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Datasheet for the decision of 25 February 2025

Case Number: T 0589/22 - 3.3.08

Application Number: 10717531.7

Publication Number: 2419741

IPC: G01N33/74

Language of the proceedings: EN

Title of invention:
RISK ASSESSMENT FOR ANTIBIOTICS TREATMENT IN PATIENTS SUFFERING FROM PRIMARY NON-INFECTIOUS DISEASE BY DETERMINING THE LEVEL OF PROCALCITONIN

Patent Proprietor:
B.R.A.H.M.S GmbH

Opponent:
Radiometer Medical ApS

Headword:
Procalcitonin levels to assess the risk of antibiotic treatment / B.R.A.H.M.S

Relevant legal provisions:
EPC Art. 83
RPBA 2020 Art. 13(2)

Keyword:
Sufficiency of disclosure - main request (no) - auxiliary requests 1 to 5 (no)
Late-filed auxiliary requests 6 and 7 - Admission into the appeal proceedings (no)

Decisions cited:
T 1790/17, G 0002/21, T 0814/12, T 0019/90, T 1020/11, T 0707/18, T 0072/04

Catchword:

Europäisches Patentamt
European Patent Office
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Beschwerdekammern

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Case Number: T 0589/22 - 3.3.08

D E C I S I O N
of Technical Board of Appeal 3.3.08
of 25 February 2025

Appellant: (Opponent)	Radiometer Medical ApS Akandevej 21 2700 Bronshoj (DK)
Representative:	Huenges, Martin Mössinger, Julia Maiwald GmbH Elisenhof Elisenstraße 3 80335 München (DE)
Respondent: (Patent Proprietor)	B.R.A.H.M.S GmbH Neuendorfstrasse 25 16761 Hennigsdorf (DE)
Representative:	Buchanan, Luke Hertin und Partner Rechts- und Patentanwälte PartG mbB Kurfürstendamm 63 10707 Berlin (DE)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 21 December 2021 concerning maintenance of the European Patent No. 2419741 in amended form**

Composition of the Board:

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

Summary of Facts and Submissions

I. European patent No. 2 419 741 is based on European patent application No. 10 717 531.7, filed as an international application published as WO 2010/118855. The patent was opposed on the grounds of Article 100(a) in conjunction with Articles 54 and 56 EPC, and of Article 100(b) and (c) EPC. The opposition division held that the main request (claims as granted) lacked an inventive step and that auxiliary request 1 filed during oral proceedings fulfilled the requirements of the EPC.

II. The opponent (appellant) lodged an appeal against the decision of the opposition division.

III. With its reply to the statement of grounds of appeal, the patent proprietor (respondent) submitted a main request and auxiliary requests 1 to 5.

IV. With a letter dated 10 April 2024, filed in reaction to the board's communication under Article 15(1) RPBA, the respondent submitted further arguments and new auxiliary requests 6 and 7. With a later letter, it submitted new document D17.

V. The claims of the main request are the claims that were found allowable by the opposition division. Claim 1 of the main request reads as follows:

"1. In-vitro diagnostic method for the identification of a subject suffering from a primary non-infectious disease having an increased risk of mortality potentially being induced by the administration of an antibiotic to said subject, comprising the steps of:

i. determining in a sample of blood, plasma or serum from said subject suffering from a primary non-infectious disease the level of Procalcitonin (PCT) or a fragment thereof or a precursor or fragment thereof having a length of at least 12 amino acid residues,

ii. correlating the determined level to a potential risk induced by the administration of an antibiotic,

iii. wherein a concentration of PCT or a fragment or a precursor or fragment thereof having a length of at least 12 amino acid residues below 200 pg/mL in said sample correlates to an increased risk induced by the potential administration of an antibiotic and wherein said subject does not exhibit any symptoms of a bacterial infection."

Claim 1 of **auxiliary request 1** differs from claim 1 of the main request in that the threshold level of PCT is 50 pg/mL, instead of 200 pg/mL.

Claim 1 of **auxiliary request 2** differs from claim 1 of the main request in that the primary non-infectious disease is specified to be cardiac disease.

