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Datasheet for the decision of 29 September 2021

Case Number: T 2513/17 - 3.3.01

Application Number: 11769677.3

Publication Number: 2558863

IPC: G01N33/564, G01N33/573

Language of the proceedings: EN

Title of invention:
COMPOSITIONS AND METHODS FOR CHARACTERIZING A MYOPATHY

Patent Proprietor:
The Johns Hopkins University

Opponent:
Euroimmun Medizinische Labordiagnostika AG

Headword:
Myopathy diagnosis/JOHNS HOPKINS UNIVERSITY

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

Keyword:
Grounds for opposition - novelty, inventive step, sufficiency of disclosure (yes)

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Case Number: T 2513/17 - 3.3.01

D E C I S I O N
of Technical Board of Appeal 3.3.01
of 29 September 2021

Appellant: (Opponent)	Euroimmun Medizinische Labordiagnostika AG Seekamp 31 23560 Lübeck (DE)
Representative:	Richter, Carsten EUROIMMUN Medizinische Labordlagnostika AG Seekamp 31 23560 Lübeck (DE)
Respondent: (Patent Proprietor)	The Johns Hopkins University 3400 North Charles Street Baltimore, MD 21218 (US)
Representative:	Hiebl, Inge Elisabeth Kraus & Weisert Patentanwälte PartGmbB Thomas-Wimmer-Ring 15 80539 München (DE)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 12 September 2017 rejecting the opposition filed against European patent No. 2558863 pursuant to Article 101(2) EPC**

Composition of the Board:

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

Summary of Facts and Submissions

I. European patent 2 558 863 is based on application 11769677.3, which was filed as an international application published as WO 2011/130647. The patent is entitled "Compositions and methods for characterising a myopathy" and was granted with four claims. The patent claims priority from two earlier applications, US patent application number 61/324,857 (first priority) and US patent application number 61/371,798 (second priority).

Claim 1 as granted reads as follows:

"1. An in vitro method for diagnosing an auto-immune-mediated necrotizing myopathy in a mammalian subject by determining the presence of autoantibodies specific for a 3-hydroxy-3-methylglutaryl coenzyme A reductase (HMGCR) protein or a fragment thereof having anti-HMGCR autoantibody binding activity in the subject comprising the steps of:
a) performing an immunoassay by contacting a biological sample obtained from the subject with a HMGCR protein or a fragment thereof having anti-HMGCR autoantibody binding activity,
b) detecting the presence of auto-antibodies in the sample which specifically bind the HMGCR protein or the fragment thereof having anti-HMGCR autoantibody binding activity, wherein the presence of autoantibodies which specifically bind the HMGCR protein or the fragment thereof having anti-HMGCR autoantibody binding activity is indicative that the subject has the myopathy."

II. An opposition was filed against the granted patent, the opponent requesting revocation of the patent in its

entirety on the grounds of lack of novelty and inventive step (Articles 54(2) and 56 EPC and Article 100(a) EPC), and insufficiency of disclosure (Article 100(b) EPC); additionally, the validity of the priority claim was challenged.

III. By its decision announced at oral proceedings, the opposition division decided that the patent as granted fulfilled the requirements of the EPC and rejected the opposition under Article 101(2) EPC.

IV. The opponent (appellant) lodged an appeal against that decision, requesting that the decision of the opposition division be set aside and that the patent be revoked in its entirety.

V. With its reply to the grounds of appeal, the patent proprietor (respondent) requested that the appeal be dismissed.

VI. Summons for oral proceedings before the board were issued. In a subsequent communication pursuant to Article 15(1) RPBA, the board provided its preliminary opinion on some issues, including a preliminary opinion concerning the admission of O16.

VII. By letter dated 27 August 2021, the respondent submitted new claim requests as auxiliary requests I and II.

VIII. Oral proceedings before the board took place as scheduled. At the end of oral proceedings, the chairwoman announced the board's decision.

