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Datasheet for the decision of 13 October 2020

Case Number: T 2306/16 - 3.3.01

Application Number: 07785730.8

Publication Number: 2064553

IPC: G01N33/68

Language of the proceedings: EN

Title of invention:
DIAGNOSTIC TEST TO EXCLUDE SIGNIFICANT RENAL INJURY

Patent Proprietor:
Antibodyshop A/S

Opponent:
Gentian AS

Headword:
NGAL for detection of acute renal failure/ANTIBODYSHOP

Relevant legal provisions:
EPC Art. 100(a), 123(2), 83, 54, 56

Keyword:
Novelty - main request and auxiliary requests 1 and 2 (no) - auxiliary request 3 (yes)
Amendments - allowable, auxiliary request 3 (yes)
Sufficiency of disclosure - auxiliary request 3 (yes)
Inventive step - auxiliary request 3 (yes)

Decisions cited:
T 0172/99

Catchword:

Europäisches Patentamt
European Patent Office
Office européen des brevets

Beschwerdekammern

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Chambres de recours

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Case Number: T 2306/16 - 3.3.01

D E C I S I O N
of Technical Board of Appeal 3.3.01
of 13 October 2020

Appellant: (Patent Proprietor)	Antibodyshop A/S Tuborg Havnevej 15, st. 2900 Hellerup (DK)
Representative:	Høiberg P/S Adelgade 12 1304 Copenhagen K (DK)
Respondent: (Opponent)	Gentian AS P.O. Box 733 1509 Moss (NO)
Representative:	Reitstötter Kinzebach Patentanwälte Sternwartstrasse 4 81679 München (DE)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 12 August 2016 revoking European patent No. 2064553 pursuant to Article 101(3)(b) EPC**

Composition of the Board:

Chairman	A. Lindner
Members:	T. Sommerfeld
	L. Bühler

Summary of Facts and Submissions

I. European patent No. 2064553 is based on European patent application No. 07785730.8, which was filed as an international application and published as WO 2008/017306. The patent is entitled "Diagnostic test to exclude significant renal injury" and was granted with 14 claims.

Claim 1 as granted reads as follows:

"1. An *in vitro* method of diagnosing, monitoring or determining the risk of developing acute renal failure in a human subject, wherein said method discriminates between a subject who does not have acute renal failure and is not at immediate risk of developing acute renal failure, and a subject who may have acute renal failure or is at risk of developing acute renal failure, said method comprising the steps of

i) determining the concentration of human neutrophil gelatinase-associated lipocalin (NGAL) in a sample of urine, plasma or serum from the subject, and
ii) comparing said concentration with a predetermined cutoff value chosen so that an NGAL concentration below the cutoff value categorizes the subject as not having and not being at immediate risk of developing acute renal failure,
wherein said cutoff value is a concentration of 150 ng/mL or a lower value for a urine sample, and wherein said cutoff value is a concentration of 200 ng/mL or a lower value for a plasma or serum sample."

II. Opposition to the granted patent was filed, the opponent requesting that the patent be revoked in its

entirety on the grounds of lack of novelty and inventive step (Articles 54(2), 56 and 100(a) EPC), lack of sufficiency of disclosure (Article 100(b) EPC) and added subject-matter (Article 100(c) EPC); additionally, the opponent contested the validity of the priority claim.

III. In its decision, which was announced at the oral proceedings, the opposition division revoked the patent under Article 101(2) and (3)(b) EPC.

IV. The patent proprietor (appellant) lodged an appeal against that decision. With the statement of grounds of appeal, the appellant requested that the decision be set aside and the patent be maintained as granted (main request) or, alternatively, according to one of the first to eighth auxiliary requests, all of which were filed with the grounds of appeal. It also submitted a new document, D19.

The **main request** consists of the claims as granted.

Claim 1 of the **first auxiliary request** differs from claim 1 of the main request in that the cutoff values for urine samples are further defined as being a concentration "between 150 ng/mL and 100 ng/mL, such as 125 ng/mL, or a concentration between 100 ng/mL and 50 ng/mL, such as 75 ng/mL".