Claim 1 of **auxiliary request 3** combines the amendments of auxiliary requests 1 and 2.

Claim 1 of **auxiliary request 4** differs from claim 1 of the main request in that the primary non-infectious disease is specified to be acute heart failure.

Claim 1 of **auxiliary request 5** combines the amendments of auxiliary requests 1 and 4.

Auxiliary requests 6 and 7 are based on auxiliary request 4 and 5, respectively, with the additional specification: "…wherein the primary non-infectious disease is acute heart failure with shortness of breath…".

VI. The following documents are cited in this decision:

D1 Maisel A. *et al.* European Journal of Heart Failure vol. 14, pages 278 to 286 (2012)
D3 WO 2008/040328 A2
D13 Nieminen M.S. *et al.* European Heart Journal vol. 26, pages 384 to 416 (2005)
D16 Infection - Wikipedia, The Wayback Machine
D17 Declaration of Prof. Dr. Stefan Anker

VII. The parties' submissions relevant to the decision are discussed in the reasons for the decision below.

VIII. The appellant requested that the decision under appeal be set aside and the patent be revoked in its entirety. It further requested that document D17 and auxiliary requests 6 and 7 not be admitted into the proceedings. Furthermore, it requested that the arguments presented in item II-1 of its statement of grounds of appeal under Article 83 EPC be admitted in appeal proceedings.

IX. The respondent requested that the appeal be dismissed (main request) or that the appealed decision be set aside and the patent be maintained on the basis of one of the auxiliary requests 1 to 7. Furthermore, it requested that the arguments presented in item II-1 of the statement of grounds of appeal under Article 83 EPC

not be admitted and that document D17 and auxiliary requests AR6 and AR7 be admitted into the appeal proceedings.

Reasons for the Decision

Admittance and consideration of a new line of argument under Article 83 EPC

1. The respondent requested that appellant's argument in item II-1 of the statement of grounds of appeal not be admitted under Article 12(4) RPBA. In short, the argument under dispute was that, because all patients in the patent's examples exhibited shortness of breath, which was a symptom of bacterial infection, none of them fell within the scope of claim 1. According to the respondent, this line of argument had not been presented during opposition proceedings under Article 83 EPC, but rather under Article 56 EPC and it was also only addressed by the opposition division under Article 56 EPC. It thus constituted a distinct attack underlying different legal requirements.

2. The board disagrees. Contrary to the respondent's arguments, the objected line of argument had already been presented in opposition proceedings under insufficiency of disclosure in appellant's letter dated 10 September 2021, section V, point 57, which states:

> *"Again, the study reported in the opposed patent involves patients that are outside the claim scope."*

Moreover, also the appealed decision addressed this argument under Article 83 EPC:

> "*The opponent alleged that it is not plausible that the method of claim 1 achieves the claimed purpose,*

i.e., that a PCT concentration below 200pg/mL correlates to an increased risk of an adverse outcome (mortality) upon administration of an antibiotic" (item 9.1),

and concluded that:

"*As discussed above under inventive step the examples disclose a group of patients afflicted with AHF to which antibiotic therapy administered at detected low levels of PCT lead to an increased rate of mortality*" (item 9.3).

The argument under inventive step referred to is found on page 4, third paragraph, of the appealed decision and reads:

"Given that the claim requires that the subject does not exhibit any symptoms of bacterial infection any of the patients showing cough or shortness of breath are excluded from the claim. As such the patients described in the patent ([0049]) and having shortness of breath did not fulfil the claim requirements".

Besides, both the appealed decision (item 9.1) and the minutes of oral proceedings before the opposition division (item 9.2) refer, in the context of these arguments, to "CLBA Chapter II C.7.2", which is the chapter in the Case law of the Boards of Appeal of the European Patent Office, both in 9th edition 2019 or 10th edition 2022, (the latter hereinafter referred to as CLBA), that concerns the level of disclosure required for medical use. Hence, this argument was already on file in the context of Article 83 EPC and was then further elaborated in the statement of grounds of appeal.

