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Datasheet for the decision of 13 June 2024

Case Number: T 2540/19 - 3.3.07

Application Number: 15202422.0

Publication Number: 3042646

IPC: A61K9/00, A61K31/535, A61K31/5575, A61K31/542, A61K45/06, A61K31/215

Language of the proceedings: EN

Title of invention:
PHARMACEUTICAL COMPOSITIONS HAVING DESIRABLE BIOAVAILABILITY

Patent Proprietor:
Alcon Research, Ltd.

Opponents:
Instone, Terry/Read, Howard Graham/Appleyard Lees IP LLP
Bausch & Lomb Incorporated
ZAKLADY FARMACEUTYCZNE POLPHARMA S.A.
Generics [UK] Limited (trading as Mylan)

Headword:
Travoprost pharmaceutical compositions / ALCON

Relevant legal provisions:
EPC Art. 100(c), 76(1)
RPBA 2020 Art. 13(2), 13(1)

Keyword:
Amendments - added subject-matter (yes)

Decisions cited:
G 0001/06, G 0002/10

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Case Number: T 2540/19 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 13 June 2024

Appellant: (Patent Proprietor)	Alcon Research, Ltd. 6201 South Freeway Fort Worth, TX 76134-2099 (US)
Representative:	Elkington and Fife LLP Prospect House 8 Pembroke Road Sevenoaks, Kent TN13 1XR (GB)
Respondent: (Opponent 1)	Instone, Terry/Read, Howard Graham/Appleyard Lees IP LLP 15 Clare Road Halifax Yorkshire HX1 2HY (GB)
Representative:	Appleyard Lees IP LLP 15 Clare Road Halifax HX1 2HY (GB)
Respondent: (Opponent 2)	Bausch & Lomb Incorporated 1400 North Goodman Street, Area 62 Rochester, NY 14609 (US)
Representative:	Maiwald GmbH Elisenhof Elisenstraße 3 80335 München (DE)
Respondent: (Opponent 3)	ZAKLADY FARMACEUTYCZNE POLPHARMA S.A. ul. Pelplinska 19 83-200 Starogard Gdanski (PL)
Representative:	Bird & Bird LLP Maximiliansplatz 22 80333 München (DE)

Respondent: (Opponent 4)	Generics [UK] Limited (trading as Mylan) Building 4 Trident Place Mosquito Way Hatfield Hertfordshire AL10 9UL (GB)
Representative:	Gill Jennings & Every LLP The Broadgate Tower 20 Primrose Street London EC2A 2ES (GB)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 8 July 2019 revoking European patent No. 3042646 pursuant to Article 101(3)(b) EPC.**

Composition of the Board:

Chairman	A. Usuelli
Members:	E. Duval
	A. Jimenez

Summary of Facts and Submissions

I. Five oppositions were filed against the patent on the grounds that its subject-matter lacked novelty and inventive step, it was not sufficiently disclosed and it extended beyond the content of the (earlier) application as filed.

II. The appeal was filed by the patent proprietor (appellant) against the decision of the opposition division to revoke the patent.

The decision was based on:
- the patent as granted as the main request,
- auxiliary requests 1, 2 and 3 filed on 8 February 2019,
- auxiliary requests 4 and 5 filed during the oral proceedings on 11 April 2019, and
- all remaining auxiliary requests filed on 14 August 2018 and 8 February 2019.

III. Claim 1 of the main request pertained to:

"An aqueous ophthalmic pharmaceutical composition, comprising:
a therapeutic agent which is travoprost; and
a surfactant which is an ethoxylated and hydrogenated vegetable oil;
wherein:
the amount of therapeutic agent is below 0.01 w/v % of the composition;
the amount of surfactant is less than 0.3 w/v % of the composition; and
the composition is free of benzalkonium chloride."

IV. The opposition division decided that:

(a) The main request, as well as auxiliary requests 1 and 2, contravened the requirements of Articles 76(1) and 123(2) EPC.

