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Datasheet for the decision of 14 March 2024

Case Number: T 1859/22 - 3.3.07

Application Number: 12169866.6

Publication Number: 2535044

IPC: A61K9/16

Language of the proceedings: EN

Title of invention:
Enterically coated cysteamine bitartrate and cystamine

Patent Proprietor:
The Regents of the University of California

Opponent:
Alfred E. Tiefenbacher (GmbH & Co. KG)

Headword:
Enterically coated cysteamine bitartrate and cystamine / THE REGENTS OF THE UNIVERSITY OF CALIFORNIA

Relevant legal provisions:
EPC R. 103(1)(a)
EPC Art. 100(c), 76(1)

Keyword:
Amendments - added subject-matter (yes)
Reimbursement of appeal fee - substantial procedural violation (no)

Decisions cited:
T 2249/08, T 3035/19, G 0002/10

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Case Number: T 1859/22 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 14 March 2024

Appellant: (Opponent)	Alfred E. Tiefenbacher (GmbH & Co. KG) Van-der-Smissen-Str. 1 22767 Hamburg (DE)
Representative:	Hamm&Wittkopp Patentanwälte PartmbB Jungfernstieg 38 20354 Hamburg (DE)
Respondent: (Patent Proprietor)	The Regents of the University of California 1111 Franklin Street, 12th Floor Oakland, CA 94607 (US)
Representative:	Page White Farrer Bedford House 21a John Street London WC1N 2BF (GB)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 21 June 2022 rejecting the opposition filed against European patent No. 2535044 pursuant to Article 101(2) EPC.**

Composition of the Board:

Chairman	M. Steendijk
Members:	E. Duval
	L. Basterreix

Summary of Facts and Submissions

I. The appeal was filed by the opponent (appellant) against the decision of the opposition division to reject the opposition filed against the patent in suit.

II. Claim 1 of the patent as granted read as follows:

"A composition comprising cysteamine bitartrate and cystamine, or a pharmaceutically acceptable salt thereof, and one or more enteric coating materials that provide delivery of the cysteamine bitartrate and cystamine, or pharmaceutically acceptable salt thereof, to a region of the small intestine in which the pH is between 4.5 and 6.5."

III. The appealed decision cited the following documents:

D1: Scientific Discussion for Cystagon® established by the EMEA, 2004
D24: Owen et al., "Development of cysteamine hydrochloride pellets for cystinotic infants", European Hospital Pharmacy, Vol. 4, No. 3, 1997
D25: Rowe, Raymond C. et al., "Handbook of Pharmaceutical Excipients" Pharmaceutical Press, 2006, Ed. 5

IV. The opposition division decided in particular that:

(a) D24 and D25 were not admitted for lack of *prima facie* relevance.

(b) The patent complied with the requirements of Article 76(1) EPC. Neither the combination of cysteamine bitartrate and cystamine nor the

definition of the enteric coating in granted claim 1 introduced any added subject-matter.

V. With their reply to the appeal, the patent proprietor (respondent) defended their case on the basis of the patent as granted as main request and auxiliary requests 1-3 submitted on 4 February 2022.

Claim 1 of auxiliary request 1 was identical to claim 1 as granted.

Claim 1 of auxiliary request 2 further specified that the composition comprised "granules of cysteamine bitartrate and cystamine" and "one or more enteric coating materials encasing the granules".

Claim 1 of auxiliary request 3 differed from claim 1 as granted by the addition of the feature "wherein the composition is granulated and formulated as a compressed tablet or as a filling of a capsule".

VI. The Board set out its preliminary opinion in a communication under Article 15(1) RPBA.

VII. Oral proceedings were held before the Board.

VIII. The parties' requests were the following:

(a) The appellant requested that the decision under appeal be set aside and that the patent be revoked in its entirety. The appellant further requested that the appeal fee be reimbursed.

(b) The respondent requested that the appeal be dismissed, or, alternatively, that the patent be

maintained on the basis of one of auxiliary requests 1-3 filed on 4 February 2022.

IX. The appellant's arguments may be summarized as follows:

(a) A reimbursement of the appeal fee was equitable because the opposition division had committed a substantial procedural violation in their exercise of discretion not to admit D24 and D25 into the proceedings.

