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**Datasheet for the decision
of 30 June 2015**

Case Number: T 2100/10 - 3.4.02

Application Number: 99965213.4

Publication Number: 1137933

IPC: G01N27/447

Language of the proceedings: EN

Title of invention:

SEPARATION OF PHOTSENSITIZER ISOMERS AND STEREOISOMERS BY
LASER-INDUCED FLUORESCENCE CAPILLARY ELECTROPHORESIS

Applicant:

THE UNIVERSITY OF BRITISH COLUMBIA

Headword:

Relevant legal provisions:

EPC 1973 Art. 56, 84, 111(1)

Keyword:

Claims - support in the description (no) (main request)
Inventive step - auxiliary request (yes)

Decisions cited:

T 0094/05

Catchword:



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Case Number: T 2100/10 - 3.4.02

D E C I S I O N
of Technical Board of Appeal 3.4.02
of 30 June 2015

Appellant:
(Applicant)

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Decision under appeal:

**Decision of the Examining Division of the
European Patent Office posted on 28 April 2010
refusing European patent application No.
99965213.4 pursuant to Article 97(2) EPC.**

Composition of the Board:

Chairwoman T. Karamanli
Members: A. Hornung
F. Narganes-Quijano

Summary of Facts and Submissions

I. The applicant (appellant) appealed against the decision of the examining division refusing European patent application No. 99965213.4 on the basis of Article 97(2) EPC.

The requests then on file were refused by the examining division for the following reasons, respectively:

- The subject-matter of claim 1 of the main request did not involve an inventive step (Article 56 EPC).
- The subject-matter of claim 1 of the first auxiliary request was not clear (Article 84 EPC).
- The subject-matter of claim 1 of the second auxiliary request was not compliant with the requirements of Article 123(2) EPC.
- The subject-matter of claim 1 of the third auxiliary request was not clear (Article 84 EPC) and did not comprise an inventive step (Article 56 EPC).
- The subject-matter of claim 1 of the fourth auxiliary request was not clear (Article 84 EPC) and did not comprise an inventive step (Article 56 EPC).
- The subject-matter of claim 1 of the fifth auxiliary request was not clear (Article 84 EPC).

II. With its statement of grounds of appeal the appellant filed amended claims according to a new main request as its sole request. The appellant gave reasons why these claims overcame the objection of lack of inventive step raised by the examining division.

III. In response to the board's clarity objections, raised in an attendance note about a phone conversation, the appellant, in a letter dated 6 June 2014, filed amended claims, replacing the claims of its previous request, and amended description pages.

IV. In a communication annexed to the summons to oral proceedings, the board expressed doubts that the subject-matter of claim 1 of the request then on file met the requirements of Articles 83 and 84 EPC 1973. The board also indicated that, according to its provisional opinion, if these objections were overcome, claim 1 would define patentable subject-matter with respect to the available prior art.

The board raised further deficiencies regarding the amended description pages as filed with letter of 6 June 2014 and indicated that it might consider a remittal of the case to the department of first instance for adapting the description.

V. With a letter dated 26 May 2015 the appellant maintained its main request filed with letter dated 6 June 2014 and filed amended claims 1 to 14 and amended description page 13 according to a new auxiliary request. The appellant further stated that in the event that the decision to refuse the patent application could be set aside on the basis of either the main request or the auxiliary request, then the request for oral proceedings was withdrawn.

VI. The appellant requested that the decision of the examining division be set aside and a patent be granted on the basis of the main request filed with letter dated 6 June 2014 or of the auxiliary request filed with letter dated 26 May 2015.

VII. Independent claim 1 according to the main request reads as follows:

"A method of separating stereoisomers of benzoporphyrin derivatives (BPDs) with a capillary electrophoresis system, which method comprises:

selecting the capillary inner diameter, capillary length, field strength, separation temperature, pH, buffer system, ionic strength, chiral selector, and organic solvent of a capillary electrophoresis system to result in separation of BPD stereoisomers,

injecting a sample containing said BPD stereoisomers into said capillary electrophoresis system, and

separating said stereoisomers,

wherein said pH is from 8.05 to 9.6,

wherein said buffer system is borate,

wherein said ionic strength is from 200 to 360 mM borate,

wherein said chiral selector is a bile salt,

wherein said organic solvent is selected from the group consisting of dimethylformamide (DMF), isopropanol or acetonitrile, and

wherein said separating results in baseline separation, such that there is no detectable overlap between the compounds being separated during elution."

