all requests filed by the respondent in reply to the appellant's Grounds of Appeal and it intends to overcome an objection raised under Article 54 EPC in the statement of Grounds of Appeal (*infra*).

5. In reply to the board's communication pursuant to Article 15(1) RPBA, the respondent has filed new documentary evidence, namely post-published document D7. Although document D7 is a late filed document, its filing has been made in direct reply to the board's communication and its introduction into the proceedings has not been contested by the appellant. Indeed, in view of the high relevance of document D7 (cf. points 20.3 and 20.4 *infra*), the board does not see any reason not to admit it into the proceedings.

6. Thus, the board, in the exercise of its discretion, decides not to admit the late filed Main Request and Auxiliary Request 2 into the appeal proceedings but to admit the late filed Auxiliary Request 1 and document D7 into the proceedings (Article 13(1) RPBA).

Auxiliary Request 1
Articles 123(2), (3), 84 and 83 EPC

7. The amendments introduced into Auxiliary Request 1 do not lead to an extension in the protection conferred by the granted claims (Article 123(3) EPC) and they do not introduce any unclarity into the claims (Article 84 EPC). The subject-matter of Auxiliary Request 1 does not go beyond the content of the application as filed (Article 123(2) EPC), basis for the limitation to a skin cream, lotion or unguent is found *inter alia* on page 11, lines 17 to 27 of the application as filed.
8. In the decision under appeal, the opposition division considered the requirements of Article 83 EPC to be fulfilled (cf. page 2 of the appealed decision). The findings of the opposition division as regards Article 83 EPC were not contested by the appellant in the statement of Grounds of Appeal and thus, they are not subject-matter of the appeal proceedings. In the light of the amendments introduced into Auxiliary Request 1, the board does not see any reason to deviate from the decision of the opposition division in this respect.
9. Thus, Auxiliary Request 1 fulfils the requirements of Articles 123(2), (3), 84 and 83 EPC.

Article 100(a) EPC - Article 54 EPC

10. The appellant, relying on document D1, considered the subject-matter of claim 1 not to be novel (cf. point IX *supra*). In document D1, it is stated that "*(w)e have preliminary data showing the presence of soluble TLR2 in serum and in monocyte supernatants. An enzyme-linked immunosorbent assay (ELISA) specific for TLR2 is under development to investigate this further*" (cf. page 479, right-hand column, at about the end of the first paragraph of document D1). However, there is no identification of the detected sTLR2 polypeptides let

alone a characterization of their molecular weights. Thus, the subject-matter of claim 1 is not explicitly disclosed in document D1.

11. It remains to be assessed whether the subject-matter of claim 1 is implicitly disclosed in document D1. Appellant's argument relies mainly on the assumption that, using the specific (TL2.1 and TL2.3) anti-TLR2 antibodies disclosed in document D1, the skilled person would inevitably have obtained sTLR2 polypeptides with molecular weights falling within the scope of claim 1, as shown in Figure 1 of the post-published document D7 (cited as expert opinion; cf. point IX *supra*). In the board's view, appellant's argument is not based on certainty but rather on considerations of probability and likelihood which, according to the established case law of the Boards of Appeal, are not justified in the examination of novelty (cf. decision T 464/94 of 21 May 1997; point 16 of the Reasons).

12. In the present case, a skilled person would necessarily have to repeat the teachings of document D1 in order to identify the sTLR2 polypeptides. However, the data on these sTLR2 polypeptides is acknowledged in document D1 to be only preliminary and there is no disclosure of the method and conditions used for obtaining these preliminary data. Although reference is made in document D1 to specific anti-TLR2 antibodies, other anti-TLR2 antibodies were also available in the prior art (cf. *inter alia*, page 6, paragraphs [0053] and [0054] of the patent-in-suit; page 6681, left-hand column, second paragraph of post-published document D2, cited as expert opinion) and, as shown in Figure 1 of post-published document D7 (cited as expert opinion), different anti-TLR2 antibodies have a different specificity. It is also worth noting that the

preliminary data referred to in document D1 are obtained from human blood cells and tissues, whereas the starting material in the studies reported in document D7 are human breast milk and intestinal epithelial cells. Important is also the presence of certain variability among the detected sTLR2 polypeptides depending on *inter alia* the type and conditions of the sample used (cf. page 3, right-hand column, second and last paragraphs of post-published document D7, cited as expert opinion). For all these reasons, the board cannot follow appellant's argument and considers the subject-matter of claim 1 not to be implicitly disclosed by document D1.