3. For completeness, the board notes that, contrary to the respondent's argument, there is no statement in the board's communication under Article 15(1) RPBA that the

above-mentioned arguments of the appellant were only presented and addressed under inventive step. In fact, in item 15 of the communication, the board explicitly referred to the appellant's submissions mentioned above to conclude that the line of argument had been submitted already during first instance, also in the context of sufficiency of disclosure, even if at oral proceedings this argument may have been discussed under inventive step.

4. Accordingly, the line of argument presented in item II-1 of the statement of grounds of appeal under Article 83 EPC is part of appellant's appeal case according to Article 12(2) RPBA and the board has no discretion under Article 12(4) RPBA not to admit it into the appeal proceedings.

Admittance of document D17 into the appeal proceedings

5. Document D17 was filed after notification of the board's communication under Article 15(1) RPBA and therefore Article 13(2) RPBA applies. According to Article 13(2) RPBA, any amendment to a party's appeal case at such a late stage of appeal proceedings is, in principle, not to be taken into account unless there are exceptional circumstances, which have been justified with cogent reasons by the party concerned. Exceptional circumstances are new or unforeseen developments in the appeal proceedings, such as new objections raised by the board or another party, which lie outside the sphere of influence of the party affected by them (CLBA, V.A.4.5.4).

6. The respondent argued that document D17, a declaration of D1's author, was submitted as a legitimate and timely response to a new objection raised by the board,

namely in reaction to the board's preliminary opinion relying on a speculative statement in document D1.

7. The board disagrees with the respondent that there are exceptional circumstances justified by cogent reasons to submit new evidence at this late stage of the proceedings. Contrary to the respondent's arguments, no new objection or a new interpretation of established EPO practice on sufficiency of disclosure have been raised in the communication pursuant to Article 15(1) RPBA. The board merely took up an objection raised by the appellant, as is apparent from points 19 and 20 of the communication wherein reference is explicitly made to passages of the statement of the grounds of appeal. Even if the board's opinion was different to the decision of the opposition division on the same subject, this is to be seen as a normal development in the appeal proceedings, which does not justify the submission of new evidence. Indeed, an objection that was unsuccessful before the opposition division may be considered persuasive and successful by the board, this being one of the possible outcomes of an appeal.

8. As to the respondent's arguments that the board, by disregarding the necessity of verifiable facts for objections under Article 83 EPC, deviated from the established EPO practice in its preliminary opinion, the following is noted. Contrary to these arguments, the board in fact applied this very same standard, as is confirmed by the conclusion of item 20 of the communication: "Thus there are serious doubts substantiated by verifiable facts, based on document D1, as to whether a PCT level of below 200 pg/ml PCT, on its own, can be considered as an indicator of an increased mortality in the selected patients who are being administered antibiotics" (emphasis added).

Hence, the board merely weighed the facts and arguments on file and, applying the established legal standards, came to a different conclusion to that reached by the opposition division.

9. Finally, the arguments that D17 is *prima facie* relevant and is a simple declaration from D1's author do not play a role for admission under Article 13(2) RPBA. While, as argued by the respondent relying on decision T 1790/17, clarification of points in the written proceedings may require submission of new evidence, the board notes that in particular in an *inter partes* proceedings, it is necessary for procedural fairness that all parties are aware of all arguments and evidence at the earliest time point in the appeal proceedings. Since, as discussed above, the objections that the new documentary evidence addresses were already in the proceedings since before the appeal proceedings, there is no justification for filing any further evidence at such a late stage of the proceedings. This cannot be seen as a mere further clarification of points raised earlier in the proceedings. For the sake of completeness, the board moreover notes that the appellant's arguments addressed by document D17 do not play a role in the board's decision on Article 83 EPC (see below), so also in view of this, there is no reason to consider document D17.

10. In view of the above, the board came to the conclusion that there were no exceptional circumstances within the meaning of Article 13(2) RPBA, which would justify the admittance of document D17. Document D17 was not admitted into the appeal proceedings.