(b) The patent was not entitled to the claimed priority, and, consequently, the subject-matter of auxiliary requests 3 and 4 lacked novelty.

(c) None of the remaining auxiliary requests were admitted into the proceedings.

V. With their statement setting out the grounds of appeal, the appellant defended their case on the basis of the patent as granted as the main request, and filed auxiliary requests 1-15.

Claim 1 of each of the auxiliary requests 1-15 likewise specified that:
- the amount of therapeutic agent is below 0.01 w/v % of the composition; and
- the amount of surfactant is less than 0.3 w/v % of the composition.

VI. Each of the opponents 1-5 (respectively respondents 1-5) replied to the appeal.

VII. By letter dated 17 March 2022, respondent 5 withdrew their opposition.

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

IX. Oral proceedings were held before the Board. During the oral proceedings, the appellant filed a new auxiliary 1

and renumbered previous auxiliary requests 1-16 into auxiliary requests 2-16.

Claim 1 of this new auxiliary request 1 differed from the main request in that the amount of surfactant was amended to "not more than 0.25 w/v % of the composition".

X. The parties' requests were the following:

(a) The appellant requested that the decision under appeal be set aside and that the case be remitted to the opposition division for consideration of the remaining grounds of opposition, or that the patent be maintained, based on the patent as granted (main request), or, alternatively, on the basis of one of auxiliary request 1 submitted during the oral proceedings, or auxiliary requests 2-16 filed with the statement of grounds of appeal.

(b) Each of respondents 1-4 requested that the appeal be dismissed. They further requested that the case be remitted to the opposition division for assessment of inventive step and sufficiency of disclosure if the Board found the further requirements of the EPC to be met.

Lastly, respondents 1, 3 and 4 requested that none of auxiliary requests 1, 2, 5-7 and 9-16 be admitted into the proceedings, and respondent 2 requested that none of the auxiliary requests 1, 2, 6 and 9-16 be admitted into the proceedings.

XI. The appellant's arguments may be summarised as follows:

(a) The combination of features found in claim 1 of the main request was clearly and unambiguously disclosed in the grand-parent application as filed, in particular in the passage running from page 10, line 29 to page 11, line 18. The amount of therapeutic agent "below 0.01 w/v %" was disclosed as preferred ("still more typically") on page 11, lines 8-14. The amount of surfactant "less than 0.3 w/v %" was also disclosed as preferred ("even more typically") on page 11, lines 15-18. A preference for the value 0.3 w/v% could also be derived from figure 1, which showed that this amount of surfactant satisfied the condition that the free fraction of travoprost in the filtrate be greater than 1%. Lastly, the combined ranges were aligned with all examples exhibiting the benefits of the invention. Thus the main request complied with the requirements of Article 76(1) EPC.

(b) The filing of new auxiliary request 1 was justified by the surprising developments during the proceedings and by the new objection against the combination of the upper limits 0.01 w/v% and 0.3 w/v%.

XII. The respondents' arguments may be summarised as follows:

(a) The subject-matter of claim 1 of the main request resulted from selections from multiple lists, including the amount of therapeutic agent of less than 0.01 w/v % and the amount of surfactant of less than 0.3 w/v %.

(b) The late filed auxiliary request 1 was not to be admitted, because it introduced new issues without

prima facie overcoming the existing issue of added subject-matter, and because its late filing was not justified by any exceptional circumstances.

Reasons for the Decision

1. Main request (patent as granted), article 100(c) EPC

1.1 The patent in suit derives from a second generation divisional application. The grand-parent application as filed was published under the PCT as WO 2009/117316 A2 (i.e. D52).

Following G 1/06, to comply with Article 76(1) EPC, it is necessary and sufficient that anything disclosed in the patent be directly and unambiguously derivable from what is disclosed in each of the preceding applications as filed.

1.2 The invention relates to topical pharmaceutical compositions (e.g., multi-dose ophthalmic compositions) having relatively low concentrations of surfactant that promote the bioavailability of a therapeutic agent, such as the prostaglandin travoprost (see the Technical field of the Invention, first page of the description).