VIII. Independent claim 1 according to the auxiliary request differs from claim 1 of the main request only in that the claimed pH range is "from 9.2 to 9.6", instead of "from 8.05 to 9.6".

IX. The present decision refers to the following documents.

D1: "Capillary electrophoresis analysis of polyhaematoporphyrin, a photosensitizer used in photodynamic therapy", Ellen N. L. Chan et al., Journal of Chromatography, 636 (1993), 171- 178.

D2: "Separation of porphyrins and porphyrin isomers in capillary electrophoresis using mixed ionic surfactant -

bovine serum albumin buffer systems", Nian Wu et al., Journal of Chromatography A, 659 (1994), 435 - 442.

Reasons for the Decision

1. Main request

1.1 Amendments

The board is satisfied that the present amended set of claims 1-15 fulfills the requirements of Article 123(2) EPC.

In particular, present claim 1 is based on claims 1, 3, 4, 6, 8, 16, 18, 19, 21 and 24 as originally filed.

The basis for the definition in claim 1 of the expression "baseline separation" can be found on page 8, lines 14 - 17 of the description of the application as originally filed.

1.2 Clarity

The subject-matter of claim 1 is not supported by the description as required by Article 84 EPC 1973.

1.2.1 Present claim 1 defines a method of separating stereoisomers of benzoporphyrin derivatives (BPD) such that the separation results in "baseline separation", meaning that no detectable overlap exists between the stereoisomers of BPD being separated during elution. According to the description as filed, such a result is obtained only under certain experimental conditions.

Since the description of the application as filed on page 12, lines 6 - 18 explains in detail that the baseline separation is *not* achieved for a pH lower than 9.2 but only from 9.2 to 9.6, present claim 1, which claims baseline separation for an extended pH range from 8.05 to 9.6, lacks support from the description (Article 84 EPC 1973).

- 1.2.2 The appellant argued that claim 1 not only specified a pH range from 8.05 to 9.6 but also referred to baseline separation of the stereoisomers. Thus, the skilled person would understand that he had to select *the* adequate pH within the claimed pH range from 8.05 to 9.6 in order to achieve the claimed result of baseline separation. The appellant stated that the skilled person reading page 13, lines 12 - 16 of the description as filed would recognise that this passage "contains specific comments about pH which are applicable in certain circumstances, but [...] there is no need to be restricted to a pH of at least 9.2 in all circumstances covered by present claim 1".

The board is not convinced by this argument since, on the one hand, the description unequivocally discloses that a pH outside the pH range of 9.2 to 9.6 does not result in baseline separation and, on the other hand, the description does not give any indication whether and, if yes, how, it is feasible to adjust the experimental circumstances covered by claim 1 so that a pH below 9.2 would nevertheless result in baseline separation. The information that a pH below 9.2 would also provide baseline separation and the underlying circumstances is, however, absent from the description. Article 84 EPC 1973 requires that a claim shall be supported by the description. The board interprets this requirement of Article 84 EPC 1973 in the sense that claim 1 must reflect the actual contribution to the art in such a way that the skilled person is able to perform the invention in the entire range claimed (cf. decision T 94/05, Reasons, point 3.1).

Allowing a claim with a pH range below 9.2, on the basis of hypothetical experimental circumstances to be adjusted so as to achieve baseline separation, would thus exceed the application's actual contribution to the art as disclosed in the description.

1.3 In view of the above, the main request is not allowable.

2. Auxiliary request

2.1 Amendments

Basis for the lower limit of 9.2 of the claimed pH range can be found, for instance, in original claim 17. The board is satisfied that the present amended set of claims 1-14 fulfills the requirements of Article 123(2) EPC.