IX. The documents cited during the proceedings before the opposition division and the board include the following:

O1 Targoff I.N. et al. 1990, Arthritis & Rheumatism 33(9):1361-1370
O2 Reeves W.H. et al. 1986, Proc. Natl. Acad. Sci. USA 83:9507-9511
O4 Dimitri D. et al. 2007, Muscle Nerve 35:389-395
O5 Targoff I.N. et al. 2006, Arthritis & Rheumatism 54(11):3682-3689
O6 Mammen A.L. 2010, Ann. N.Y. Acad. Sci. 1184:134-153
O14 Christopher-Stine L. et al. 2010, Arthritis & Rheumatism 62(9):2757-2766
O15 Mammen A.L. et al. 2011, Arthritis & Rheumatism 63(3):713-721
O16 "Versuchsbericht" by Dr Bianca Teegen (12 pages)
O17 Declaration of Dr Michael Mahler (3 pages)
O21 Alvarado-Cardenas M. et al. 2016, Autoimmunity Reviews 15:1161-1166

X. The appellant's submissions, in so far as relevant to the present decision, may be summarised as follows.

Novelty

There were no significant differences between the disclosures of O14 and the first priority document, but the fact remained that the disclosure of the priority document was not enabling. The same was true for document O15 and the second priority document.

Inventive step

Document O6 could be considered the closest prior art. It disclosed the usefulness of antibody detection assays and suggested that a specific group of patients had antibodies against SRP (signal recognition particle) while others might have them (pages 143 and 144); it thus prompted the skilled person to identify new autoantibodies. There was hence motivation to look for other autoantibodies in this group of patients and a 50% likelihood of finding HMGCR autoantibodies since, as taught in the patent in paragraphs [0095] and [0096], 50% of the patients (i.e. 16 of the 32 patients who did not have anti-SRP autoantibodies) displayed HMGCR autoantibodies. Accordingly, by following the procedure for identification of antigens, which was routine at the priority date and used by the inventors, the skilled person would inevitably arrive at the HMGCR autoantibodies. As to documents O1, O2, O4 and O5, cited by the respondent as evidence that there would be many other possible targets, they were not common general knowledge and were related to other diseases.

The claimed subject-matter also lacked inventive step when documents O14 or O15 were taken as closest prior art.

Sufficiency of disclosure

The disclosure of the patent did not allow the skilled person to carry out the whole subject-matter claimed without undue burden.

In Example 8 of the patent, the test had a sensitivity of only 6% (45 out of 750). Moreover, some patients had autoantibodies but did not test positive (reference was made to paragraph [0070]). Since patients could have the same condition but different autoantibodies, the

assay would not detect such patients. Thus, the method was not very sensitive. Paragraph [0096] in Example 1 of the patent presented evidence of an immunoblot that did not work.

Immunofluorescence (IFT) was given in the patent as a possible diagnostic method, but there was no information on how to perform it, and O16 showed that it did not work in a high number of cases: it only worked in 10% of the cases, the right tissue had to be taken and the skilled person had to make too many selections, and it was not straightforward to distinguish positive from negative results.

Moreover, for ELISA-positive samples, results were discrepant since IFT results were almost all negative.

Claim 1 required more than just a correlation, it also involved putting it into practice by means of a diagnostic assay. The diagnostic reliability was, however, questionable since different methods could lead to different results.

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

Novelty

The disclosure of O14 was completely comprised in the first priority document, corresponding to pages 18 to 49. The disclosure of the priority document in fact went beyond that of O14 since it characterised the target protein as being HMGCR, in contrast to O14, and specifically taught autoantibodies against HMGCR (page 52, claims).

Inventive step

Document O6 was the closest prior art, and the technical effect associated with the distinguishing feature was the identification of a unique subset of patients with myopathy (patent, last sentence of paragraph [0116] and paragraph [0118]). Hence the technical problem could also be formulated as the identification of a unique subset of patients with myopathy. It was not obvious to arrive at this subset of patients because the information in paragraph [0095] of the patent was only part of the invention and not available in the prior art. O6 provided no suggestion or pointer towards HMGCR; page 144, left column, last five lines of the first full paragraph would be interpreted as meaning that patients could have one or more other autoantibodies or even none at all. The remaining prior art, such as O1, O2, O4 and O5, did not provide any pointer either; instead they presented a wide variety of other possible autoantibody targets. Without the knowledge of the patent, the skilled person would not have arrived at this subgroup of patients from O6 in an obvious way.

Sufficiency of disclosure

The invention was not the development of some kind of assay but the establishing of a correlation between the target HMGCR and a new group of patients, i.e. the provision of a new disease marker, the presence of which could be correlated with the presence of the disease. It was not contested that this correlation was present.