Claim 1 of the **second auxiliary request** is based on claim 1 of the first auxiliary request, with a further amendment defining the cutoff values for plasma or serum samples as being a concentration "between 200 ng/mL and 150 ng/mL, such as 175 ng/mL or 160 ng/mL or 155 ng/mL, or a concentration between 150 ng/mL and 100 ng/mL, such as 125 ng/mL".

In the **third auxiliary request**, claim 1 was further amended to define the cutoff values for urine samples as being "between 150 ng/mL and 100 ng/mL, such as 125 ng/mL". Dependent claims 2 to 12 are specific embodiments of the method of claim 1.

V. The opponent (respondent) replied to the statement of grounds of appeal, requesting that the appeal be dismissed and that the sixth, seventh and eighth auxiliary requests not be admitted into the proceedings. The respondent moreover provided arguments regarding added subject-matter, priority, novelty, inventive step and sufficiency of disclosure.

VI. A summons to oral proceedings before the board was issued, followed by a communication pursuant to Article 15(1) RPBA.

VII. In view of the appellant's request that oral proceedings take place by videoconference, the board sent a further communication, enquiring whether the respondent agreed to this. By its fax dated 22 September 2020, the respondent informed the board that it would not be attending the oral proceedings.

VIII. The oral proceedings before the board took place by videoconference, in the absence of the respondent. At the end of the oral proceedings, the chairman announced the board's decision.

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

D5 Mishra et al., The Lancet (2005) 365, 1231-1238

D6 W02005/121788
D7 Bangert et al., Inflamm. Res. (2007), Suppl. 2, 104-105
D8 Haase et al., Am. J. Kidney Diseases (2009) 54, 6, 1012-1024
D10 Uttenthal, Clinical Laboratory International (CLI) (2007)
D11 Cai et al., Clin. J. Am. Soc. Nephrol. (2010) 5, 2229-2235
D12 Kjelsden et al., J. Immunol. Methods (1996) 198, 155-164
D13 Xu et al., J. Immunol. Methods (1994) 171, 245-252
D16 Bläser et al., Clinica Chimica Acta (1995) 235, 137-145
D17 Wheeler et al., Crit. Care Med. (2008), 36, 1297-1303
D18 W02006/066587
D19 Bennett et al., Clin. J. Am. Soc. Nephrol. (2008) 3, 665-673

X. The appellant's submissions may be summarised as follows:

Main request: interpretation of claim 1

The method claimed in claim 1 of the main request was a method that made it possible to identify all patients at risk of developing acute renal failure, with a negative predictive value of 100%. Any cutoff value below the upper limit of the given ranges provided such a negative predictive value of 100%. The choice of the appropriate cutoff involved a trade-off: the cutoff should be as high as possible, so as to identify all patients that had or were at risk of having acute renal failure, but at the same time should be able to

correctly exclude all patients that were not at risk, as was illustrated in the figure on page 10 of the grounds of appeal.

Main request, first and second auxiliary requests: novelty

Document D5 was concerned with the diagnosis of acute renal failure and not with the identification of patients that did not have a risk of developing acute renal failure. D5 identified cutoff values with a 100% negative predictive value, but the skilled person would immediately realise that the NGAL levels measured in D5 were too low and could not be correct. At the time when the patent was filed, groups working in the same area reported NGAL levels in normal serum of above 60 ng/mL (D13, D16, D17 and D18), i.e. much higher than the level reported in D5. Even the authors of D5 recognised this, in their later publication D17 and again in D19. D17 attributed the differences to the measurement techniques, but in fact the same methods had been used in D5 and D17. D5 was thus not an enabling disclosure and therefore should not be considered as part of the prior art.

Third auxiliary request: inventive step

Claim 1 defined ranges for the cutoff value for urine and plasma or serum samples. While some of these cutoff values for urine were also disclosed in D5, it was apparent from Table 2 of D5 that they did not have a negative predictive value of 100%. As for the claimed cutoff values for serum and plasma, these were not disclosed in D5: extrapolating from the values that were disclosed in Table 2, one would conclude that the claimed cutoff values for plasma and serum would have a

negative predictive value far below 100%. Hence, starting from D5 the skilled person would consider that much lower cutoff values were needed than those stated in the claim, and would not be motivated to use higher cutoff values instead.

