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Datasheet for the decision of 29 July 2025

Case Number: T 0684/23 - 3.3.10

Application Number: 09790996.4

Publication Number: 2313364

IPC: C07C279/12, A61P13/12, C07K16/44

Language of the proceedings: EN

Title of invention:
METHODS FOR DETECTING SYMMETRICAL DEMETHYLARGININE

Patent Proprietor:
IDEXX LABORATORIES, INC.

Opponent:
Zoetis Services LLC

Headword:

Relevant legal provisions:
EPC Art. 100(a), 56

Keyword:
Inventive step - (no)

Decisions cited:

Catchword:

Europäisches Patentamt
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Boards of Appeal

Chambres de recours

Boards of Appeal of the
European Patent Office
Richard-Reitzner-Allee 8
85540 Haar
GERMANY
Tel. +49 (0)89 2399-0

Case Number: T 0684/23 - 3.3.10

D E C I S I O N
of Technical Board of Appeal 3.3.10
of 29 July 2025

Appellant: (Opponent)	Zoetis Services LLC 10 Sylvan Way Parsippany NJ 07054 (US)
Representative:	Dörries, Hans Ulrich df-mp Patentanwälte Rechtsanwälte PartG mbB Theatinerstraße 16 80333 München (DE)
Respondent: (Patent Proprietor)	IDEXX LABORATORIES, INC. One Idexx Drive Westbrook, ME 04092 (US)
Representative:	Hoffmann Eitle Patent- und Rechtsanwälte PartmbB Arabellastraße 30 81925 München (DE)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 8 February 2023 rejecting the opposition filed against European patent No. 2313364 pursuant to Article 101(2) EPC.**

Composition of the Board:

Chair	P. Gryczka
Members:	R. Pérez Carlón
	T. Bokor

Summary of Facts and Submissions

I. The appellant (opponent) lodged an appeal against the opposition division's decision rejecting the opposition against European patent No. 2 313 364.

II. Notice of opposition had been filed on grounds including lack of inventive step (Article 100(a) EPC).

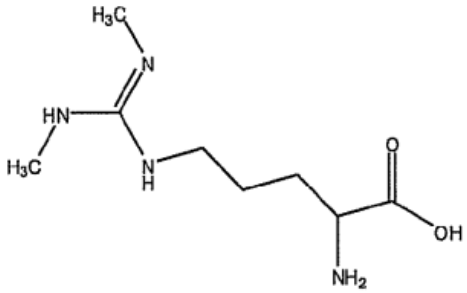
III. The following documents are relevant to the present decision:

D5 WO 02/04465 A1
D6 DE 10 2005 060 057 A1
D7 WO 2006/078813 A2
D8 Kielsen *et al.*, "Symmetric dimethylarginine (SDMA) as endogenous marker of renal function - a meta-analysis", *Nephrol. Dial. Transplant.*, (2006), 21: 2446-51
D20 Harlow, Lane, editors: "Antibodies: A Laboratory Manual", Cold Spring Harbor Laboratory, 1988, Chapter 5 "Immunizations", pages 72-87, and Chapter 14 "Immunoassays", pages 555-604
D23 Expert opinion of Rainer Böger
D28 Fleck *et al.*, "Serum concentrations of asymmetric (ADMA) and symmetric (SDMA) dimethylarginine in patients with chronic kidney diseases", *Clinica Chimica Acta* 336 (2003), pages 1-12

IV. The patent as granted, which is the respondent's (patent proprietor) main request in appeal, includes the following six independent claims:

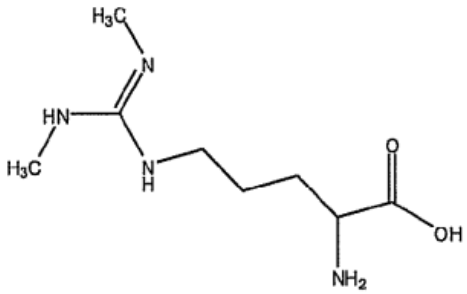
"1. An isolated antibody specific for free symmetrical dimethylarginine (SDMA) in a biological sample, wherein

free SDMA is not part of a polypeptide chain, wherein free SDMA is SDMA of the formula,



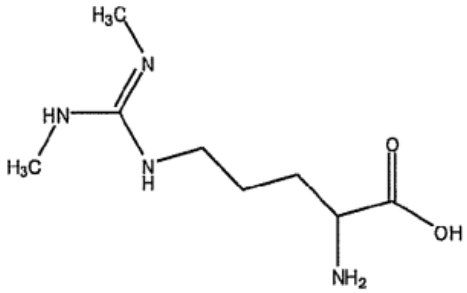
4. A device for determining the presence of SDMA in a sample comprising a solid support having bound thereto an anti-SDMA antibody of any one of claims 1-3.

