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Datasheet for the decision of 25 March 2021

Case Number: T 0555/17 - 3.3.01

Application Number: 07836873.5

Publication Number: 2057466

IPC: G01N33/53, A61K35/30, A61K39/395, A61K35/24, C07K14/00, C07K16/00

Language of the proceedings: EN

Title of invention:
METHODS AND COMPOSITIONS FOR TREATMENT AND DIAGNOSIS OF AUTOIMMUNE ENCEPHALITIS OR EPILEPSY

Patent Proprietors:
The Trustees of The University of Pennsylvania
CHILDREN'S HOSPITAL OF PHILADELPHIA

Opponent:
Ravo Diagnostika GmbH

Headword:
Diagnosis of autoimmune encephalitis/TRUSTEES

Relevant legal provisions:
EPC Art. 100(b), 112(1)(a)

Keyword:
Grounds for opposition - insufficiency of disclosure (no)
Referral to the Enlarged Board of Appeal - (no)

Decisions cited:
T 1474/12

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Case Number: T 0555/17 - 3.3.01

D E C I S I O N
of Technical Board of Appeal 3.3.01
of 25 March 2021

Appellant: (Patent Proprietor 1)	The Trustees of The University of Pennsylvania 3160 Chestnut Street, Suite 200 Philadelphia, PA 19104-6283 (US)
Appellant: (Patent Proprietor 2)	CHILDREN'S HOSPITAL OF PHILADELPHIA 34th Street and Civic Center Boulevard Philadelphia, PA 19104 (US)
Representative:	Bösl, Raphael Konrad Patentanwälte Isenbruck Bösl Hörschler PartG mbB Prinzregentenstraße 68 81675 München (DE)
Respondent: (Opponent)	Ravo Diagnostika GmbH Oltmannsstrasse 5 79100 Freiburg (DE)
Representative:	Rudolph, Ulrike Patentanwaltskanzlei Dr. U. Rudolph In der Schanz 10 69198 Schriesheim (DE)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 22 December 2016 concerning maintenance of the European Patent No. 2057466 in amended form**

Composition of the Board:

Chairwoman	M. Pregetter
Members:	T. Sommerfeld
	P. de Heij

Summary of Facts and Submissions

I. European patent 2 057 466 is based on application 07836873.5, which was filed as an international application and published as WO 2008/021408. The patent is entitled "Methods and compositions for treatment and diagnosis of autoimmune encephalitis or epilepsy" and was granted with 14 claims.

Claim 1 as granted reads as follows:

"1. A method of diagnosing an anti-NMDA receptor encephalitis in a subject, comprising the step of testing a biological sample obtained from the subject for an antibody to an NR subunit of an NMDA receptor, whereby a presence of said antibody in said biological sample indicates said anti-NMDA receptor encephalitis, and wherein the anti-NMDA receptor encephalitis is associated with dystonic movement, dyskinesias, or autonomic instability, thereby diagnosing said anti-NMDA receptor encephalitis in a said subject."

II. Opposition was filed against the granted patent, the opponent requesting revocation of the patent in its entirety on the grounds of exclusion from patentability, lack of novelty and inventive step (Articles 53(c), 54(2) and 56 EPC and Article 100(a) EPC) and insufficiency of disclosure (Article 100(b) EPC).

III. By an interlocutory decision announced at oral proceedings on 11 October 2016, the opposition division decided that the patent could be maintained in amended form on the basis of auxiliary request 3 filed during oral proceedings (Articles 101(3)(a) and 106(2) EPC).

The opposition division considered that the claims as granted (main request) did not fulfil the requirements of Article 83 EPC. The claims according to auxiliary requests 1 and 2 were also considered to contravene Article 83 EPC. Auxiliary request 3, however, was considered to fulfil the requirements of the EPC, in particular Articles 84, 83, 54 and 56 EPC.

IV. The patent proprietors (appellants) lodged an appeal against that decision. In their statement of the grounds of appeal, dated 28 April 2017, the appellants requested that the patent be maintained as granted (main request) or, alternatively, on the basis of the claims according to auxiliary requests 1 to 4, all filed with the grounds of appeal.

V. In its reply to the appellants' statement of grounds of appeal, the opponent (respondent) requested that the appeal be dismissed. Moreover, it requested that auxiliary request 3 not be admitted into the proceedings.

