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Datasheet for the decision of 16 June 2025

Case Number: T 2008/22 - 3.3.08

Application Number: 17206796.9

Publication Number: 3318881

IPC: G01N33/68, G01N33/92

Language of the proceedings: EN

Title of invention:
METHOD TO MONITOR GAUCHER'S DISEASE

Patent Proprietor:
Centogene GmbH

Opponent:
Sanofi

Headword:
Gaucher's disease/CENTOGENE

Relevant legal provisions:
EPC Art. 83
RPBA 2020 Art. 12(4)

Keyword:
Sufficiency of disclosure - main request (no) - auxiliary requests 1 to 9 (no)
Late-filed auxiliary request 10 - Admission into the appeal proceedings (no)
Late-filed documents - admitted (no)

Decisions cited:
T 0435/20, T 0063/06

Catchword:

Europäisches Patentamt
European Patent Office
Office européen des brevets

Beschwerdekammern

Boards of Appeal

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Case Number: T 2008/22 - 3.3.08

D E C I S I O N
of Technical Board of Appeal 3.3.08
of 16 June 2025

Appellant: (Patent Proprietor)	Centogene GmbH Am Strande 7 18055 Rostock (DE)
Representative:	Bohmann, Armin K. Bohmann Anwaltssozietät Nymphenburger Straße 1 80335 München (DE)
Appellant: (Opponent)	Sanofi 54 Rue La Boétie 75008 Paris (FR)
Representative:	Garner, Stephen, Robinson, Alexander J. Mathys & Squire The Shard 32 London Bridge Street London SE1 9SG (GB)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 27 June 2022 concerning maintenance of the European Patent No. 3318881 in amended form**

Composition of the Board:

Chairwoman	T. Sommerfeld
Members:	D. Pilat
	D. Rogers

Summary of Facts and Submissions

I. European patent No. 3 318 881 was granted on the basis of European patent application No. 17 206 796.9, which was a divisional application from the European patent application No. 12 728 976.7, filed as an international patent application published as WO 2012/167925.

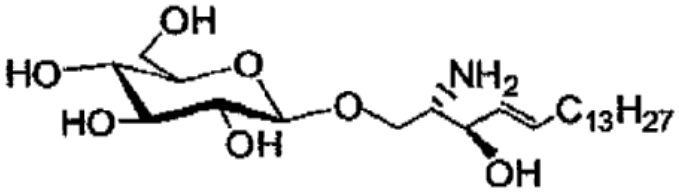
II. The patent was opposed on the grounds of Article 100(a) EPC, in conjunction with Articles 54 and 56 EPC, and of Article 100(b) and (c) EPC. In an interlocutory decision, the opposition division concluded that Article 100(c) EPC prejudiced the maintenance of the patent as granted, that auxiliary requests 1 and 2 were not allowable for lack of compliance with Articles 123(2)/76 EPC, that auxiliary request 3 was not allowable for lack of compliance with Article 54 EPC, but that the patent could be maintained in amended form on the basis of auxiliary request 4, which was held to meet the requirements of the EPC.

III. The patent proprietor and the opponent (appellants I and II, respectively) both lodged an appeal against said decision. Appellant I submitted auxiliary requests 1 to 9 with their statement of grounds of appeal and auxiliary request 10 with their reply to appellant II's appeal.

IV. Claims 1 and 7 of the main request (claims as granted) read:

"1. A method for determining the course of Gaucher's disease in a subject comprising the step of determining at several points in time a level of a biomarker present in a sample from the subject, wherein the

sample is selected from the group consisting of a blood sample, a serum sample, a plasma sample, a whole blood sample and a sample from whole blood collected on a dry blood filter card, wherein the biomarker is free lyso-Gb1 of formula (I)



(I),

and wherein the level of the biomarker is indicative of the severity of the disease in the subject.

...

7. The method of any one of claims 1 to 6, wherein the biomarker is detected by means of immunoassay, mass spectrometric analysis, biochip array, functional nucleic acids and/or a fluorescent derivative of free lyso-Gb1."

V. Claim 1 of **auxiliary requests 1 to 3 and 5 to 7** is identical to claim 1 of the main request. Claim 1 of **auxiliary request 4** differs from claim 1 of the main request by insertion of features from dependent claim 4. Claim 1 of **auxiliary requests 8 to 10** differs from claim 1 of the main request by insertion of the second alternative set out in dependent claim 2 of the main request. Claim 7 of the main request has remained unamended (except for renumbering and adaptation of claim dependencies) in auxiliary requests 1 to 8. In **auxiliary request 9**, claim 5 corresponds to claim 7 of the main request, which has been amended by deletion of the alternatives "biochip array" and "functional nucleic acids". In **auxiliary request 10**, this claim has been deleted.