(b) The parent application did not disclose the combination of cysteamine bitartrate and cystamine. Relying on information in D1 regarding Cystagon™ amounted to erroneously supplementing the disclosure of the parent application with common general knowledge rather than determining its implicit disclosure.

Furthermore, the feature "to a region of the small intestine in which the pH is between 4.5 and 6.5" of claim 1 resulted from an inadmissible generalization. According to paragraph [0036] of the parent application as filed, the enteric coating material should not provide delivery of the drug to a region of the small intestine in which the pH was between 4.5 and 6.5, but should provide a continuous delivery of the drug during the unit dosage form’s transit within the small intestine.

The criteria of Article 76(1) EPC were thus not met.

X. The respondent's arguments may be summarized as follows:

(a) The opposition division correctly exercised their discretion not to admit D24 into the proceedings, by considering its *prima facie* relevance.

(b) The parent application as filed as a whole disclosed the combination of cysteamine bitartrate and cystamine in paragraphs [0030]-[0033] and [0051]. In addition, the references to Cystagon™ in the parent application as filed provided implicit basis for this combination.

Furthermore, paragraphs [0034]-[0036] of the parent application disclosed not only a region of the small intestine having a pH between 4.5 and 6.5, but also disclosed the feature of providing delivery to that region.

The criteria of Article 76(1) EPC were thus met.

Reasons for the Decision

1. Request for reimbursement of the appeal fee

1.1 In the first instance proceedings, the appellant submitted D24 and D25 by letter dated 4 February 2022, i.e. on the last date for making submissions under Rule 116(1) EPC. D24 relates to cysteamine hydrochloride-containing pellets for the treatment of cystinosis, and D25 identifies the Eudragit® L100-55 enteric coating mentioned in D24. In the same letter, the appellant relied on D24 and D25 in the context of inventive step both as part of the objection starting from D1 and in a new objection starting from D24.

According to the appealed decision, the opposition division admitted neither D24 nor D25 for lack of *prima facie* relevance, considering that D24 did not address the same technical problem as the patent nor pertained to the same active principle i.e. not the same cysteamine salt.

The appellant contends that two substantial procedural violations occurred, namely:
- the unreasonable exercise of discretion not to admit D24 and D25 into the proceedings, and
- the inadequate reasoning in the appealed decision regarding inventive step in view of D24 and D25, by not admitting D24 and D25 into the proceedings after the parties extensively discussed these documents in the assessment of inventive step.
A reimbursement of the appeal fee would accordingly be equitable.

1.2 For the following reasons, the Board concurs that the opposition division's exercise of discretion is contradicted by their comprehensive discussion of D24 and D25.

As explained in the Case Law of the Boards of Appeal (10th edition, 2022, IV.C.4.5.3), *prima facie* relevance is ascertained on the face of the facts, i.e. with little investigative effort, which reflects the need for procedural expediency in considering and admitting late-filed facts and evidence.

In the case at hand, during the oral proceedings before the opposition division, the parties extensively debated the issue of inventive step, including starting from D24 or in view of D1 in combination with D24, and taking D25 into account (see the minutes, page 4). Only

thereafter did the opposition division open the discussion on admittance of D24 and D25. Following this discussion and after deliberation, the chairperson announced that D24 and D25 were not admitted, that the requirements of Article 56 EPC were fulfilled, and that the opposition was rejected.

Furthermore, in the Board's opinion, the detailed reasoning given in the appealed decision for the decision not to admit D24 and D25 goes beyond a mere assessment of *prima facie* relevance, but in fact explains entirely why, in the opposition division's view, the criteria of inventive step would still be fulfilled if D24 and D25 were taken into account (see §1.4, pages 7-10 of the decision).

Accordingly, the Board considers that, having assessed D24 and D25 as to their content and found them to be not prejudicial to inventive step, the opposition division's additional exercise of discretion not to admit D24 and D25 was under these circumstances not only unnecessary, but also inconsistent with the actual consideration of these documents in full during the proceedings and in the decision.

1.2.1 However, the Board considers that, even if the opposition division's exercise of discretion were to be seen as constitutive of a procedural violation, this would not be a substantial one and would not justify a reimbursement of the appeal fee, because, as explained above, the decision sufficiently explains why D24 and D25 did not lead, or would not have led, to a finding of lack of inventive step.