XI. The respondent's arguments were submitted in writing. Where relevant for the present decision, they may be summarised as follows:

Main request: interpretation of claim 1

The patent did not provide explicit definitions of the groups of subjects between which a discrimination was to be made. From Figure 1 and paragraphs [0014] and [0015] it could be assumed that the inventors had performed a conventional quantitative determination of the maximum urinary concentration of NGAL in said group of patients, correlating said data retrospectively with the observation of whether or not said patients had developed acute renal failure, and retrospectively determining a cutoff value discriminating between patients who did not have acute renal failure and those who had developed acute renal failure.

Priority

Since the disclosures of the patent application and the priority document were practically identical, priority was not validly claimed for the subject-matter of claim 1, for the reasons given under Article 123(2) EPC. Accordingly, documents D7 and D10 were citable prior art.

Main request, first and second auxiliary requests: novelty

Document D5 (and D6) disclosed NGAL as a biomarker for acute renal injury after cardiac surgery in children, and identified a urinary cutoff value of 50 ng/mL that made it possible to predict whether patients would develop acute renal failure later on (D5: page 1234, right-hand column to page 1235, left-hand column and page 1236, middle of right-hand column; D6: paragraphs [0062] and [0064] and Figure 6).

Third auxiliary request: added subject-matter

There was no basis for the selection of the specific bodily fluid samples, in particular in combination with the respective cutoff value ranges. The application as filed did not teach that specific ranges applied to specific sample types: on the contrary, on page 6, lines 15 to 21 and lines 30 to 35, it was stated that the cutoff values for plasma or serum and urine were similar. Since only urine samples had been analysed, it had to be concluded that in fact the cutoff values for plasma or serum samples had to be extrapolated from the values for urine samples and would therefore indeed have to be similar. Finally, while the description as granted had been adapted to the wording of claim 1, paragraph [0021] still referred, "wrongly and not supported by the original disclosure", to plasma and serum cutoffs as being similar to those of urine.

Third auxiliary request: sufficiency of disclosure

The lack of clear teaching in the contested patent on the criteria making it possible to identify a subject as not having acute renal failure and not being at immediate risk of developing it, or alternatively as possibly having acute renal failure or being at risk of

developing it, meant that the skilled person would not be able to carry out the invention without undue burden. The skilled person would have to run their own research programme to define medical parameters for patients who were "not at immediate risk of developing acute renal failure" and patients who were "at risk of developing acute renal failure" and to correlate such patients with a suitable cutoff range for each of the different bodily fluid samples (urine, plasma, serum). Moreover, the invention was based on a single "study of unselected adult patients admitted to intensive care" (patent, paragraph [0015]) and only urine samples had been analysed. It was however apparent, e.g. from D8, that the type of primary disease ultimately resulting in acute renal failure drastically affected the NGAL cutoff value to be chosen. The antibody used for NGAL detection also had an impact, because it was known from D11 and D12 that several molecular forms of human NGAL existed in urine and blood which were apparently immunologically different. As to the serum and plasma samples, there was no data at all in the contested patent. Finally, the claimed subject-matter was defined by unfamiliar parameters such as the selection criterion of the group of patients and the discrimination criterion, for which the patent did not fulfil the "particular obligation to disclose all the information necessary reliably to define the new parameter" (T 172/99, catchword).

Third auxiliary request: novelty

The lower value of 100 ng/mL for urinary NGAL was explicitly disclosed in D5 (Table 2) and D6 (Table 2). Since the claims were not restricted to particular negative predictive values, in particular not to a

value of 100%, the subject-matter of claim 1 was anticipated by D5 or D6.

Third auxiliary request: inventive step

Documents D5 and D6 were the closest prior art and, since there was no comparative data making it possible to define any surprising advantageous effect associated with the claimed subject-matter, the problem was formulated as the provision of an alternative method of diagnosing, monitoring or determining the risk of developing acute renal failure. The solution, which consisted in defining a different range of cutoff values, was just an arbitrary modification with a foreseeable outcome. Moreover, document D18 explicitly stated on page 23, first and second paragraphs, that urinary NGAL values below a range of 370 to 329 ng/ml and plasma NGAL values below 436 to 355 ng/ml were not diagnostic for renal disorders, and this provided a motivation to look for cutoff values below said ranges.

XII. The appellant requests that the decision under appeal be set aside and the patent be maintained as granted (main request) or, alternatively, according to one of the first to eighth auxiliary requests, all filed with the statement of grounds of appeal.