2.2 Clarity

2.2.1 Claim 1 is limited to the pH range of 9.2 to 9.6. Hence, the board is satisfied that the objection of lack of support, raised in point 1.2 above, against claim 1 of the main request is overcome.

2.2.2 The board is satisfied that the further clarity objections raised by the examining division in the appealed decision have also been overcome by amendment:

- The wording of claim 1 then on file, "wherein said separated stereoisomers are isolatable", objected by the examining division as being unclear, has been removed from present claim 1.
- The expression "baseline separation", considered unclear by the examining division, has been clarified in present claim 1 by stipulating that there is no detectable overlap between the compounds being

separated during elution.

2.2.3 In follows from the above that the requirements of Article 84 EPC 1973 are fulfilled.

2.3 Sufficiency of disclosure

By limiting claim 1 to the pH range of 9.2 to 9.6, the board is satisfied that the objection of lack of sufficiency of disclosure, raised in point 5 of the annex to the summons to oral proceedings, is overcome.

2.4 Novelty

Novelty of the claimed subject-matter was not objected by the examining division. The board does also not raise a lack of novelty objection in view of the available prior art documents. Consequently, the requirements of Article 54(1) EPC 1973 are fulfilled.

2.5 Inventive step

The claimed subject-matter comprises an inventive step in view of the available prior art documents.

2.5.1 Technical field

The technical field of the invention is the separation of stereoisomers of benzoporphyrin derivatives (BPD) by using capillary electrophoresis. According to the description, the BPD are to be used as photosensitizers in photodynamic therapy for cancer treatment.

2.5.2 Closest prior art

According to the appealed decision, D1 was considered to represent the closest prior art for the requests then on file. Since the technical field of the claimed invention remained unchanged, D1 could, in principle, still be considered as the closest prior art for the subject-matter of the claims of the present auxiliary request, especially in view of the other available prior art documents, such as document D2 or document US 5,171,749 cited in the patent application, which do not come closer to the claimed invention.

However, D1 does not exactly belong to the technical field of the present invention as defined in point 2.5.1 above because D1 discloses a separation method of polyhaematoporphyrin (PHP) instead of benzoporphyrin derivative (BPD). For this reason alone, the board is of the opinion that the claimed method is not obvious in view of D1.

But even in case that D1 would be considered as a reasonable starting point for the assessment of inventive step, namely on the basis of the facts that PHP is simply another porphyrin photosensitizer used in photodynamic therapy for cancer treatment and that the separation in D1 is carried out by capillary electrophoresis, the board is of the opinion that the skilled person, starting from D1, would not arrive at the claimed method in an obvious manner.

2.5.3 Differences between claim 1 and the closest prior art

The claimed method differs from the method of D1 by the following differing features (i) to (v):

- (i) The components to be separated are stereoisomers of BPD.
- (ii) The ionic strength is from 200 to 360 mM borate.
- (iii) The chiral selector is bile salt.

(iv) The organic solvent is selected from a group consisting of DMF, isopropanol or acetonitrile.

(v) The separation process provides baseline separation.

2.5.4 Objective technical problem

The differing features (i) to (v) might be seen as to solve the following problems of:

- providing an alternative porphyrin to be separated by capillary electrophoresis (feature (i)),
- selecting the adequate process parameters (features (ii) to (iv)), and
- achieving the mentioned degree of separation of the porphyrin (feature (v)).

2.5.5 Non-obviousness of the claimed solution

- Feature (i)

D1, identifying PHP as "one of the photosensitizers currently under trial" in photodynamic therapy, is concerned about optimizing the capillary electrophoresis in order to study the precise composition of PHP. D1 concludes that "in future work, we aim to focus on optimising capillary electrophoresis conditions for resolution and collection of fractions of individual oligomers".

It is true that the claimed stereoisomers of BPD are known photosensitizers, but the board sees no obvious reason to select these specific photosensitizers from the very large number of photosensitizers known in the art. The examining division referred to the abstract of D2 and stated in general terms that D2 gave a hint towards BPD. The board, however, does not accept this statement, since D2 refers to six types of porphyrins, including coproporphyrin having type I and III separated isomers (cf. abstract of D2), but not to BPD.