Main request

Claim construction

11. Claim 1 is directed to an in vitro diagnostic method for the identification of a subject suffering from a primary non-infectious disease having an increased risk of mortality potentially being induced by the administration of an antibiotic to said subject. Being a diagnostic claim, the purpose of the method is a technical feature of the claim. To achieve this purpose, the diagnostic method includes determining the levels of procalcitonin (PCT) in a sample of blood, plasma or serum from the subject, wherein a concentration of PCT below 200 pg/mL is indicative of an increased risk induced by administration of an antibiotic in a subject that does not exhibit any symptoms of a bacterial infection.

12. Hence, the predictive value of the diagnostic method is restricted to those subjects "suffering from a primary non-infectious disease" (preamble) who do "not exhibit any symptoms of a bacterial infection" (end of item iii). The diagnostic method then allows to identify within this group of subjects those subjects who have an increased risk of mortality potentially being induced by the administration of an antibiotic; in other words, those subjects to whom administration of an antibiotic is contraindicated.

13. The concept of a "subject suffering from a primary non-infectious disease" is interpreted as that the subject has an underlying disease, which can be any disease with the only limitation that it is not an infectious disease. Because this refers however to the primary disease, it does not exclude that a secondary disease may be infectious. In fact, the very problem underlying the invention is that, because infectious diseases

often superimpose on a non-infectious primary disease, there is a need to be able to distinguish those patients who indeed have a superimposed bacterial infection and therefore benefit from antibiotic therapy against those who don't, for whom antibiotic therapy is even contraindicated (patent, paragraphs [0003] and [0004]).

14. As to the further limitation that the subject does not exhibit any symptoms of a bacterial infection, its interpretation was a matter of dispute. The respondent argued that a symptom of bacterial infection referred to symptoms which were indicative of bacterial infection. The board, however, agrees with the appellant that such a symptom is merely a symptom that can be attributed to a bacterial infection but whose presence is not necessarily diagnostic of a bacterial infection. Hence, as argued by the appellant, claim 1 excludes subjects who exhibit any symptoms of a bacterial infection, whether they have a bacterial infection or not. On the other hand, it does not exclude subjects who may indeed have a bacterial infection but do not present any symptoms of such.

15. The presence of a (single) symptom on its own may indicate a particular disease but rarely allows to make a diagnosis of a specific disease. This is why medical practitioners usually need to rely on a combination of symptoms (and often additional data) to be able to make a differential diagnosis, thereby distinguishing one disease or condition from others that have similar signs or symptoms. In the particular case of bacterial infections, symptoms are typically non-specific in that they can also be caused by diseases other than a bacterial infection, e.g by a viral infection or even by non-infectious diseases. These include malaise,

fever, chills, localized redness, swelling and pain, which are however not exclusive of bacterial infections (D16, page 2, "Bacterial or viral"; D13, paragraph bridging pages 394 and 395 referring to "a decrease in general condition" as a symptom of a bacterial infection).

16. The board hence agrees with the appellant that "shortness of breadth" may be such a symptom of a bacterial infection, e.g. as a symptom of pneumonia, which may be of bacterial origin (D3, page 1, line 16 and page 2, lines 4 and 5; see also page 2, lines 20 to 22; lines bridging pages 5 and 6; see also page 10, lines 6 to 9; and D1, page 279, last sentence of Introduction) and is not, as argued by the respondent, to be understood as an exclusive symptom of acute heart failure. Contrary to respondent's arguments, there is no reason to introduce any limitations to the claim which are not there; the patent itself states that shortness of breadth "may have different causes, among them heart diseases" (paragraph [0025]). Accordingly, even if "shortness of breadth" may be disclosed in the patent as a symptom of acute heart failure, which it certainly also is, it is nevertheless also a symptom of bacterial infection (D1, last sentence of Introduction on page 279) and as such one of the symptoms that are excluded by the claim. Accordingly, claim 1 excludes subjects with shortness of breadth.