The respondent requests that the appeal be dismissed and that the sixth, seventh and eighth auxiliary requests not be admitted into the proceedings.

Reasons for the Decision

1. The appeal is admissible.

2. The oral proceedings took place in the absence of the respondent, who had been duly summoned but decided not to attend, as notified in its fax dated 22 September 2020. In accordance with Rule 115(2) EPC, the board decided to continue the proceedings in its absence.

Moreover, pursuant to Article 15(3) RPBA, the board was not obliged to delay any step in the proceedings, including its decision, by reason only of the absence at the oral proceedings of any party duly summoned. Accordingly, the absent respondent was treated as relying only on its written case.

Main request

3. Interpretation of claim 1

3.1 Claim 1 of the main request is directed to an in vitro method of diagnosing, monitoring or determining the risk of developing acute renal failure in a human subject, wherein said method is based on the determination of NGAL in a sample of urine, plasma or serum from the subject. According to the claimed method, a measured concentration of NGAL which falls below a predetermined cutoff value makes it possible to conclude that the subject does not have and is not at immediate risk of developing acute renal failure, while a concentration above said cutoff value indicates that the subject may have acute renal failure or is at risk of developing acute renal failure. This is because, as explained by the appellant and stated in the patent (e.g. paragraphs [0019] and [0021]), the cutoff values falling within the claimed ranges all have a negative predictive value of 100%, which is required in order

for the method to be able to discriminate between the two groups of patients recited in the claim.

4. Novelty (Article 100(a) EPC

4.1 Document D5 discloses the use of NGAL as a biomarker for acute renal injury after cardiac surgery and teaches that "all children who subsequently developed acute renal injury had a concentration of urinary NGAL above an arbitrary cutoff value of 50 µg/L, whereas only one of 51 controls had a value above this arbitrary cutoff" (page 1235, left-hand column, last four lines of first paragraph; results illustrated in Figure 2). Similar results were obtained for serum NGAL concentrations, namely that "none of the 51 children who never developed acute renal injury had a value above an arbitrary cutoff of 50 µg/L, whereas ten of 20 children who developed acute renal injury had a concentration in serum above this value" (page 1235, left-hand column, last five lines of second paragraph; results illustrated in Figure 3). In the Discussion section, D5 concludes that "Our results indicate that NGAL is not only a powerful immediate early biomarker for acute renal injury, (...), but is also a valid discriminatory marker for the entire duration of the study" (page 1236, right-hand column, last five lines of second paragraph).

4.2 Hence, the board concludes that document D5 discloses a method of determining the risk of developing acute renal failure in a human subject with all the features of the method as claimed in claim 1 of the main request. The cutoff value of 50 µg/L (i.e. 50 ng/mL) identified in D5 for urine samples falls within the claimed range of "150 ng/mL or lower" for urine

samples, and has a negative predictive value of 100%, as shown in Table 2 of D5.

4.3 The appellant argued that the skilled person would immediately recognise that D5's teaching was erroneous, and therefore not enabling for any clinically relevant cutoff values, because all other groups working in the same area (D13, D16), and even the group of D5 in later publications (D17, D19), had provided completely different NGAL levels in normal urine. Since D5 was a non-enabling disclosure it did not form part of the prior art.

4.4 While there might have been prior art that taught significantly higher serum NGAL values in healthy individuals than those indicated in D5 (as described at length by the appellant in its statement of grounds of appeal), the board disagrees that the skilled person would immediately consider the disclosure of D5 to be necessarily erroneous. Rather, the skilled person would have considered that these divergent measurements could have to do with the different populations analysed or different methods used, for example. This is also acknowledged in the patent itself, which states in paragraph [0018] that the cutoff level "will depend on the characteristics of the patient population or group to which the test is applied". It must moreover be noted that the control levels are quite different from publication to publication, even among the rest of the prior art. Furthermore, the later publications by the authors of D5 hypothesise that the discrepancies have to do with different measuring methods (D17, page 1300, right-hand column, lines 51 to 53), or even state that the results support the findings of document D5 (D19, page 670, left-hand column, lines 7 to 11). Hence, the board fails to see any indication in the prior art

allowing a conclusion that the skilled person would simply have discarded the data of D5 as incorrect. Accordingly, the disclosure of D5 is considered enabling.