5. A method for detecting the presence or amount of free SDMA in a biological sample, the method comprising:
(a) contacting the sample with the anti-SDMA antibody specific for free SDMA according to any one or more of claims 1-3 in a biological sample and an SDMA comprising SDMA conjugated to a label, and
(b) detecting the presence or amount of the label associated with the antibody, thereby determining the presence or amount of SDMA in the sample, wherein free SDMA is not part of a polypeptide chain, wherein free SDMA is SDMA of the formula



6. A method for detecting the presence or amount of free SDMA in a biological sample, the method comprising:

(a) contacting the sample with the anti-SDMA antibody specific for free SDMA according to any one or more of claims 1-3 in a biological sample and conjugated to a label and with an SDMA conjugate comprising SDMA conjugated to a solid support;
(b) detecting the presence or amount of the label associated with the solid support, thereby determining the presence or amount of SDMA in the sample,
wherein free SDMA is not part of a polypeptide chain,
wherein free SDMA is SDMA of the formula



9. A method for determining renal function in an animal subject comprising:
(a) conducting the method of any one of claims 5-8 to determine the amount of free SMDA [sic] *in a biological sample obtained from the subject, and*
(b) determining the renal function by comparing the amount of SDMA in the sample to one or more SDMA standards that correlate to renal function in an animal.

10. A method for diagnosing renal disease in a subject comprising:
(a) determining the amount of SDMA in a biological sample from the subject according to any of claims 5-8;
(b) comparing the amount of SDMA in the sample to the amount of SDMA in the sample of a healthy subject;
(c) diagnosing that the subject has renal disease when the amount of SDMA in the sample from the subject is higher than the SDMA in the sample from the healthy

subject."

V. The opposition division concluded that examining inventive step starting from D8 was against all principles of the problem-solution approach. If a skilled person would nevertheless decide to start from D8, the claimed solution, characterised by the antibody in claim 1, would not have been obvious in view of the prior art and was thus inventive.

VI. With the response to the grounds of appeal the respondent filed its first to eleventh auxiliary requests. Auxiliary request 12 was filed with a letter dated 29 November 2024.

Claim 1 of the first auxiliary request specifies a reactivity of less than 5%, compared with reactivity for SDMA, for one or more of asymmetrical dimethylarginine (ADMA), L-arginine and N-methylarginine.

Auxiliary request 2 only has the claims directed to the device and methods in auxiliary request 1.

Auxiliary request 3 differs from auxiliary request 2 by specifying a reactivity of the antibody of less than 1%.

Auxiliary request 4 has all the claims of the patent as granted except dependent claim 2.

Auxiliary request 5 has the four independent claims relating to methods of the patent as granted.

Auxiliary request 6 has the claims to a method for determining renal function and for diagnosing renal

disease of the patent as granted.

Auxiliary request 7 relates to the use of the antibody in claim 1 of the patent as granted for detection of SDMA in a biological sample of an animal subject.

Claim 1 of auxiliary request 8 relates to an antibody having the features of claim 1 of auxiliary request 1, and further specifies an SDMA concentration of between 1 and 100 µg/mL.

Claim 1 of auxiliary requests 9 to 11 specifies the nature of the biological sample in claim 1 of the patent as granted.

Lastly, auxiliary request 12 has the claims of auxiliary request 1 to an antibody, to a device and to methods for detecting SDMA, but lacks those for determining renal function and diagnosing renal disease.

VII. The appellant's arguments concerning the issue of inventive step over D8 were as follows.

Document D8, disclosing that SDMA was a suitable marker for evaluating renal function, was a suitable starting point for examining inventive step. The problem of providing an improved method for determining renal function and diagnosing renal disease was not credibly solved by the subject-matter of any of the requests on file, given the absence of comparative data. The sole problem credibly solved was the provision of an alternative. The claimed solution, which was characterised by the antibody in claim 1, would have been a straightforward choice for the skilled person in view of the common general knowledge, D5, D6 or D7, and

thus lacked an inventive step. Even if the problem were to be considered that of providing an improvement, the alleged advantages were inherent in immunoassays and the claimed solution was not inventive, either.