VI. Oral proceedings before the board took place on 25 March 2021. During the oral proceedings, the appellants withdrew the pending auxiliary requests 1, 2 and 4 and the respondent submitted a request for referral of a question to the Enlarged Board of Appeal. At the end of the oral proceedings, the chairwoman announced the board's decision.

VII. The submissions of the appellants, in so far as they are relevant to the present decision, may be summarised as follows:

Main request, claim 1: sufficiency of disclosure

Claim 1 was directed to a diagnostic method comprising the step of testing a biological sample for the presence of an antibody to an NR subunit of an NMDA receptor. The subunit was not part of the test, let alone as a detector antigen. Any test could be used and whenever it identified such an antibody, then the diagnosis of anti-NMDA receptor encephalitis was made. The claim did not require that the antibody bind to one single subunit, and it did not exclude the possibility that the subunit was part of a heteromer (as envisaged in paragraph [0021] of the application as filed). Since the claim was clear in itself, there was no need to use the description to interpret it. The tests disclosed in the patent provided guidance on how to carry out the invention, but none of them was part of the claim, so even if one such test did not work, the claim was still enabled over its whole scope (see e.g. paragraphs [0078] and [0079]). The contribution of the invention was the establishment of a link between autoimmune encephalitis and the presence of autoantibodies, thereby defining a new patient group, namely the group of auto-NMDAR encephalitis. The respondent's arguments related to mechanistic considerations which were irrelevant for the claim. The respondent had not discharged its burden of proof that the invention did not work.

Request for referral to the Enlarged Board of Appeal

There was no diverging case law because T 1474/12, which the respondent relied on, was an isolated case which was not even cited in other decisions. In addition, the opposition division had stated in its decision that the conclusions of T 1474/12 did not apply to the present case (page 7 of the appealed

decision). There was thus no need for a reply to the proposed question to the Enlarged Board of Appeal in order to come to a decision in the present case.

VIII. The respondent's arguments, in so far as they are relevant to the present decision, may be summarised as follows:

Main request, claim 1: sufficiency of disclosure

The patent taught the detection of autoantibodies against the NMDA receptor by using an NMDA antigen, but made clear that either the complete NMDAR (tetramer) or heteromers with at least the subunits NR1 and NR2 had to be used, whereas single NMDAR subunits expressed in HEK cells did not work. Claim 1, however, required that the patients' autoantibodies be detected using an NMDAR subunit as a detector antigen. The claimed diagnostic method was not made available in the patent, because the patent presented contradictory data and so the skilled person would not know how to make the method work. The claim was unclear because there were different possible interpretations; hence the description had to be used to interpret it. Since the claim was very broad, showing only one way of carrying out the invention was not enough for enablement; on the contrary, it had to be shown that the invention was feasible over the whole scope of the claim. However, the claim comprised embodiments which were described in the patent as not working. The burden of proof was not on the opponent, since the patent itself showed that the invention did not work over the whole scope claimed. This deficiency could not be resolved by post-published evidence that contradicted the patent's teaching.

Request for referral to the Enlarged Board of Appeal

The conclusions reached by the present board were not in line with decision T 1474/12, which stated that a claim was not sufficiently disclosed when it encompassed embodiments which were explicitly shown in the patent not to lead to the claimed and desired effect. In view of this divergence in case law, a referral to the Enlarged Board of Appeal was necessary.

IX. The appellants requested that the decision under appeal be set aside and that the patent be maintained as granted or, alternatively, on the basis of auxiliary request 3, filed with the statement of grounds of appeal.

The respondent requested that the appeal be dismissed and that auxiliary request 3 not be admitted into the proceedings. Moreover, it requested that a question be referred to the Enlarged Board of Appeal.

Reasons for the Decision

1. The appeal is admissible.

Main request

2. Article 100(b) EPC

2.1 Claim 1 is directed to a method of diagnosing an anti-NMDA receptor encephalitis in a subject, comprising the step of testing a biological sample obtained from the subject for an antibody to an NR subunit of an NMDA

receptor, whereby a presence of said antibody in said biological sample indicates anti-NMDA receptor encephalitis; claim 1 further lists a number of encephalitis-related symptoms characterising the disease to be diagnosed (for the complete wording of the claim, see section I). For the purposes of Article 83 EPC / 100(b) EPC, the patent application must contain an enabling disclosure of testing for an antibody to an NR subunit of an NMDA receptor and it must be rendered at least plausible that such testing is suitable for diagnosing an anti-NMDA receptor encephalitis in a subject.