4.5 The main request is thus not allowable, because it lacks novelty over D5 (Article 100(a) EPC).

First and second auxiliary requests

5. Novelty (Article 54 EPC)

5.1 Claim 1 of these requests defines the cutoff value for a urine sample as being between 150 and 100 ng/mL, such as 125 ng/mL, or a concentration between 100 ng/mL and 50 ng/mL, such as 75 ng/mL. Because the cutoff value of 50 ng/mL for urine samples is still encompassed in claim 1 of these requests, these requests also lack novelty over D5, for the same reasons as given above for the main request.

5.2 The first and second auxiliary requests are thus also not allowable, because they fail to comply with Article 54(2) EPC.

Third auxiliary request

6. Article 123(2) EPC

6.1 Claim 1 of the third auxiliary request differs from claim 1 as originally filed in that the following amendments have been inserted:

"1. An *in vitro* method of diagnosing, monitoring or determining the risk of developing acute renal failure in a human subject, wherein said method discriminates

between a subject who does not have acute renal failure and is not at immediate risk of developing acute renal failure, and a subject who may have acute renal failure or is at risk of developing acute renal failure, said method comprising the steps of
i) determining the concentration of human neutrophil gelatinase-associated lipocalin (NGAL) in a sample of ~~bodily fluid~~ urine, plasma or serum from the subject, and
ii) comparing said concentration with a predetermined cutoff value chosen so that an NGAL concentration below the cutoff value categorizes the subject as not having and not being at immediate risk of developing acute renal failure,
wherein said cutoff value is a concentration between 150 ng/mL and 100 ng/mL, such as 125 ng/mL, for a urine sample, and wherein said cutoff value is a concentration between 200 ng/mL and 150 ng/mL, such as 175 ng/mL or 160 ng/mL or 155 ng/mL, or a concentration between 150 ng/mL and 100 ng/mL, such as 125 ng/mL for a plasma or serum sample."

6.2 The board considers that it is implicit that the method of original claim 1 is an vitro method, because the claim explicitly states that the concentration of NGAL is to be determined in a sample. As to the further amendments, the board considers that they are based in original claims 2 and 3, which further define the method of claim 1 as filed as shown:

"2. The method of claim 1, wherein the sample is a urine sample and the cutoff value is a concentration of 250 ng/mL or a lower value, such any [sic] value between 250 ng/mL and 200 ng/mL, such as 225 ng/mL, or any value between 200 ng/mL and 150 ng/mL, such as 175 ng/mL or 160 ng/mL or 155 ng/mL, or any value between

150 ng/mL and 100 ng/mL, such as 125 ng/mL, or any value between 100 ng/mL and 50 ng/mL, such as 75 ng/mL."

"3. The method of claim 1, wherein the sample is a plasma or serum sample and the cutoff value is 250 ng/mL or a lower value, such any [sic] value between 250 ng/mL and 200 ng/mL, such as 225 ng/mL, or any value between 200 ng/mL and 150 ng/mL, such as 175 ng/mL or 160 ng/mL or 155 ng/mL, or any value between 150 ng/mL and 100 ng/mL, such as 125 ng/mL."

6.3 According to originally filed claims 2 and 3, the sample of bodily fluid is urine (claim 2) or plasma or serum (claim 3) and the cutoff value is a concentration of 250 ng/mL or lower or a value to be chosen from subranges of this larger range, including the range "between 150 ng/mL and 100 ng/mL, such as 125 ng/mL", for the urine sample or the ranges "between 200 ng/mL and 150 ng/mL, such as 175 ng/mL or 160 ng/mL or 155 ng/mL, (...), such as 125 ng/mL" for the plasma or serum sample. Hence, all the claimed ranges are disclosed in combination with the respective samples.

6.4 Accordingly, the board considers that claim 1 of the main request does not add subject-matter.

6.5 The respondent raised a further objection under Article 123(2) EPC as regards the description as granted, arguing that the adapted description of the patent as granted still referred to plasma cutoffs "similar to that of urine" at paragraph [0021]. However, the board fails to see how this can be part of an objection under Article 123(2) EPC; rather, it would appear to be an objection under Article 84 EPC, which may have to be

dealt with when adapting the description to the allowable claim set.