VIII. The respondent's arguments were as follows.

Document D8 was not a suitable starting point for examining inventive step as it did not relate to antibodies. If it were nevertheless considered suitable, the problem underlying the claimed invention would be to provide an improved method for determining SDMA in a biological system. The claimed solution, characterised by the antibody in claim 1, was not taught by the prior art and was thus inventive.

IX. The board informed the parties by a communication dated 7 November 2024 of its preliminary view that the claimed subject-matter was not inventive in view of D8.

X. The respondent requested in reply that a new technical member from one of the biotechnology boards be added to the board or that the case be reallocated to a different board.

The board stated in a communication dated 16 December 2024 that it saw no need for either. The request was not maintained at the oral proceedings before the board on 29 July 2025.

XI. The parties' final requests were as follows:

The appellant requested that the appealed decision be set aside and the patent revoked, and that auxiliary requests 9 to 12 and amended paragraph [0077] not be admitted into the proceedings.

The respondent requested:
that the appeal be dismissed;
alternatively, that the patent be maintained:
- in amended form, in a given case with paragraph [0077] of the description as filed with the statement of grounds of appeal,
- with the claims filed as auxiliary requests 1 to 11 with the statement of grounds of appeal, of which auxiliary requests 1 to 8 correspond to requests filed in opposition proceedings,
- or with the claims of auxiliary request 12, filed with a letter dated 29 November 2024; and
that the case be remitted to the opposition division and a different apportionment of costs be awarded if the objections in the context of sufficiency of disclosure to be found in points III.5.1 and III.5.3 of the statement of grounds of appeal were admitted into the proceedings;
that the objections against novelty of claim 4 over D1 and D3 not be admitted into the proceedings; and
that the technical expert be permitted to make submissions if required.

XII. At the end of the oral proceedings, the decision was announced.

Reasons for the Decision

1. The appeal is admissible.

Inventive step

2. The invention relates to an antibody specific for free symmetrical dimethylarginine (SDMA) in a biological sample (claim 1), to a device containing it (claim 4),

and to methods using the antibody in claim 1 for detecting SDMA (claims 5, 6), determining renal function (claim 9) and diagnosing renal disease (claim 10).

3. D8

3.1 Document D8 discloses inulin clearance as the gold standard for determining the glomerular filtration rate of kidney-impaired patients. Measuring inulin clearance was cumbersome and expensive, and in practice serum creatinine values were typically used. However, serum creatinine values suffered from inter-individual variability and their determination required accurate 24-hour timed urine collections, which was not always easy (see first paragraph, right-hand column on page 2446).

Document D8 evaluates SDMA as an endogenous marker of renal function (see title). Based on 18 studies involving 2136 patients, D8 discloses that systemic SDMA correlates both with inulin clearance and with serum creatinine (see page 2446, Results). D8 concludes that SDMA can be a reliable marker of renal function (see page 2446, Conclusions).

In the left-hand column of page 2449, lines 36 to 39, D8 discloses that the methods for determining SDMA then known were HPLC and GL-MS. Both techniques are expensive (page 2449, right-hand column, lines 14 and 13 from bottom).

D8 is silent on antibodies.

3.2 The opposition division concluded that taking D8 as a starting point went against all principles of the

problem-solution approach. According to the opposition division, the closest prior art, like the patent, should have been from the technical field of antibodies for diagnosis. The respondent agreed with this conclusion in appeal.

The board, however, considers that a document disclosing free SDMA as an endogenous marker of renal function pertains precisely to the technical field of the claimed invention. Like D8, the claimed invention aims at determining SDMA for diagnosing renal disease. D8 belongs to the technical field of the problem addressed (renal function) and does not need to belong to the technical field of the claimed solution (antibodies) too. D8 is a suitable starting point for examining inventive step.

Since the board arrived at the conclusion that the claimed subject-matter was not inventive starting from D8, the question of whether another document comes even closer to the claimed invention can remain unanswered.

4. Problem underlying the claimed invention

In view of D8, the respondent formulated the problem underlying the claimed invention as providing an improved method for evaluating renal function, achieving lower costs, improved time effectiveness and increased reliability.

5. Solution

The proposed solution is the antibody specific for free SDMA in biological systems in claim 1, the device containing it in claim 4 and the methods in claims 5,

6, 9 and 10 including the antibody in claim 1.

