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Datasheet for the decision of 1 February 2023

Case Number: T 0809/16 - 3.3.04

Application Number: 06836771.3

Publication Number: 1951232

IPC: A61K31/485, A61K9/22, A61K47/10, A61K9/36

Language of the proceedings: EN

Title of invention:

METHODS OF REDUCING ALCOHOL-INDUCED DOSE DUMPING FOR OPIOID SUSTAINED RELEASE ORAL DOSAGE FORMS

Patent Proprietor:

ALZA Corporation

Opponents:

Reckitt Benckiser (Brands) Limited
Wibbelmann, Jobst
Ledl, Andreas / Buehler, Dirk
Develco Pharma Schweiz AG
Generics [UK] Limited
Josef Hödl

Headword:

Opioid dosage forms for reducing adverse effects associated with alcohol-induced dose dumping/ALZA

Relevant legal provisions:
EPC Art. 56

Keyword:
Inventive step - (no) - obvious selection among a number of commonly known possibilities

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Beschwerdekammern

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Case Number: T 0809/16 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 1 February 2023

Appellant (Opponent 2)	Wibbelmann, Jobst Wuesthoff & Wuesthoff Patent- und Rechtsanwälte Schweigerstrasse 2 81541 München (DE)
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Respondent: (Patent Proprietor)	ALZA Corporation 1900 Charleston Road Mountain View, CA 94043-7210 (US)
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Representative:	Lederer & Keller Patentanwälte Partnerschaft mbB Unsöldstraße 2 80538 München (DE)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 3 February 2016 concerning maintenance of the European Patent No. 1951232 in amended form**

Composition of the Board:

Chairwoman	M. Pregetter
Members:	S. Albrecht
	M. Blasi

Summary of Facts and Submissions

I. European patent No. 1 951 232 ("the patent") is based on European patent application No. 06836771.3 ("application as filed"). The patent was granted with ten claims.

II. Opposition proceedings were based on the grounds for opposition under Article 100(a) EPC for lack of novelty, lack of inventive step and an exception to patentability pursuant to Article 53(c) EPC; Article 100(b) EPC; and Article 100(c) EPC.

III. The documents filed during the opposition proceedings included:

D12: R. J. Meyer *et al.*, "FDA's ACPS Meeting, October 2005 Awareness Topic: Mitigating the Risks of Ethanol Induced Dose Dumping from Oral Sustained/Controlled Release Dosage Forms", October 2005 (four pages in total)

D38: A. S. Hussain, "Preventing Alcohol Induced Dose Dumping is a Desired Product Design Feature", ACPS Meeting, 26 October 2005 (13 pages in total)

IV. The opposition division decided that the patent in amended form in the version of auxiliary request 4 and the invention to which it related met the requirements of the EPC.

Claim 1 of this request reads as follows:

"1. An osmotic opioid sustained release dosage form for use for reducing adverse effects associated with

alcohol-induced dose dumping in patients who are orally receiving the dosage form, wherein:
the dosage form, when tested using an in vitro test method that employs a test medium that comprises aqueous alcohol at a concentration of 20% volume/volume, releases less than or equal to 50 weight percent of the dose of the opioid in a period of 2 hours following initiation of the in vitro test method;
and wherein the dosage form comprises a semi-permeable membrane."

In its decision, the opposition division concluded, *inter alia*, that the subject-matter of claim 1 of auxiliary request 4 involved an inventive step starting from documents D12 and D38.

V. The patent proprietor and opponents 2, 3, 4, 5 and 6 each lodged an appeal against the opposition division's decision. Opponent 1 did not file any appeal and is therefore a party as of right to the appeal proceedings.

VI. With its statement of grounds of appeal, the patent proprietor submitted nine sets of claims of a main request and auxiliary requests 1 to 8. The set of claims of auxiliary request 8 was identical to the claim request held allowable by the opposition division.

VII. The board scheduled oral proceedings in line with the parties' requests.

VIII. In a letter dated 5 August 2020, opponent 6 withdrew the appeal and became a party as of right to the appeal proceedings.

IX. In a communication pursuant to Article 15(1) RPBA 2020, the board drew the parties' attention to the points to be discussed during the oral proceedings.

X. In a letter dated 28 November 2022, opponent 6 informed the board that he would not be attending the oral proceedings.

XI. Likewise, in a letter dated 2 December 2022, opponent 1 informed the board that it would not be attending the oral proceedings.

XII. On 1 February 2023, oral proceedings took place in the presence of the patent proprietor and opponents 2, 3, 4 and 5 and, in accordance with Rule 115(2) EPC and Article 15(3) RPBA 2020, in the absence of opponents 1 and 6. During the oral proceedings, the patent proprietor withdrew its appeal, thus becoming the respondent to the opponents' appeals in the proceedings. The respondent requested that the appeals be dismissed and that the patent be maintained in amended form considered allowable by the opposition division as its sole request. At the end of the oral proceedings, the Chair announced the board's decision.