The claims were directed to a diagnostic assay which could be put into practice in several ways, as

disclosed on page 12 of the patent, all known to the skilled person. The patent provided at least one way of carrying out the invention, namely by ELISA as described on paragraph [0157]. O16 confirmed that ELISA worked and also showed that IFT worked in 10% of the patients (page 2, section 2.2, last sentence of the first paragraph), further elaborating that what had not worked was the selection of the appropriate cells. O17 and O21 also provided post-published evidence that the invention worked.

It was also normal that discrepancies occur and that experiments could be needed to optimise the assays, but these would be routine. Paragraph [0070] related to healthy patients, so it was not evidence that the assay failed. To the contrary, it showed that the assay was highly specific. As to paragraph [0097], no test was 100% specific, as concluded by the opposition division on page 5, section 12.4 of the decision.

XII. The appellant requested that the decision of the opposition division be set aside and that the patent be revoked in its entirety.

The respondent requested that:
- the appeal be dismissed or, alternatively, that the decision be set aside and that the patent be maintained on the basis of auxiliary requests I or II, both filed with the letter dated 27 August 2021
- document 016 not be admitted into the proceedings.

Reasons for the Decision

1. The appeal is admissible.

2. Novelty (Articles 54(2) and 100(a) EPC)

2.1 The appellant raised objections for lack of novelty of the granted claims (main request) over documents O14 and O15. These documents were published, respectively, after the first priority and after the second priority of the current patent, and the appellant essentially argued that neither of the priority claims was valid because the disclosure of the priority documents did not disclose the claimed subject-matter in an enabling way.

2.2 According to the respondent, 014 and 015 are both comprised in the second priority document, filed on 9 August 2010, while 014 is comprised in the first priority document, filed on 16 April 2010. During oral proceedings, the appellant agreed that there were no relevant differences between the disclosures of O14 and O15 and the priority documents. The board notes that indeed the first priority document comprises the manuscript of 014, while the second priority document comprises the manuscripts of 014 and 015. Moreover, as argued by the respondent, the disclosure of the first priority document even goes beyond that of O14 since it identifies the target protein as being HMGCR and discloses autoantibodies to it (claims on page 52 of the first priority document), while O14 only characterises the potential target protein by reference to its molecular weight. It follows that O14 and O15, being entirely comprised in the priority documents, cannot be used against novelty of the claimed subject-matter because regardless of whether their disclosure anticipates the granted claims, the fact is that the same disclosure is in priority document(s) filed before the publication dates of 014 and 015. Accordingly,

either the priority is valid and O14 and O15 are not prior art, or the priority is not valid (because not all claimed features are enablingly disclosed in the priority document), in which case O14 and O15 cannot be considered novelty-destroying either.

2.3 The granted claims are thus not anticipated by the disclosures of documents O14 and O15. Article 100(a) EPC in combination with Article 54(2) EPC does not prejudice the maintenance of the patent as granted.

3. Inventive step (Articles 56 and 100(a) EPC)

3.1 It is common ground that document O6, which is a review about antibody-mediated myopathy, is the closest prior art. The distinguishing feature from the claimed subject-matter is that O6 discloses the detection of another autoantibody, namely against SRP instead of HMGCR, for the diagnosis of the same disease. Since there is no surprising technical effect linked to the distinguishing feature, the technical problem can be formulated as the provision of an alternative diagnostic method for autoimmune-mediated necrotising myopathy: this formulation of the technical problem was put forward by both parties in their written submissions and maintained at oral proceedings by the appellant. At oral proceedings, the respondent relied on paragraph [0116], last sentence of the patent to present an alternative formulation of the technical problem, namely as a method for the identification of a unique subset of patients with myopathy. In any case, the solution is the method as claimed, and the board is satisfied that the problem, however formulated, has been solved; this has not been disputed by the appellant.

3.2 Document O6 teaches that some but not all patients with necrotising myopathy have autoantibodies against SRP (page 143, left column, section "Anti-signal recognition particle autoantibodies"). It moreover hypothesises that patients that do not display anti-SRP antibodies might have other as yet unidentified autoantibodies (page 144, left column, last two sentences of the first full paragraph). Hence, as argued by the appellant, the skilled person would, in view of these teachings of O6, be motivated to look for other autoantibodies in the patients who do not display anti-SRP autoantibodies.