According to established case law, one of the preconditions for reimbursement of the appeal fee under

Rule 103(1)(a) EPC is that a substantial procedural violation has taken place. A substantial procedural violation is an objective deficiency affecting the entire proceedings (see Case Law of the Boards of Appeal, 10th edition, 2022, V.A.11.6).

Here, contrary to the appellant's position, the full reasoning in the appealed decision leaves no doubt that, if the opposition division had instead taken the stance that D24 and D25 were formally part of the opposition proceedings, they would have reached the same conclusion on inventive step.

The Board cannot accept either the appellant's view that a wrong exercise of discretion is necessarily to be considered as a substantial procedural violation justifying a reimbursement of the appeal fee. In this respect, the Board's reasoning is similar to the views expressed in decision T 2249/08 (see point 6.7 of the reasons), wherein the opposition division's exercise of discretion and decision not to allow a particular objection into the proceedings did not appear to the Board to have been decisive, such that the procedural violation, if any, could not have been substantial.

Accordingly, the appellant's request for reimbursement of the appeal fee is refused.

2. Main request (patent as granted), Articles 100(c) and 76(1) EPC

The patent derives from a divisional application. Claim 1 of the main request pertains to a composition comprising cysteamine bitartrate and cystamine, or a pharmaceutically acceptable salt thereof, and one or more enteric coating materials that provide delivery of

the cysteamine bitartrate and cystamine, or pharmaceutically acceptable salt thereof, to a region of the small intestine in which the pH is between 4.5 and 6.5.

The active compounds used in the claimed invention are two different sulfhydryl agents, namely:

- cysteamine, known in the treatment of cystinosis, and
- cystamine, which is contemplated in the treatment of neurodegenerative diseases (see paragraphs [0002], [0017], [0030], [0031] of the patent).

For the following reasons, the Board concludes that claim 1 of the main request exceeds the limits of what a skilled person would derive directly and unambiguously, using common general knowledge, from the parent application as filed as a whole.

2.1 Combination of cysteamine bitartrate and cystamine

Contrary to the respondent's view, the parent application as filed does not unambiguously disclose the combined presence of cysteamine bitartrate and cystamine in the composition of the invention.

2.1.1 In paragraph [0030], the passage "the compositions of the disclosure can contain any cysteamine or cystamine, cysteamine or cystamine derivative, or combination of cysteamine or cystamines. The active agents in the composition, i.e., cysteamine or cystamine, may be administered in the form of a pharmacologically acceptable salt" does not clearly disclose a combination of cysteamine *and* cystamine. The word "combination" does not unambiguously indicate that both cysteamine and cystamine are present in the same

composition, as it could also refer e.g. to a plurality of cystamine derivatives.

2.1.2 In paragraph [0031], the indication that the disclosure aims to "overcome the problems associated with cysteamine and cystamine delivery" does not mean that both are present in the same composition.

2.1.3 Paragraph [0032] mentions methods "for the treatment of cystinosis, the treatment of neurodegenerative disease [...] using enterically coated cysteamine and cystamine, respectively." Considering the word "respectively", this passage does not teach the combined presence of cysteamine and cystamine in the same composition either.

2.1.4 Paragraph [0033] states that "The disclosure provides composition [*sic*] comprising enterically formulated cysteamine and cystamine derivatives. Examples of cysteamine derivatives include hydrochloride, bitartrate and phosphocysteamine derivatives. Cystamine and cystamine derivatives include sulfated cystamine". The Board concurs with the appellant that the expression "composition" is ambiguous, as it could be corrected either to "a composition" or to "compositions", and that the interconnection "and" in "cysteamine and cystamine derivatives" could also indicate that "derivatives" refers to both cysteamine and cystamine. But even supposing that the first sentence refers to a single composition comprising both cysteamine and cystamine derivatives, it would still be necessary not only to take cysteamine bitartrate as the cysteamine (derivative), but also cystamine itself, or a pharmaceutically acceptable salt thereof, as the cystamine derivative. The parent application as filed contains no disclosure of this specific combination.

2.1.5 Lastly, the expression "the enterically coated cysteamine and cystamine compositions" of paragraph [0051] does not disclose either a composition comprising both active ingredients.

2.1.6 The respondent argues that the word "or" in the expression "combination of cysteamine or cystamines" of paragraph [0030], or the wording of paragraphs [0031] and [0032], do not exclude, or could mean, that cystamine and cysteamine are combined in the same composition. However, the gold standard of G 2/10 requires that the amended subject-matter be directly and unambiguously disclosed, and not simply that it be compatible with the original disclosure.