Sufficiency of disclosure (Article 83 EPC)

17. Article 83 EPC requires that the application discloses the invention in a manner sufficiently clear and complete for it to be carried out by the skilled person. Since claim 1 is directed to a diagnostic method, the purpose of the method (i.e. "identification

of a subject suffering from a primary non-infectious disease having an increased risk of mortality potentially being induced by the administration of an antibiotic to said subject") is an effect that has to be achieved and thus is a functional technical feature of the claim (G 1/03, OJ 2004, 413, point 2.5.2 of the Reasons). Hence, for the requirements of Article 83 EPC to be fulfilled, the patent has to provide suitable evidence that the claimed method allows the diagnosis to be made, or this must be derivable from the prior art or common general knowledge (CLBA, C.II 7.2.1, in particular T 814/12 clarifying that the requirements of Article 83 EPC for a medical use claim apply by analogy to diagnostic use claims).

18. In the patent's Examples, all patients included in the study had shortness of breath, this being in fact an inclusion requirement (opposed patent, paragraph [0049]: "To be eligible patients had to report shortness of breath as their primary complaint upon presentation to the emergency department"). Since, as discussed above, shortness of breath is a symptom of bacterial infection, none of the examples of the patent falls within the scope of the claim. Hence, they cannot provide evidence that the claimed method allows the claimed diagnostic purpose to be achieved. As concluded in the appealed decision (item 9.3), the Examples of the patent disclose that in a group of patients afflicted with acute heart failure (AHF), detection of low levels of PCT, in particular below the threshold of 200pg/mL, is associated with an increased mortality when an antibiotic is administered. This does not necessarily lead to the conclusion that the same applies to the different patient group to which the claim is limited. There is likewise no other teaching in the patent that supports the conclusion that the

method has the claimed diagnostic effect in the patient group as claimed, i.e. patients with a non-infectious primary disease who do not exhibit symptoms of a bacterial infection. There were also no arguments that this would be rendered plausible from the prior art or common general knowledge. Accordingly, the board comes to the conclusion that the claimed subject-matter is not sufficiently disclosed.

19. Under Article 83 EPC, the proof of a claimed therapeutic effect must be provided in the application as filed, in particular if, in the absence of experimental data in the application as filed, it would not be credible to the skilled person that the effect is achieved. A deficiency in this respect cannot be remedied by post-published evidence (decision G 2/21, point 77 of the Reasons). By analogy, the same applies to a claimed diagnostic effect (T 814/12, points 26 and 27 of the Reasons). Hence a reference to the BACH (Biomarkers in Acute Heart Failure) trial in post-published document D1 is of no help in this context. In any case, the same conclusion would also apply to the study in document D1 because also in this study AHF patients with "shortness of breath" were included, thus also patients that do not belong to the same patient group which is claimed.

20. Since the initial plausibility of the claimed diagnostic benefit is not established in the patent application, nor is it rendered plausible by the prior art or common general knowledge, it is not necessary to provide serious doubts supported by verifiable facts to establish that the in-vitro diagnostic method claimed does not meet the requirements of Article 83 EPC. Hence the conclusions of the decisions cited by the respondent, T 19/90 (point 3.3 of the Reasons),

T 1020/11 (point 6 of the Reasons), T 707/18 (point 12 of the Reasons) and T 72/04 (point 3 of the Reasons), are not applicable to the present case. It would be odd to require that the appellant provides verifiable facts to substantiate serious doubts, when the patent application itself and the prior art provide no information on whether the technical effect on which the claimed diagnostic method is based is actually achieved.

21. Thus, the board concludes on the basis of the evidence on file that the main request does not meet the requirements of Article 83 EPC.

Auxiliary request 1
Sufficiency of disclosure

22. Claim 1 of **auxiliary request 1** differs from claim 1 of the main request in that the threshold level of PCT is 50 pg/mL, instead of 200 pg/mL.

23. Claim 1 of auxiliary request 1 only reduces the threshold level of PCT to 50 pg/mL, but otherwise defines the subject to be diagnosed in accordance with claim 1 of the main request.