VI. The documents cited in this decision include the following:

D14 Gomes Muller M.V. *et al.*; Brazilian Journal of Pharmaceutical Sciences, vol. 46, no. 4, pages 643 to 649, 2010

D17 Abstract of Bednar R. Laboratoriumsmedizin vol. 18(5), pages 196 to 199, 1994

D18 Grabowski, G.A.; The Lancet, vol.372, pages 1263 to 1271, 2008

D19 Weinreb, N. J. *et al.*; Genetics in Medicine, vol. 12, no. 1, pages 44 to 51, 2010,

D20 Zimran A. et al.; The Lancet, vol.12, no.2, pages 349 to 352, 1989

VII. In a communication under Article 15(1) RPBA, the parties were informed of the board's provisional opinion on the issues of the case.

VIII. With letter dated 18 October 2024, appellant I announced that it would not attend oral proceedings and requested a decision on the state of the file.

IX. The board cancelled oral proceedings.

X. The parties' submissions, insofar as they are relevant to the decision, are discussed in the Reasons for the decision, below.

XI. The parties' requests, insofar as relevant to the present decision, are as follows:

Appellant I requested that the decision be set aside and the patent be maintained as granted (main request)

or, alternatively, on the basis of the claims of any of auxiliary requests 1 to 10.

Appellant II requested that the decision under appeal be set aside and the patent be revoked in its entirety, and that document D17 not be admitted into the appeal proceedings Moreover, it requested that auxiliary request 10 not be admitted in the appeal proceedings.

Reasons for the Decision

1. Both parties had conditionally requested oral proceedings. However, by informing that it would not attend oral proceedings (see section VIII.), appellant I has in fact withdrawn its request for oral proceedings. As for appellant II, the order of this decision is in agreement with its main request. The present decision could thus be issued without holding oral proceedings.

Admittance of documents D17 to D20 (Article 12(4) RPBA)

2. Document D17 was submitted with appellant I's statement of grounds of appeal, while documents D18 to D20 were submitted with appellant I's reply to appellant II's grounds of appeal. Admission of these documents is thus at the board's discretion pursuant to Article 12(4) RPBA. According to Article 12(4) RPBA, any part of a party's appeal case which does not meet the requirements in Article 12(2) RPBA is to be regarded as an amendment, which may be admitted only at the discretion of the board, and the party shall clearly identify each amendment and provide reasons for submitting it in the appeal proceedings.

3. Appellant I has not provided any justification as to why these documents have not been submitted already during first instance proceedings or as to why they should be admitted into appeal proceedings. The board thus sees no reasons to admit them into the proceedings (Article 12(4) RPBA).

Main request (claims as granted) and auxiliary requests 1 to 9

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

4. Article 83 EPC stipulates that the application shall disclose the invention in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art. The subject-matter of an application must be sufficiently disclosed based on the application as a whole, including examples, and taking into account the common general knowledge of the skilled person. At least one way of enabling the person skilled in the art to carry out the invention must be disclosed, but this is sufficient only if it allows the invention to be performed in the whole range claimed, and the disclosure must be reproducible without undue burden. The related ground for opposition is in Article 100(b) EPC.

5. Claim 1 of the main request is directed to a method for determining the course of Gaucher's disease in a subject comprising determining at several points in time a level of free lyso-Gb1 in a sample from a subject. Dependent claim 7 defines the means of detection (for the full wording of the claims, see section IV above). It encompasses immunoassays as means of detection of free lyso-Gb1, to be used for the purpose of claim 1, i.e. for determining the course of Gaucher's disease. Accordingly, the enablement of the claimed method requires that immunoassays for detection

of free lyso-Gb1 are sufficiently disclosed in the patent, which means that also the antibodies necessary for use in such immunological assays have to be sufficiently disclosed.

6. As argued by appellant II, the patent does not describe or suggest how to obtain the antibodies necessary for use in such an immunological assay. In fact, neither the patent nor the prior art discloses how to generate and obtain an antibody or fragment thereof capable of distinguishing free lyso-Gb1 at low concentrations from other similar molecules, such as glucosylceramide (GlcCer or Gb1) or from lyso-Gb3, which might be present at much higher concentrations in said samples, so as to enable the skilled person to perform immunoassays capable of determining the course of Gaucher's disease.

7. The relevant target molecule, Lyso-Gb1, is a small molecule comprising a single hexose ring joined to a short (C_{13}) lipid tail. Without suitable epitopes for antibody recognition required for the design of an antibody having a sufficiently high specificity and affinity, lyso-Gb1 is expected to be a challenging and unconventional target in the sense of decision T 435/20 (see below). Neither the prior art nor the patent discloses that glucosylsphingosine (lyso-Gb1) is a suitable antigen and that screening methods exist that would allow the selection of antibodies that specifically detect only free lyso-Gb1 at low concentration, knowing that there are many other structurally related small molecules that could be present - even at higher concentrations - in the sample of a subject in whom the course of Gaucher's disease is to be determined.

8. Although the board acknowledges that raising and screening antibodies involves only routine experimentation, this is the case only if the skilled person knows from the disclosure in the patent or from common general knowledge (i) which antigens are suitable for raising antibodies having the desired properties and (ii) which screening process should be used to select these antibodies without undue burden. These two criteria are set out in decision T 435/20 for enablement of antibodies against an unconventional target (point 28 of the Reasons). Thus, the board considers that in the absence of available lyso-Gb1-binding antibodies, which must also be specific and have a high affinity to its target, or of means of obtaining them without an undue burden, the development of such an antibody would require significant research efforts going beyond routine experimentation.