XIII. The cases of appellant-opponents 2, 3, 4 and 5 relevant to this decision can be summarised as follows.

Each of documents D12 and D38 represented promising starting points for the assessment of inventive step. The subject-matter of claim 1 differed from these disclosures in that the dosage form was osmotic. In the absence of any technical effect linked to this difference, the objective technical problem was the provision of an alternative drug design releasing less

than or equal to 50 wt% of the opioid in a period of two hours in a test medium comprising 20% (volume/volume) ethanol. The solution to this problem proposed in claim 1 would have been obvious since osmotic opioid sustained release dosage forms having a semi-permeable membrane were commonly known in the art at the effective date of the patent.

XIV. The respondent's case relevant to this decision can be summarised as follows.

Documents D12 and D38 could be considered the closest prior art. Neither of these documents disclosed osmotic opioid sustained release dosage forms. The objective technical problem was thus to be worded, in line with pages 20 and 21 of the application as filed, as the provision of a sustained release dosage form which did not dose dump when co-ingested with alcohol. The solution proposed in claim 1 would not have been rendered obvious by the prior art. Documents D12 and D38 merely invited the skilled person to investigate the ruggedness of dosage forms *in vitro* without providing any technical information as to how a solution to the technical problem might be achieved. Undoubtedly, osmotic opioid sustained release dosage forms having a semi-permeable membrane formed part of the skilled person's common general knowledge at the earliest priority date of the patent. However, so did many other types of opioid sustained release dosage forms. Absent any pointer in the prior art towards osmotic opioid sustained release dosage forms as a solution to the objective technical problem, an inventive step had to be acknowledged for the claimed subject-matter.

XV. The parties' final requests relevant to this decision were as follows.

The appellants requested that the decision under appeal be set aside and that the patent be revoked in its entirety.

The respondent requested that the appeals be dismissed and that the decision under appeal be upheld, i.e. that the patent be maintained in amended form in the version considered allowable by the opposition division.

Opponent 6, after having withdrawn the appeal, neither maintained any earlier request nor submitted any new requests.

Opponent 1 did not file any request in the appeal proceedings.

Reasons for the Decision

1. The appeals are admissible. They meet the requirements of Articles 106 to 108 and Rule 99(2) EPC.

2. Claim format

For the respondent's benefit, the board assumes that claim 1 is a claim in the format under Article 54(5) EPC and, hence, is directed to a second medical use.

3. Inventive step (Article 56 EPC)

The closest prior art

3.1 It was common ground that documents D12 and D38 can be taken as the closest prior art in the assessment of inventive step of claim 1. Both starting points had been considered in the decision under appeal.

Content of document D12

3.2 Document D12 (see title) is a position paper by the FDA entitled "FDA's ACPS meeting, 26 October 2005 Awareness Topic: Mitigating the Risks of Ethanol Induced Dose Dumping from Oral Sustained/Controlled Release Dosage Forms".

3.3 This paper is divided into two sections.

3.3.1 The first section has four paragraphs and provides background information on the phenomenon of alcohol-induced dose dumping from modified release dosage forms. Among other things, it reports (see third paragraph in conjunction with citation No.4 of document D12) that the FDA had concluded in July 2005 that the overall risk versus benefit profile of an opioid (i.e. a hydromorphone) modified-release drug product, marketed as Palladone™ ("Palladone"), was unfavourable due to alcohol-induced dose dumping.

3.3.2 In the second section (see page 2, second full paragraph to the bottom of page 3), the authors of document D12 ("the authors") take a position on the awareness topic to be discussed at the FDA's meeting of 26 October 2005. Notably, the authors consider that the FDA's finding on Palladone necessitated the

"development of a general regulatory approach to address the issue of whether alcohol undermines the release characteristics of the drug for new drug applications and already marketed products that utilize a controlled-release mechanism" (see page 2, second full paragraph, first sentence). In their view, this approach should preferably not involve *in-vivo* evaluation. Instead, they propose a system that classifies products into "vulnerable" and "rugged" categories based on the mechanism of drug release. In case of class uncertainty, they suggest verifying the class using a suitable *in-vitro* test of alcohol-induced dose dumping potential (see page 3, last paragraph).

Content of document D38

3.4 Document D38, entitled "Preventing Alcohol Induced Dose Dumping is a Desired Product Design Feature", is a reproduction of 13 slides presented at the FDA's ACPS Meeting of 26 October 2005 by one of the authors of document D12, Ajaz S. Hussain.

3.5 As submitted by appellant-opponent 5 in writing (see statement of grounds of appeal, page 9, last paragraph; page 10, first paragraph) and orally, and confirmed by the respondent at the oral proceedings, document D38 has the same starting point as document D12, i.e. the FDA's safety concerns for the opioid modified-release drug product Palladone (see point 3.3.1 above; paragraph [0050] of the patent).