24. The board considers that since the patent does not provide any supporting evidence for the diagnostic effect that the risk of mortality is achieved in subjects receiving antibiotics with PCT levels below 50 pg/ml, as shown in Figure 2B and 3B of the patent, but additionally who do not exhibit any symptoms of a bacterial infection, the sufficiency of the disclosure for claim 1 of auxiliary request 1 must be denied for the same reasons as set out above for claim 1 of the main request.

Auxiliary requests 2 and 4
Sufficiency of disclosure

25. Claim 1 of **auxiliary requests 2 and 4** differs from claim 1 of the main request in that the primary non-infectious disease is specified to be cardiac disease or acute heart failure, respectively.

26. Apart from the definition of the underlying primary disease, claim 1 of auxiliary requests 2 and 4 still defines the subject to be diagnosed in accordance with claim 1 of the main request. As the patent does not provide evidence which would support the diagnostic effect, namely that the risk of mortality is achieved in subjects receiving antibiotics with PCT levels below 200 pg/ml, and who do not exhibit any symptoms of a bacterial infection, the sufficiency of disclosure for claim 1 of auxiliary requests 2 and 4 must be denied for the same reasons as set out for claim 1 of the main request.

Auxiliary requests 3 and 5
Sufficiency of disclosure

27. Claim 1 of **auxiliary requests 3 and 5** differs from claim 1 of auxiliary requests 2 and 4, respectively, in that the threshold level of PCT is 50 pg/mL, instead of 200 pg/mL.

28. Again claim 1 of auxiliary requests 3 and 5 still defines the subject to be diagnosed in accordance with claim 1 of the main request. As the patent does not provide evidence which would support the diagnostic effect, namely that the risk of mortality is achieved in subjects receiving antibiotics with PCT levels below

50 pg/ml, and who do not exhibit any symptoms of a bacterial infection, regardless of whether or not they have a bacterial infection, the sufficiency of disclosure for claim 1 of auxiliary requests 3 and 5 must be denied for the same reasons as set out above for claim 1 of the main request.

29. Thus, the board concludes on the basis of the evidence on file that none of the auxiliary requests 1 to 5 meet the requirements of Article 83 EPC.

Admittance of auxiliary requests 6 and 7 (Article 13(2) RPBA)

30. The respondent essentially argued that the new line of arguments under Article 83 EPC led to a new legal situation to which the respondent should legitimately be allowed to react. By specifying that the primary non-infectious disease is acute heart failure with shortness of breath, it was made clear that shortness of breadth was associated with the underlying disease acute heart failure and was not to be considered a symptom of bacterial infection. Hence, these auxiliary requests addressed the issue of sufficiency of disclosure, did not introduce a lack of clarity, were *prima facie* allowable and were not detrimental to procedural economy. They should thus be admitted, as they fulfilled the criteria for admission listed in CBLA V.A.4.5.10.

31. For the reasons set out above in relation to the admittance of document D17, the board considers that no new objection was raised by the board in its preliminary opinion; nor has there been a new or unforeseen development in the appeal proceedings. For this reason alone, the board cannot acknowledge any exceptional circumstance that would justify admittance

of auxiliary requests 6 and 7. Furthermore, they also do not *prima facie* overcome the existing objection of sufficiency of disclosure, but introduce new problems of clarity in claim 1. The board agrees with the appellant that "wherein the primary non-infectious disease is acute heart failure with shortness of breath" *prima facie* contradicts the exclusion defined in the last sentence of claim 1, so that for this reason too, auxiliary requests 6 and 7 are not clearly allowable.

32. In this respect, the board disagrees with the respondent that decision T 1790/17, stating that the board still had to consider and balance all relevant circumstances when using its discretion under Article 13(2) RPBA, should be followed. This decision on an ex parte case does not apply in the present case, which, contrary to T 1790/17, addresses objections already raised in the statement of grounds of appeal instead of objections and concerns raised by the board (T 1790/17, point 7 of the reasons).

33. The board therefore decided not to admit auxiliary requests 6 and 7 into the appeal proceedings under Article 13(2) 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