6. Success of the claimed solution

The parties were divided on whether the claimed subject-matter credibly solved the problem of providing an improved method for evaluating renal function in all aspects. In the following, this will be considered to be the case. As the conclusion on inventive step is nevertheless negative, it is not necessary to elaborate further on this point.

7. It remains to be examined whether the claimed solution would have been obvious to a skilled person in view of the prior art.

7.1 The respondent did not dispute that the link between SDMA and renal function was known from D8. It argued, however, that D8 contained no motivation to seek better measurement methods.

D8 summarises the drawbacks of known markers of renal function, proposes plasma SDMA levels as a suitable alternative and discloses that the available detection methods, HPLC and GC-MS, were expensive and not suitable for widespread clinical application (see corresponding passages in point 3.1 above). D8 thus provides motivation to seek alternative methods of measuring SDMA, contrary to the respondent's argument.

7.2 It was undisputed that immunoassays were known and widespread before the priority date: see only as an example paragraph [0003] of D6, disclosing that a number of haptens, including amino acids, were usually detected by immunoassays. It was also undisputed that immunoassays were known to be more convenient, cheaper

and faster than HPLC and GC-MS. A skilled person, seeking an improved detection method, would thus have considered an immunoassay an obvious solution. It is implicit for the skilled person that an immunoassay requires a suitable antibody.

According to the respondent, the antibody in claim 1 is totally specific and able to detect SDMA in biological samples such as serum. The board will examine the claimed subject-matter using this interpretation.

Claim 1 merely specifies the pre-eminent properties of an antibody for an SDMA assay: total specificity and direct application on serum. An assay relying on an antibody with those properties would have been an obvious improvement to a skilled person. This is the case regardless of whether an antibody with those properties was within the reach of a skilled person at the filing date: what is relevant is whether the features in claim 1 are obvious.

7.3 The respondent relied on the declaration D23 by R. Böger to show that the focus at the priority date was on ADMA, not on its symmetrical isomer. However, the information that SDMA was a suitable marker for renal function is in the closest prior-art document D8. This argument is thus not convincing.

7.4 The respondent argued that D8 was cautious in its conclusion and only disclosed that SDMA had promise as a marker. There was thus no expectation of success.

However, the link in D8 between renal disease and free SDMA in plasma and the lack of simple measurement methods are sufficient incentive, regardless of whether SDMA could become a standard, routinely used,

therapeutic marker.

7.5 The respondent argued that no immunoassays for free SDMA were known at the filing date, let alone in a complex biological environment. A skilled person for this reason would not have found a pointer to the claimed solution. The prior art D5, D6 and D7 sought to determine ADMA and not SDMA.

This argument is not convincing. A secondary document such as D5 to D7 inevitably differs from the claimed invention at least by one feature, otherwise it would have been novelty-destroying.

7.6 The respondent also argued that the prior art did not suggest selectivity of SDMA over ADMA and that cross-reactivity was moreover to be expected. The claimed invention was not obvious for this reason either.

This argument is not convincing. D8 discloses that both SDMA and ADMA can be found in the plasma of subjects. Seeking an improved, reliable method for measuring the former whilst preventing false positives, an antibody which could selectively measure SDMA in the presence of ADMA would have been an obvious improvement.

7.7 The respondent argued that D8 related to the determination of renal disease in combination with ADMA in the context of cardiology practice, whereas the claimed invention provided a method of general validity. For this reason too, an inventive step should be acknowledged.

The data in D8 relates to patients with cardiovascular problems, and due to data availability it does not deal with patients having other types of health problems. D8

reviewed publications containing data of SDMA and renal markers, which were only provided in studies relating to the isomer ADMA, i.e. in the context of cardiovascular diagnosis. A skilled reader would however not have considered the conclusions in D8 to be applicable only for patients with cardiovascular issues.

7.8 The parties were divided on whether the preparation of the antibody in claim 1 involved difficulties in view of the requirements in the Guidelines, G.II.6.2, and with reference to the general methods for the preparation of antibodies against haptens in D20 (see pages 72 and 78).

The board however fails to see the relevance of this issue in the present context. If the claimed antibody could not have been obtained by standard methods, its preparation could have been an invention in itself. However, the claimed antibody needs to be inventive on its own: it cannot be rendered inventive by means of any arguable difficulty in obtaining it.