13. Further novelty objections raised by the appellant in its Grounds of Appeal were not further pursued during the oral proceedings and are considered by the board not to be relevant. Indeed no prior art document on file anticipates a first or second medical use of any of the sTLR2 polypeptides of claim 1, a skin cream, lotion or unguent containing it or its use as ingredient in a functional food or cosmetic.
14. Thus, the the subject-matter of Auxiliary Request 1 fulfils the requirements of Article 54 EPC.

Article 100(a) EPC - Article 56 EPC

15. In view of the arguments put forward by the parties under Article 56 EPC, the following points are of relevance for a correct application of the problem-and-solution approach:
 - 15.1 Claim 1 is a product-claim directed to several polypeptides defined by specific features including solubility, molecular weight and degree of similarity

to defined TLR2 sequences. There is, however, no reference in claim 1 to any specific anti-TLR2 antibody, to a specific (bio)activity or to the use of any of these polypeptides which is based on a particular activity.

- 15.2 For a particular product, the source and method of its obtention are not relevant insofar as they do not confer a specific characteristic, feature and/or property to this product, which allows to distinguish it from the same product when obtained by other methods and/or from other sources. If a particular method disclosed in the prior art renders the obtention of a claimed product obvious, the fact that this is not the case for other methods does not contribute to the inventive activity of a claim referring to the product.
16. According to the established case law, the closest prior art for assessing inventive step is normally a document disclosing subject-matter conceived from the same purpose as the claimed invention and having the most relevant technical features in common, i.e. requiring the minimum of structural modifications (cf. "Case Law of the Boards of Appeal of the EPO", 7th edition 2013, I.D.3.1, page 167). Applying these criteria, the board, contrary to the respondent and the opposition division, shares appellant's view that the closest prior art is represented by document D1.
17. Although document D6 relates to a soluble form of a membrane-bound (CD14) receptor obtained from human breast milk, there is no reference in this document to the TLR2 membrane-receptor or to sTLR2 polypeptides. In the present case and with the evidence on file, the board does not consider the source of the sTLR2

polypeptides (human breast milk or serum) to be of any relevance, since neither the patent itself, the prior art or the post-published documents on file disclose any specific feature or property associated to these sTLR2 polypeptides when isolated from different sources. On the contrary, no differences are expected when using different sources, as shown for instance by the reference in dependent claim 3 to the sTLR2 polypeptides of claim 1 obtainable from milk as being also obtainable by immuno-precipitation of other mammalian fluids such as serum, plasma or intestinal content.

18. Although document D1 does not refer to human breast milk but only to human blood cells and tissues (serum, plasma, monocyte supernatants), the purpose of this document is focused on the expression and regulation of TLR2 and on the elucidation of its role, in particular, in response to different microbial products. In this context, there is an explicit reference in document D1 to the presence of sTLR2 in serum and in monocyte supernatants (cf. page 479, right-hand column, at about the end of the first paragraph of document D1; point 10 *supra*). The relevance of these findings is clearly emphasized in document D1 itself by a reference to the development of a specific (ELISA) assay for TLR2 and the interest to investigate further.

19. Starting from document D1, the objective technical problem to be solved is the actual identification and characterization of these sTLR2 polypeptides. As a solution to this problem the patent proposes the soluble polypeptides according to claim 1, which solve the posed problem. It has to be noted that the presence or absence of biological activity of the sTLR2 polypeptides is not relevant for the formulation of

this problem. Firstly, this feature is not required for the sTLR2 polypeptides of claim 1 (cf. point 15.1 *supra*) and, secondly, the presence of activity is inherent to the product itself. From the evidence on file there is no reason to expect that the sTLR2 polypeptides cited in document D1 have different activities than sTLR2 polypeptides isolated from other sources, in particular, from human breast milk (cf. point 15.2 *supra*).

20. The board is convinced that, in the light of the prior art, it would have been obvious for a skilled person to arrive at the polypeptides of claim 1 without undue experimentation or application of any inventive skill, which polypeptides are not required to be isolated or in a substantially pure or homogeneous form.