1.3 Claim 1 of the main request relates to an aqueous ophthalmic pharmaceutical composition which is free of benzalkonium chloride (BAC) and comprises:

- a therapeutic agent which is travoprost; and
- a surfactant which is an ethoxylated and hydrogenated vegetable oil.

The composition of claim 1 is defined by the following features in combination:

- the amount of therapeutic agent is below 0.01 w/v % of the composition; and
- the amount of surfactant is less than 0.3 w/v % of the composition.

The relevant question is whether this combination of features remains within the limits of what a skilled person would derive directly and unambiguously, using common general knowledge, and seen objectively and relative to the date of filing, from the whole of the grand-parent application as filed (following the "Gold standard" of G 2/10).

1.4 The appellant saw a basis for the above combination in the passage from page 10, line 29 to page 11, line 18 of the grand-parent application as filed. This passage recites lists of upper and lower limits for the amounts of surfactant and therapeutic agent.

The claimed upper limit of 0.01 w/v % for the amount of therapeutic agent is the narrowest value recited on page 11, lines 12-14 ("such composition typically includes less than 5 w/v %, more typically less than 0.05% w/v % and still more typically less than 0.01 w/v % such therapeutic agent").

The claimed upper limit of 0.3 w/v % for the surfactant concentration derives from lines 15-18 of the same page ("The composition also typically includes less than 0.5 w/v %, more typically less than 0.4 w/v%, even more typically less than 0.3 w/v % and even possilby [*sic*] less than 0.15 w/v % such surfactant").

1.5 The above passage on page 11 cited by the appellant does not single out the claimed combination of upper limits of 0.01 w/v % and 0.3 w/v %. In addition, the grand-parent application discloses further, narrower upper limits for the therapeutic agent in claim 14 ("less than about 0.006 w/v %") and for the surfactant in claim 9 ("less than 0.3%, 0.2% or 0.15%"). Contrary to the appellant's view, the question of added subject-matter cannot be assessed having regard to the passage on page 11 in isolation, but must take account of the whole of the grand-parent application as filed. This follows from the standard for disclosure set out in G 2/10. Considering the overall disclosure of the grand parent application, the respective upper limits for the amounts of surfactant and therapeutic agent are each selected from the various values disclosed separately in the original disclosure, and no preference is explicitly expressed for the selected alternatives over the other recited values.

Furthermore, in the Board's opinion, the issue of added subject-matter must be addressed by reference to the skilled person, who has a technical reading of the original disclosure. As can be understood from the original disclosure (see 1.2 above; see page 3, lines 24-26), the invention is precisely predicated on a connexion between travoprost and the surfactant, and their respective amounts. The specific combination of less than 0.01 w/v % therapeutic agent with less than 0.3 w/v % surfactant however represents a new piece of technical information. In particular, a pointer to the combination of upper limits cannot be artificially derived by drawing a parallel between the expressions used in the lists spelled out on page 11, i.e. from the the fact that the amounts of therapeutic agent and of surfactant are respectively disclosed to be "still more

typically" below 0.01 w/v % and "even more typically" below 0.3 w/v % (see page 11, lines 8-18).

1.6 The appellant also sought to derive a preference for the value 0.3 w/v% from figure 1 of the grand-parent application. Figure 1 shows the results of a filtration assay intended as a model for travoprost bioavailability, wherein the free fraction of travoprost, i.e. in the filtrate, is measured. According to page 24, lines 16-21, it is desired to have free fraction of travoprost greater than 1%, preferably greater than 2% and most preferably greater than 4%. The appellant's argument is that the figure shows that an amount of surfactant of less than 0.3 w/v % satisfies the condition that the free fraction of travoprost in the filtrate be greater than 1%.