3.3 It is also true that the skilled person would know routine methods for searching for autoantibodies in the samples of patients with necrotising myopathy but without anti-SRP antibodies. However, there is no pointer in O6 or the remaining prior art to HMGCR as a possible autoantigen against which autoantibodies would be present and could be relied on as a diagnostic marker for autoimmune-mediated necrotising myopathy. To the contrary, other autoantibodies are disclosed not only in O6 (page 139, section "Myositis-specific autoantibodies and their associated clinical features", starting in the left column), but also in O1, O2, O4 and O5. Hence, the skilled person starting from the teachings of O6 would not necessarily identify HMGCR autoantibodies nor would be in a one-way street situation.

3.4 The board is thus not convinced by the appellant's arguments that the skilled person following exactly the same procedure as the inventors would inevitably arrive at the HMGCR autoantibodies. The fact is that there was no pointer in the prior art to HMGCR autoantibodies as a marker for autoimmune myopathy. Moreover, the

indication in the patent that as many as 50% of the autoimmune myopathy patients had such antibodies (paragraphs [0095] and [0096], describing that 16 of the 32 patients that had no anti-SRP antibodies had anti-HMGCR antibodies) was only disclosed in the patent and not in the prior art.

3.5 In its statement of grounds of appeal (page 9), the appellant also appears to rely on documents O14 and O15 for the discussion of inventive step. However, as stated in point 2.2, the priority claim can only be held invalid and O14 and O15 considered prior art if these documents are not enabling. Since the appellant has not provided any reasoning why these non-enabling documents would nevertheless lead the skilled person in an obvious way to the claimed subject-matter, this attack must fail.

3.6 Accordingly, the claimed subject-matter is considered to involve an inventive step. Article 100(a) EPC in combination with Article 56 EPC does not prejudice the maintenance of the patent as granted.

4. Sufficiency of disclosure (Articles 83 and 100(b) EPC)

4.1 Article 83 EPC stipulates that the application must disclose the invention in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art. At least one way of enabling the skilled person in the art to carry out the invention must be disclosed, this being sufficient only if it allows the invention to be performed in the whole range claimed.

4.2 As argued by the respondent, the invention is the provision of a new disease marker, based on the finding

that detection of autoantibodies against HMGCR can be used for the diagnosis of autoimmune necrotising myopathy. There is ample evidence in the patent supporting this finding. Moreover, the carrying out of diagnostic tests based on this finding is extensively disclosed in paragraphs [0064] to [0079] of the patent, and an example is provided using ELISA. Accordingly, at least one way of carrying out the invention is disclosed, and the disclosure of the patent allows the invention to be performed in the whole range claimed. Moreover, there is no evidence on file that the invention did not work; to the contrary, post-published documents O16, O17 and O21 confirm that the invention could be carried out. Certainly the skilled person would have to determine the appropriate conditions to use any particular detection method of HMGCR autoantibodies, but this is within the realm of what a skilled person would routinely do.

4.3 The board is therefore not convinced by the appellant's arguments that the skilled person would be faced with undue burden when carrying out the invention. To the contrary, the skilled person would have to follow routine experimentation when putting the teachings into practice for different diagnostic methods. The fact that there could be discrepancies between different immunoassays or that some assays might not work under given conditions (O16) again would be issues that could be solved by routine experimentation. It is true that some assays might be more complex than others, but the skilled person, relying on their general knowledge in the field, would be in a position to identify and solve problems and to properly analyse the results. Also, the fact that some immunoassays might not have a sensitivity or specificity of 100% is outside the scope

of the invention, which is not directed to particular diagnostic assays.

4.4 The claims of the main request are thus considered to relate to subject-matter sufficiently disclosed in the patent. Article 100(b) EPC does not prejudice the maintenance of the patent as granted.

5. Admission of document O16

5.1 With the reply to the grounds of appeal, the respondent requested that document 016 be not admitted into the proceedings, arguing that the opposition division had improperly exercised its discretion under Article 114(2) EPC when admitting this document into the proceedings. In the communication pursuant to Article 15(1) RPBA, the board provided its preliminary opinion concerning the admission of O16, indicating that it saw no reason to revert the decision of the opposition division concerning the admission of document 016. At the oral proceedings, the parties were given an opportunity to provide their arguments, but both relied on their written comments.

5.2 The board decided to not overturn the decision of the opposition division to admit document O16 into the proceedings. However, in view of the outcome of this appeal, there is no need to further reason this part of the decision.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairwoman:

M. Schalow M. Pregetter

Decision electronically authenticated