7. Article 83 EPC

7.1 Article 83 EPC requires a European patent application to disclose the invention in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art.

7.2 The respondent argued that Article 83 EPC was not fulfilled, on the one hand because the particular patient subpopulations to be discriminated between by the claimed analytical method were not sufficiently disclosed, and on the other hand because there was lack of experimental evidence.

7.3 The board agrees that it might not be absolutely clear where the borders are between the group of patients who are at immediate risk of developing acute renal failure and the group of patients who are at risk of developing acute renal failure. However, contrary to the respondent's arguments, the board considers that this lack of clarity does not result in an undue burden for the skilled person to carry out or reproduce the invention. According to the claimed invention, the skilled person only has to determine the patient's NGAL levels in urine, plasma or serum samples and conclude whether they are above or below a given cutoff value, which can be any value within the range given in the claim: if the determined value is above the cutoff value the patient will be identified as belonging to the group of patients that "may have acute renal failure or is at risk of developing acute renal failure", while if the determined value is below the cutoff value the patient will be identified as

belonging to the group of patients that "does not have and is not at immediate risk of developing acute renal failure". Hence, the skilled person can carry out the invention without undue burden, and the board fails to see how the selection criterion of the group of patients and the discrimination criterion are to be considered unclear parameters for which the patent must fulfil the "particular obligation to disclose all the information necessary reliably to define the new parameter" (T 172/99, catchword).

7.4 It is true that the contested patent contains little experimental data and that the only information provided concerning the characteristics of the studied patient population is that they were "unselected adult patients admitted to intensive care". The board agrees that factors such as age, sex, disease state and underlying disease may all have an impact in the NGAL measurements. However, the aim of the present invention is not to identify specific cutoff values for all possible subgroups of patients but rather to identify cutoff values that apply in general to all patients with a disease requiring intensive care treatment. The inventors have thus identified the cutoff values that resulted in a negative predictive value of 100% in the studied population, and the board sees no reason to doubt that they can be applied generally. In fact, contrary to the respondent's arguments, the board fails to see how the cutoff values identified in the post-published document D8 for specific clinical settings such as after cardiac surgery, critically ill patients and after contrast infusion should invalidate the cutoff values of the method as claimed. First, it is not clear, either from the respondent's submissions on page 19 of its reply to the grounds of appeal or from Table 5 of D8, whether these values refer to urine or

to plasma/serum samples. Second, there is no indication of their negative predictive value, so these values cannot be compared to the values as claimed. Third, for two of the three exemplified clinical settings the indicated cutoff values do in fact fall within the ranges given in the claim, both for urine and for plasma or serum samples: these clinical settings are "critically ill patients" and "after contrast infusion", for which cutoff values of 155 ng/mL and 100 ng/mL respectively are given; it should be noted that the term "critically ill patients" represents a clinical setting which is as ill defined as "patients requiring intensive care", and probably covers the same group of patients. As for the third setting, "after cardiac surgery", the cutoff value for this is higher than the claimed ranges, namely 273.6 ng/mL: nonetheless, it is still true that the negative predictive value of the claimed ranges would remain 100% for this clinical setting, but the number of false positives might be higher.

7.5 The respondent further argued that the type of antibody used could also have an impact on the measured NGAL levels, and referred to documents D11 and D12 as evidence that there were immunologically different forms of NGAL in urine and blood that would not all be identified by all available anti-NGAL antibodies. While this may be the case, the board notes that the claim refers to NGAL in general. The skilled person would thus understand that the method requires the use of antibodies that recognise all forms of NGAL and that the cutoff values relate to total NGAL.

7.6 Finally, as regards the respondent's argument that the contested patent provides no data for serum or plasma samples, the board notes that the patent does in fact

teach that plasma and serum samples were analysed, as were the urine samples for which the data is presented in the patent, and that the cutoff values were calculated in the same way: i.e. the maximum cutoff value for which there was a 100% negative predictive value. The board accepts the appellant's arguments that there is no need to include the raw data in the application, the conclusions provided being plausible even in the absence of this data.

7.7 The board comes to the conclusion that the third auxiliary request fulfils the requirements of Article 83 EPC.

8. Priority - status of D7 and D10

8.1 The respondent stated that the priority claim was not valid, essentially arguing that, since granted claim 1 and the description contained subject-matter which had no basis in the application as filed, said subject-matter could not benefit from priority either, the disclosures of the priority document and of the application as filed being "practically identical".