2.2 At the priority date it was well within the ability of the skilled person to design tests which are suitable for detecting auto-antibodies against the NMDA receptor; as stated in the patent, "Methods and kits for detection of antibodies are well known in the art" (paragraph [0078]). Because the NMDA receptor is exclusively composed of NR subunits (which assemble to form a tetramer/heteromer in the functional receptor), it is clear that any antibody directed against it must be directed to one (or more) of such subunits, as recited in claim 1 as granted. The skilled person would moreover understand that development of autoimmunity against the NMDA receptor requires that this receptor be presented to the immune system, which means that the receptor must be expressed as a cell membrane receptor in its functional form as tetramer. The skilled person would also expect that the auto-antibodies are directed to the part of the NMDA receptor that is exposed at the cell surface, meaning the extracellular domains of its subunits, rather than the transmembrane or intracellular domains, and would take this into consideration when designing possible detection tests.

2.3 The patent teaches a particular type of autoimmune encephalitis which is characterised by the presence of anti-NMDA receptor auto-antibodies in patients' samples (see e.g. paragraphs [0006], [0007]) and [0020]). The board thus considers that it is rendered plausible in the patent that testing for an antibody to an NR subunit of an NMDA receptor is suitable for diagnosing that particular type of autoimmune encephalitis.

2.4 The board concurs with the appellants' interpretation of the claim that it is simply directed to a method of diagnosis to be performed in patients presenting with any of the symptoms listed, wherein the method comprises testing a patient's sample for the presence of an (auto)-antibody that binds to an NR subunit of an NMDA receptor. When such a test is positive, i.e. when such an (auto)-antibody is detected in the patient's sample, then the disease is diagnosed, meaning that the patient is said to have an anti-NMDA receptor encephalitis. The board considers that the claim is not limited to any test in particular and instead merely requires that any suitable test for the detection of an antibody as recited - i.e an antibody that binds a (meaning one or more) NR subunit - be used. Hence the board disagrees with the respondent's view that the claimed method of diagnosis implicitly requires the use of a detection antigen consisting solely of an NR subunit of the NMDA receptor and that the scope of claim 1 includes embodiments which were described in the patent as not working.

2.5 Although the skilled person would be able to develop the required tests without further guidance from the patent, the board notes that the patent does in fact provide examples of tests which could be used and which the skilled person could adopt when carrying out the

invention (e.g. Examples 1 and 4; paragraphs [0018] and [0019] and Figure 8; paragraphs [0101] and [0103]). Additionally, the patent also alerts for test formats that may not work (e.g. expression of single NR subunits in HEK cells: paragraph [0103]), thus providing the skilled person with further guidance. Contrary to the respondent's arguments, those non-working test formats are not part of the claim scope, because the claim is not restricted to any particular test and does not define which detector antigen should be used.

2.6 Accordingly, the board considers that the subject-matter of claim 1 of the main request is sufficiently disclosed in the patent (Article 100(b) EPC).

3. Referral of a question to the Enlarged Board of Appeal

3.1 At oral proceedings, after the board had announced that it considered claim 1 of the main request to be sufficiently disclosed, the respondent requested that a question be referred to the Enlarged Board of Appeal in order to ensure uniform application of the law. The question, which was submitted by the respondent in German, reads as follows:

"*Ist ein Anspruch ausreichend offenbart, wenn er Ausführungsformen umfaßt, die in der Patentschrift von den Erfindern ausdrücklich als nicht zum Erfolg führend herausgestellt sind.*"

It can be translated into English as follows (free translation by the board):

Is a claim sufficiently disclosed when it encompasses embodiments which the inventors explicitly state in the patent do not lead to success?

3.2 The board notes that, as explained above, claim 1 is not considered to encompass non-working embodiments. Thus, the board's conclusions are not in conflict with case law (e.g. T 1474/12). For that reason alone, an answer to the above question is not needed in order to come to a decision in the present case.

3.3 Accordingly, the board rejects the respondent's request for referral of a question to the Enlarged Board of Appeal (Article 112(1)a) EPC).

4. Concluding remarks

At first instance, the respondent had raised further objections to the main request but none of them was pursued in the appeal proceedings. Hence, the board comes to the conclusion that none of the grounds for opposition prejudices the maintenance of the patent as granted.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The patent is maintained as granted.

3. The request for referral to the Enlarged Board of Appeal is rejected.

The Registrar: The Chairwoman:

M. Schalow M. Pregetter

Decision electronically authenticated