20.1 The disclosure of document D1 provides appropriate methods and means for a skilled person to identify and characterize the sTLR2 polypeptides referred to in this document. Indeed, the TLR2 expression studies performed in document D1 rely on the identification and characterization of TLR2 by immuno-precipitation from cell lysates, followed by gel electrophoresis and determination of molecular weight (cf. Figure 2, page 476 of document D1). The relevance of these immuno-techniques is clearly shown throughout the entire disclosure of document D1. As explicitly acknowledged in the patent-in-suit, a skilled person is well aware of all these standard techniques, which include a purification by immuno-affinity followed by Western-blotting procedure (cf. page 5, paragraph [0046] and page 6, paragraph [0048] of the patent).

20.2 The studies and results reported in document D1, including the detection of sTLR2 in serum and monocyte supernatants, were carried out using the anti-TLR2 specific monoclonal antibodies TL2.3 and TL2.1. The document contains a bibliographic reference disclosing the method used for obtaining the TL2.1 antibody and the staining specificity of this monoclonal antibody, which is identical to the specificity of the TL2.3 antibody (cf. page 474, right-hand column, second paragraph of document D1). Although several anti-TLR2 antibodies were known in the prior art and available to the skilled person (cf. *inter alia*, page 6, paragraphs [0053] and [0054] of the patent-in-suit; page 6681, left-hand column, second paragraph of post-published document D2, cited as expert opinion), in view of the disclosure of document D1, the obvious first choice for a skilled person, when trying to solve the above formulated technical problem, would have been to use the very same antibodies used in document D1.

20.3 In Figure 1 of the post-published document D7 (cited as expert opinion), the predominant sTLR2 polypeptides profiles in breast milk are shown by Western-blot analysis. In the TL2.3 and TL2.1 gels corresponding to the anti-TLR2 monoclonal antibodies used in document D1, two sTLR2 polypeptides are detected with molecular weights of about 25 and 80 kDa (cf. Figure 1, page 4 of document D7). Although post-published document D2 (cf. page 6682, right-hand column, third paragraph, page 6683, Figure 1) uses other anti-TLR2 antibodies, the detection of several sTLR2 polypeptides in human plasma, including sTLR2 polypeptides of 25 and 83 kDa, is described therein. These other anti-TLR2 antibodies also detect the presence of sTLR2 polypeptides in human breast milk, including the sTLR2 polypeptides of 25 and 83 kDa (cf. page 6687, left-hand column, second

paragraph and page 6686, Figure 6 of document D2, cited as expert opinion). There is no evidence on file to cast any doubt on the fact that sTLR2 polypeptides obtained from different sources but having the same molecular weight are indeed the same sTLR2 polypeptides (cf. point 15.2 *supra*).

20.4 It has also been argued by the respondent that, in view of the high variability and non-stability of the sTLR2 polypeptides disclosed in document D7, the detection of a sTLR2 polypeptide having a molecular weight as indicated in claim 1 depends to a high extent on the quality of the sample used and is therefore not necessarily obvious (cf. point X *supra*). The board notes, however, that in all these studies, a sTLR2 polypeptide of a molecular weight of about 25 kDa identified and referred to as a predominant form (cf. page 3, right-hand column, second paragraph and page 4, Figure 2 of document D7, cited as expert opinion). This sTLR2 polypeptide of about 25 kDa is also shown to be highly stable and detectable at all points in time (when the sample is stored for 15 days at room temperature and for 7 days at 4°C) (cf. page 3, right-hand column, second paragraph from the bottom to page 4, left-hand column, first paragraph, page 5, Figure 4 of document D7). Indeed, the presence of sTLR2 polypeptides of about 25 and 83 kDa in human plasma is reported in post-published document D2 (cited as expert opinion) independent of any technical difficulties or stability problems. Moreover, it is standard practice in scientific studies not to rely on a single sample and/or measure but to use several samples and measures in order to have statistically significant data and results. The detection of these sTLR2 polypeptides in human serum lies within the normal technical abilities

of a skilled person using routine and standard practice.

21. Thus, in view of all the above considerations, the subject-matter of claim 1 does not fulfil the requirements of Article 56 EPC.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.
2. The patent is revoked.

The Registrar:

The Chairman:



A. Wolinski

M. Wieser

Decision electronically authenticated