8.2 As already stated in the board's communication under Article 15(1) RPBA, to which the respondent has not replied, the board notes that the respondent's line of argument, which even admits that the disclosures of the priority document and of the application are essentially identical, can hardly substantiate an objection for lack of validity of the priority claim. Rather, the board would either come to the conclusion that the relevant subject-matter contravened Article 123(2) EPC, in which case the priority issue would be irrelevant, or would conclude that the subject-matter complied with Article 123(2)EPC, in which case priority

would also be valid. As set out above, the board concludes that Article 123(2) EPC is valid, and therefore priority must also be valid.

8.3 Since documents D7 and D10 would only be citable in the event that the priority was found invalid, the board comes to the conclusion that these documents are not part of the prior art.

9. Article 54(2) EPC

9.1 In claim 1 of this request, the cutoff values are defined as being between 150 ng/mL and 100 ng/mL, such as 125 ng/mL, for a urine sample, and between 200 ng/mL and 150 ng/mL, such as 175 ng/mL or 160 ng/mL or 155 ng/mL, or between 150 ng/mL and 100 ng/mL, such as 125 ng/mL for a plasma or serum sample.

9.2 The respondent argued that the parameter range for urinary NGAL in D5 included the lower value of 100 ng/mL, as explicitly disclosed in Table 2 of D5. However, the board notes that Table 2 of D5 teaches a negative predictive value of 89% for said cutoff for urinary NGAL, which, as explained above under section 3.1, does not make it possible to discriminate between the two groups of patients, as required by the claim.

9.3 The same conclusions apply in relation to document D6, the patent application corresponding to D5, with Table 2 on page 30 being essentially identical to Table 2 of D5.

9.4 Hence, claim 1 of the third auxiliary request is novel. The third auxiliary request fulfils the requirements of Article 54(2) EPC.

10. Article 56 EPC

10.1 Document D5 (or D6) is the closest prior art. The difference from the claimed subject-matter is that it discloses cutoff values for NGAL which are below the lower limits of the ranges claimed. Contrary to the arguments of the respondent and the conclusions of the opposition division, the board considers that it is plausible that the claimed ranges, including those for the plasma and serum samples, give a 100% negative predictive value in the claimed method. Hence, the technical problem is formulated as the provision of a method which is suitable for identifying individuals who do not have and are not at risk of having acute renal failure, i.e. a method that makes it possible to exclude acute renal failure in patients while identifying non-acute renal failure patients as correctly as possible. The solution is the method as claimed, and the board considers that it solves the technical problem.

10.2 Starting from D5 (or D6), it would not have been obvious to arrive at the NGAL cutoff values of the patent as granted, because such cutoff values are indicated in D5 (or D6) as giving a negative predictive value lower than 100%. Hence, the skilled person would not think that higher cutoff values would still be capable of identifying all patients at risk of having acute renal failure, but rather would assume that lower values would have to be used in order to have a negative predictive value of 100%. The skilled person would not therefore arrive at the claimed solution in an obvious way.

10.3 The respondent further argued (page 26 of letter or reply to grounds of appeal) that the patent

proprietor's own document D18 explicitly taught that urinary NGAL values below a range of 370 to 329 ng/ml and plasma NGAL values below 436 to 355 ng/ml were not diagnostic for renal disorders (D18, page 23, first and second paragraphs), thereby providing a motivation to the skilled person to look for cutoff values below the ranges mentioned. The board fails to see how this document could prompt the skilled person to look for lower cutoff values than those mentioned above, since the document explicitly states that such lower values would not be diagnostic for renal disorders. On the contrary, the board considers that this document prompts the use of even higher cutoff values, thus teaching away from the claimed invention.

10.4 Accordingly, the board considers that claim 1 of the third auxiliary request involves an inventive step. The third auxiliary request thus complies with Article 56 EPC.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the opposition division with the order to maintain the patent with the following claims and a description to be adapted thereto:
Claims 1 to 12 of the third auxiliary request filed with the statement of grounds of appeal.

The Registrar: The Chairman:

M. Schalow A. Lindner

Decision electronically authenticated