Therefore, the board is unable to see why the skilled person would abandon the initial and explicit research programme taught by D1 and select a new component to be separated, such as the claimed stereoisomers of BPD.

- Features (ii) to (iv)

Even in case that the skilled person, starting from D1, would contemplate capillary electrophoresis for separating stereoisomers of BDP, no hint can be found in D1 about selecting the ionic strength, the chiral selector and the solvent as claimed. Indeed, D1 teaches the use of micellar additives such as sodium dodecyl sulphate (SDS) and cetyltrimethylammonium bromide (CTAB) instead of the chiral selector of bile salt as claimed. Furthermore, D1 teaches a 20 mM borate buffer which is outside the claimed range from 200 mM to 360 mM borate and also remains silent about a possible use of a solvent as claimed.

In case that the skilled person would consult D2, he would learn that a mixture of 50 mM of the bile salt sodium taurodeoxycholate (STDC) and alcohols is a pertinent additive for separating stereoisomers of coproporphyrin, but also that bile salt alone would be unsuccessful in the separation (cf. D2, page 436, left column). Hence, it is true that the skilled person would receive at least an indication of the possible use of bile salt. However, even the combination of D1 and D2 does not provide any pointer to the ionic strength of 200 to 360 mM borate nor to the claimed solvent.

- Feature (v)

The functional feature of the "baseline separation" could be seen as merely an obvious wish. However, the process parameters defined in present claim 1 is considered to be

essential to arrive at the claimed result of baseline separation. Therefore, the board is satisfied that the feature of "baseline separation", in combination with the process parameters of claim 1, constitutes a clear technical limitation suitable for contributing to the inventive step of the claimed method.

D1 discloses the separation of PHP into the different chemical compounds haematoporphyrin (HP), hydroxyethylvinyl-deuteroporphyrin (HVD) and protoporphyrin (PP). However, these compounds are not stereoisomers and the separation is not a baseline separation (cf. D1, page 174, right column, third paragraph). The only reference in D1 to separate stereoisomers is to be found on page 173, paragraph bridging left and right columns, stating incidentally that "diastereoisomers of HP show a partially resolved doublet". The partial resolution of diastereoisomers of HP shown in figure 2a of D1 is considered to be not more than a side effect, insufficiently relevant to provide the incentive to start a new research programme for a method as claimed, using capillary electrophoresis for baseline separating stereoisomers of porphyrins. Actually, in the board's view, starting from the disclosure of D1, the skilled person could not even reasonably expect that capillary electrophoresis would be capable of baseline separating not only structurally or chemically different components, but also the more challenging stereoisomers.

- 2.5.6 The board notes that, in its decision, the examining division did not raise an objection of lack of inventive step against the subject-matter of the claims of the fifth auxiliary request then on file, whose scope is broader than that of the subject-matter of present claim 1.

2.5.7 As a result, the subject-matter of claim 1 involves an inventive step (Article 56 EPC 1973).

2.6 It follows from the above that claim 1 of the auxiliary request meets the requirements of the EPC and, accordingly, this is also the case for the dependent claims 2 to 14. Therefore, a patent can be granted on the basis of claims 1 to 14 of the auxiliary request.

3. Remittal

In view of the amendments made to the claims, the description requires extensive adaptation. Since the present amended description pages are not sufficiently adapted to the amended claims, the board considers it appropriate in the circumstances of the present case to leave the full adaptation of the description to the examining division. The appellant had no objection to this course of action. The board thus remits the case to the department of first instance for adaptation of the description (Article 111(1) EPC 1973).

4. Procedural matters

In view of the appellant's conditional request for oral proceedings (see point V above), it was not necessary to hold oral proceedings because the auxiliary request is allowable.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the department of first instance with the order to grant a patent with the following claims and a description to be adapted:

Claims: Nos. 1 to 14 according to the auxiliary request filed with letter of 26 May 2015.

The Registrar:

The Chairwoman



M. Kiehl

T. Karamanli

Decision electronically authenticated