7.9 The parties also referred to the expectation of success in the context of the claimed antibody. However, whether there was a reasonable expectation of obtaining the claimed antibody has no bearing on its inventiveness. It may at best have relevance in the context of its preparation.

7.10 The respondent relied on the commercial success of the claimed invention, which was the result of long-ongoing research, as D8 relates to publications from 1970 onwards (see page 2446, Methods).

Even if D8 states that its search was from 1970

onwards, the 18 publications reviewed span from 1997 to 2006 (see Figure 1). The patent application was filed only two years after the publication of D8, and commercial success may arise from a number of factors which do not necessarily have to include any inventiveness of the claimed invention. These arguments are thus not convincing.

7.11 The respondent's arguments on inventive step with respect to the claims to a device and the method claims hinged on the inventiveness of the antibody used. The subject-matter of these claims lacks inventive step for the same reasons as claim 1.

7.12 As neither the claimed antibody nor the claimed device and methods are inventive (Article 56 EPC), the ground for opposition of Article 100(a) EPC thus precludes maintenance of the patent as granted.

8. Auxiliary requests 1 to 12

8.1 Claims 1 of auxiliary requests 1 and 12 set a threshold for cross-reactivity of the claimed antibody of 5%. As the board has examined inventive step on the assumption that the claimed antibody had no cross-reactivity at all, the conclusion on the main request also applies.

8.2 Claim 1 of auxiliary request 2 relates to a device comprising the antibody of claim 1 of auxiliary request 1. A device is an obvious constituent of an immunoassay, and by the respondent's own argument its inventiveness hinged on that of the antibody. The arguments with respect to the higher-ranked request thus also apply. The device in claim 1 of auxiliary request 3 has an even lower level of cross-reactivity (1%); the board has however examined the main request

for an antibody with total selectivity, and the conclusion thus does not change.

8.3 Claim 1 of auxiliary request 4 corresponds to claim 1 of the patent as granted. The same arguments thus apply.

8.4 Auxiliary request 5 contains only those claims in the patent as granted which related to methods. By the respondent's own argument, the gist of the invention lies in the features of the antibody, which are not inventive for the reasons already given.

The argument applies analogously to the method for determining renal function and diagnosing with the antibody in claim 1 of the patent as granted, which are the sole independent claims in auxiliary request 6.

The respondent argued that the prior art did not disclose the specific steps in these methods and that claim 1 of these requests should be considered inventive for this reason.

However, the claimed methods for detecting the presence or amount of free SDMA only contain common features of immunoassays, and nothing different is argued by the respondent. The methods for determining renal function and diagnosing renal disease merely contain the steps of determining the amount of free SDMA and comparing it with a reference, which is also trivial in itself.

8.5 Claim 1 of auxiliary request 7 relates to the use of the antibody in claim 1 of auxiliary request 1 for the detection of SDMA in a biological sample of an animal subject. The arguments above apply in the same manner.

8.6 Claim 1 of auxiliary request 8 relates to an antibody having all the features of that in claim 1 of auxiliary request 1, and stipulates in addition that the cross-reactivity set should be achieved at concentrations of SDMA of between 1 and 100 µg/mL. It was undisputed that these concentrations correspond to the levels of SDMA in plasma, as disclosed in point 4.1 of document D28. The issue of inventive step thus does not change.

8.7 Claims 1 of auxiliary requests 9 to 11 define the meaning of biological sample in claim 1 of the patent as granted. Since the board has examined claim 1 of the patent as granted on the assumption that the claimed antibody was specific for free SDMA in plasma, the conclusion for these auxiliary requests is the same.

8.8 None of the sets of claims filed as auxiliary requests are thus allowable, regardless of their admittance.

9. Other requests

In view of the board's negative conclusion on inventive step, it is not required to decide on any other of the respondent's requests. The respondent acknowledged that the amendment of paragraph [0077] of the description had no bearing on inventive step. The board did not need to decide on whether the respondent's technical expert could address the board, as no submission was offered at the oral proceedings.

9.1 Conclusion

The board therefore arrives at the conclusion that the ground for opposition in Article 100(a) EPC precludes maintenance of the patent as granted and of auxiliary requests 1 to 12.

Order

For these reasons it is decided that:

The decision under appeal is set aside.
The patent is revoked.

The Registrar: On behalf of the Chair (according to Art. 8(3) RPBA):

C. Rodríguez Rodríguez T. Bokor

Decision electronically authenticated