9. Appellant I essentially argued that the burden of proof was on the opponent and that, according to the established practice under the EPC, the patent is given the benefit of the doubt after it is granted. Since document D14 provided evidence that the generation of antibodies binding to lyso-Gb1 is sufficiently disclosed, appellant II could not discharge his or her burden of proof by merely arguing that such antibodies cannot be obtained.

10. It is true, as argued by appellant I, that the opponent bears the burden of proof when arguing that the claimed subject-matter is insufficiently disclosed. However, the patent contains no experimental evidence and/or information on how to obtain the above antibodies. It is therefore enough for appellant II to establish a lack of sufficiency of disclosure by merely raising serious doubts, e.g. by comprehensive and plausible

arguments that the common general knowledge and the patent provide insufficient information to reliably obtain an anti-lyso-Gb1 necessary for the immunoassay of claim 7 (see T 63/06, headnotes, Reasons point 3.3.1; Case law of the Boards of Appeal, 10th edition 2022, hereinafter "Case Law", III.G.5.2.2 c)). It follows that in the absence of evidence that the production of an antibody specifically binding with high affinity to the lyso-Gb1 biomarker was enabled, the burden of proof to demonstrate that suitable antibodies were either available at the relevant time or that they could have been developed on the basis of the disclosure of the patent in combination with the common general knowledge of the skilled person and without an undue burden lies with appellant I (Case Law, II.C.7.3).

11. The board cannot agree with appellant I that, based on the commercially available antibodies in document D14, the skilled person would have routinely generated more specific and/or more sensitive antibodies against its own target molecule and would also have developed antibodies against other similar small target molecules.

12. The opposition division considered that D14 established that it was possible at the date of filing to generate antibodies to glycosydic lipids, which, like lyso-Gb1, were also relatively small molecules (decision under appeal, point 15.5 of the Reasons). However, as argued by appellant II, glucosylceramide (Gb1) and lyso-Gb1 are different compounds, lyso-Gb1 being a deacetylated derivative of Gb1, but even if the structural difference was ignored, the anti-glucosylceramide antibody used in D14 does not specifically detect its own target molecule, glucosylceramide. Hence, D14

cannot be considered as evidence that specific antibodies, allowing to distinguish the small target molecule from other, similar small molecules in the sample, could be produced without undue burden. Even disregarding this fact, D14 provides no indication as to how a suitable antigen can be identified to raise antibodies specific for free lyso-Gb1, or which process for screening antibodies would be capable of identifying those suitable for monitoring the course of Gaucher disease in a subject, which must be capable of detecting free lyso-Gb1 in the blood at a concentration approximately 100 times lower than that of Gb1.

13. Under these circumstances, the board considers that appellant II has convincingly argued that neither the patent nor common general knowledge enable the skilled person to put this feature into practice. Hence the ground for opposition under Article 100(b) EPC prejudices the maintenance of the patent as granted.

14. Given that the use of immunoassays for the detection of Lyso-Gb1 for determining the course of Gaucher disease in a patient is claimed in each of auxiliary requests 1 to 9, the same rationale and conclusions as set out above for the main request apply to auxiliary requests 1 to 9. None of them fulfils the requirements of Article 83 EPC.

Auxiliary request 10

Admittance and consideration

15. Auxiliary request 10 was filed for the first time in appeal proceedings, with the reply to appellant II's appeal.

16. The primary object of appeal proceedings is to review the decision under appeal in a judicial manner (Article 12(2) RPBA). It is a matter of discretion of the board whether or not requests filed for the first time in appeal proceedings, but which could and should have been presented in the previous proceedings, are admitted and considered (Article 12(4) RPBA). In this respect, Article 12(4) RPBA requires that the appellant provides reasons for only submitting new requests in the appeal proceedings, and to indicate the basis for the amendments in the application and explain why the amendments in the request overcome the objections raised.

17. The board considers that since the reply to appellant II's grounds of appeal provided neither reasons nor explained why this new auxiliary request could not have been submitted during opposition proceedings, and how it overcame the objections raised, admittance of this new request into the appeal proceedings under Article 12(2) and (4) RPBA cannot be justified.

18. Even if, *arguendo*, the deletion of a dependent claim (relative to higher-ranking requests) in auxiliary request 10 were intended by appellant I to address the problem under Article 83 EPC in relation to claim 7 of the main request, the board agrees with appellant II that this issue had already been raised since the outset of the opposition procedure (e.g. notice of opposition, section 6.4). Thus, appellant I could and in fact should have filed amended claims in response to this objection already during opposition proceedings, but chose not to do so.

19. In summary, on the basis of the above considerations, auxiliary request 10 is not admitted into the appeal proceedings (Article 12(4) RPBA).

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The patent is revoked.

The Registrar: The Chairwoman:

C. Rodríguez Rodríguez T. Sommerfeld

Decision electronically authenticated