2.1.7 According to the respondent, the references to Cystagon™ in the parent application as filed (e.g. paragraphs [0033] and [0035]) should be seen as an implicit disclosure of the combination of cysteamine bitartrate and cystamine, taking into account the common general knowledge reflected in D1 that Cystagon™ inevitably contains cystamine.

The Board is firstly not convinced that D1 teaches that cystamine is inevitably present in Cystagon™, considering that D1 merely reports the formation or presence of cystamine as a degradation product in some batches or formulations of cysteamine bitartrate (see e.g. page 3). But in any case, such a reference to common general knowledge cannot compensate for the lack of disclosure in the parent application itself (see T 3035/19, point 1.7.3 of the reasons). The presence of cystamine in Cystagon™ could only be regarded as implicitly disclosed in the parent application if it was not explicitly mentioned therein, but was a clear

and unambiguous consequence of what is explicitly mentioned (Case Law of the Boards of Appeal, 10th edition, 2022, II.E.1.3.3). In the present case, the parent application as filed merely mentions that Cystagon™ is a cysteamine derivative or cysteamine bitartrate (see paragraphs [0033] and [0055]), but nowhere discloses or implies that Cystagon™ contains any cystamine.

2.1.8 Hence, the combination of cysteamine bitartrate and cystamine extends beyond the content of the parent application as filed.

2.2 Feature "to a region of the small intestine in which the pH is between 4.5 and 6.5"

According to claim 1, the one or more enteric coating materials is such that it provides delivery of the cysteamine bitartrate and cystamine, or pharmaceutically acceptable salt thereof, to a region of the small intestine in which the pH is between 4.5 and 6.5. In agreement with the respondent's position, the Board understands the upper limit of 6.5 in claim 1 to mean that the active agent is substantially completely delivered in the region with a pH of 4.5-6.5, i.e. claim 1 does not allow for the delivery to merely start in this region and continue at a later stage.

Paragraph [0036] of the parent application firstly states that "The coating material is selected such that the therapeutically active agent will be released when the dosage form reaches the small intestine or a region in which the pH is greater than pH 4.5". However, this passage does not disclose that the pH in the region of

the small intestine where the active agents are delivered is 4.5 to 6.5.

The same paragraph later indicates that "The pH of the small intestine gradually increases from about 4.5 to about 6.5 in the duodenal bulb to about 7.2 in the distal portions of the small intestine (ileum)". This appears to be the only passage in the parent application disclosing a region of the small intestine where the pH is 4.5 to 6.5. However, this passage does not disclose that the active agents are delivered to the duodenal bulb, let alone, more generally, to any portion of the small intestine characterised by a pH of 4.5-6.5. At most, the rest of the paragraph indicates that the coating should *begin* to dissolve within the pH range of the duodenum (which is not limited to the duodenal bulb), and *continue* to dissolve at the pH range within the small intestine. This passage neither implies a delivery to the duodenal bulb nor to a region where the pH is 4.5 to 6.5.

Paragraph [0036] further states that "the amount of enteric polymer coating should be sufficient to substantially dissolved during the approximate three hour transit time within the small intestine (e.g., the proximal and mid-small intestine)". The reference to proximal and mid-small intestine may exclude the distal portions of the small intestine (ileum), which are stated earlier in the same paragraph to have a pH of 7.2. Nonetheless, there is no basis in the parent application for equating this dissolution in the proximal and mid-small intestine with a delivery in a region where the pH is 4.5 to 6.5.

2.3 Accordingly, the main request does not meet the criteria of Article 76(1) EPC.

3. In each of auxiliary requests 1-3, claim 1 contains both the feature regarding the combined presence of cysteamine bitartrate and cystamine and the feature relating to a delivery to a region of the small intestine in which the pH is between 4.5 and 6.5. Accordingly, each of auxiliary requests 1-3 also infringes Article 76(1) EPC.

Order

For these reasons it is decided that:

The decision under appeal is set aside.

The patent is revoked.

The request for reimbursement of the appeal fee is refused.

The Registrar: The Chairman:

B. Atienza Vivancos M. Steendijk

Decision electronically authenticated