3.6 Document D38 complements the teaching of document D12 in that it provides further insights on the system proposed in document D12 for determining the potential for alcohol-induced dose dumping for a given dosage form (see point 3.3.2 above). Notably, slides 6, 8 and

11 graphically illustrate *in-vitro* drug release profiles of vulnerable product designs (i.e. dosage forms with high alcohol-induced dose dumping potential). Slides 7, 10 and 12, in turn, graphically show *in-vitro* drug release profiles of rugged product design (i.e. dosage forms with low alcohol-induced dose dumping potential). As discernible in the graphs of slides 6, 8 and 11, vulnerable product designs release about 50% or more of the drug in 20% aqueous ethanol at 2 hours following initiation of the *in-vitro* test. By contrast, rugged product designs have an *in-vitro* drug release of at most about 50% in 40% aqueous ethanol at 2 hours following initiation of the *in-vitro* test (see graphs of slides 7, 10 and 12). Since drug release in 40% aqueous ethanol represents the "worst case" dissolution test (see slide 5), it can be reasonably concluded that the rugged product designs disclosed in slides 7, 10 and 12 release less than 50% of the drug in 20% aqueous ethanol at 2 hours following initiation of the *in-vitro* test and thus exhibit an *in-vitro* drug release profile in accordance with claim 1.

The respondent's arguments on the disclosures of documents D12 and D38

3.7 The respondent submitted that documents D12 and D38 were concerned with patient safety in the United States and had been published for regulatory purposes only. In terms of content, these documents were mere invitations to perform a research programme to identify rugged product designs and were devoid of any concrete technical information. For instance, the examples in document D38 were purely prophetic examples based on computer modelling which could not be reproduced in the absence of any information on the testing conditions.

3.8 The board does not agree. Irrespective of whether the examples of document D38 are based on concrete experimental values or whether these are computer-modelled predictions, it remains that document D38 directly and unequivocally conveys the technical teaching that dosage forms exhibiting *in-vitro* drug release profiles in accordance with claim 1 have low potential for ethanol-induced dose dumping (see point 3.6 above). Undisputedly, documents D12 and D38 do not specify any testing conditions. However, as correctly observed by appellant-opponent 5, the *in-vitro* dissolution tests referred to in document D38 are standard, routine tests in the art, which the skilled person would be able to carry out without any difficulty.

3.9 The following considerations relate to document D38 taken as the closest prior art.

Difference vis-à-vis the closest prior art

3.10 The subject-matter of claim 1 differs from the closest prior-art document D38 in that the opioid sustained release dosage form is an osmotic dosage form.

3.11 Claim 1 further states that the dosage form comprises a semi-permeable membrane. In agreement with the opposition division (see point 4.1, paragraph 7 of the appealed decision), the board finds that the presence of a semi-permeable membrane is an implicit technical feature of osmotic dosage forms. This had not been disputed by the respondent.

Objective technical problem and solution

3.12 The board accepts, in favour of the respondent, that the objective technical problem to be solved is the provision of a sustained release dosage form that does not dose dump when co-ingested with alcohol.

3.13 The proposed solution to this problem is an osmotic opioid sustained release dosage form (having a semi-permeable membrane).

Obviousness of the claimed subject-matter

3.14 The claimed subject-matter would have been obvious to the skilled person having regard to the state of the art. As indicated in point 3.6 above, the closest prior art outlines how the potential for dose dumping for a given dosage form might be assessed. Hence, the closest prior art addresses the technical problem posed, and the skilled person seeking to solve it would have simply followed the approach proposed in this document and subjected commonly known opioid sustained release dosage forms to the *in-vitro* test it describes. Undisputedly, such commonly known opioid sustained release dosage forms include osmotic opioid dosage forms (having a semi-permeable membrane). As a consequence, the closest prior art combined with common general knowledge would have led the skilled person to the proposed solution.

3.15 The respondent took a different view, arguing that *in-vivo* tests were needed to establish whether any of the many known opioid sustained release dosage forms offered a solution to the technical problem posed. The skilled person would thus not have been in a mere "try-and-see" situation and would have needed a good

reason to select osmotic opioid sustained release dosage forms for testing. However, the skilled person would not have had any such reason since the prior art did not contain any pointer towards such osmotic dosage forms.

3.16 The board does not concur. As submitted by appellant-opponent 5 at the oral proceedings, the overall topic of documents D12 and D38 (see titles) is mitigating the risks of alcohol-induced dose dumping from oral sustained/controlled release dosage forms. Within this context, document D38 explicitly states that the *in-vitro* test it proposes is a reliable alternate approach to an *in-vivo* evaluation (see slide 4). Hence, *in-vivo* tests are not required to establish whether any of the many known opioid sustained release dosage forms afford a solution to the objective technical problem posed. Furthermore, in cases like the current one, where the claimed invention represents a mere obvious and consequently non-inventive selection among a number of commonly known possibilities, a separate pointer in the prior art towards the claimed subject-matter is not necessary to establish obviousness. As a consequence, the respondent's arguments are not convincing.

Overall conclusion

4. The board concludes that having regard to the appellants' objections of lack of inventive step starting from document D38 as the closest prior art, the patent as amended in the form considered allowable by the opposition division does not meet the requirements of Article 56 EPC.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The patent is revoked.

The Registrar: The Chair:

I. Aperribay M. Pregetter

Decision electronically authenticated