The Board does not find this argument persuasive. The appellant's argument is based on a target value (1% free fraction) which is itself the least preferred value in a list (1%, 2% or 4%), and in the context of an assay carried out with travoprost concentrations (0.004, 0.002 or 0.001 w/v %) which do not point specifically to the claimed upper limit (less than 0.01 w/v % travoprost). In addition, the curve extrapolated from the data in figure 1 takes a value different from 1% for a surfactant concentration of 0.3 w/v %. Hence, a different cut-off surfactant concentration is just as likely, namely up to 0.4 w/v % surfactant because it would still lead to at least 1% travoprost free fraction, or lower than 0.3 w/v % as the resulting travoprost bioavailability would be expected to be even higher. Thus, contrary to the appellant's view, the specific value 0.3 w/v % is not disclosed as preferred in figure 1, but is arbitrarily selected from the continuum of values shown therein.

1.7 Lastly, the appellant submitted that the combined ranges were aligned with all examples exhibiting the benefits of the invention. However, these examples fall within the claimed combination of ranges just as much as within other upper limits recited in the grand-parent application as filed for the therapeutic agent (i.e. from less than 5 w/v % to less than 0.006 w/v %), or any higher upper limit for the surfactant. A mere consistency with the examples in the original disclosure can in these circumstances not make up for a lack of pointer to the combined features.

1.8 As a consequence, the main request does not meet the requirement of Article 76(1) EPC.

2. Auxiliary request 1, admittance

2.1 The appellant filed auxiliary request 1 during the oral proceedings before the Board. In claim 1 of this new auxiliary request 1, the upper limit for the amount of surfactant is amended from "less than 0.3 w/v %" to "not more than 0.25 w/v %".

2.2 Auxiliary request 1 is an amendment to the appellant's case which is subject to the provisions of Article 13(2) RPBA in its version in force as of 1 January 2024. This newly filed request shall, in principle, not be taken into account unless there are exceptional circumstances, which have been justified with cogent reasons by the party concerned.

No exceptional circumstances are apparent in the presence case. Contrary to the appellant's view, the objection of added subject-matter against the combined features of claim 1, including the upper limits for the

amounts of surfactant and therapeutic agent, was already raised at the beginning of the appeal proceedings, namely in respondent 1's reply (see the passage bridging pages 13 and 14), respondent 2's reply (see §45), respondent 3's reply (see §33) and respondent 4's reply (see page 15). This issue was additionally pointed out in the Board's communication under Article 15(1) RPBA dated 13 March 2024 (see point 1.1.2.e). Lastly, this question of the combination of the concentrations of surfactant and therapeutic agent is not new in appeal, but was raised and addressed in the first instance proceedings (see the appealed decision, §2.1.1, page 10). The fact that the Board comes to a different conclusion from the opposition division on this point does not constitute exceptional circumstances.

2.3 In addition, the admittance of auxiliary request 1 is also subject to the provisions of Article 13(1) RPBA, according to which the Board shall exercise its discretion in view of, *inter alia*, whether the party has demonstrated that the amendment, *prima facie*, overcomes the issues raised by another party in the appeal proceedings or by the Board and does not give rise to new objections.

In the case at hand, the appellant indicated, as basis for the amended upper limit, examples 2 and 3 in the table at the bottom of page 24 of the grand-parent application as filed, wherein the compositions are characterised by specific components and amounts, in particular 0.25 % HCO-40 as surfactant and 0.004 % travoprost. This amendment does not *prima facie* overcome the issue of disclosure for the claimed combination of not more than 0.25 w/v % surfactant with less than 0.01 w/v % therapeutic agent, and on the

contrary raises the additional issue of intermediate generalisation of the value 0.25 w/v % out of these specific compositions.

2.4 Accordingly, the Board did not admit auxiliary request 1.

2.5 Auxiliary requests 2-16, Article 76(1) EPC

In each of the auxiliary requests 2-16, claim 1 combines the upper limits of below 0.01 w/v % therapeutic agent and less than 0.3 w/v % surfactant, as in the main request. These auxiliary requests must therefore fail under Article 76(1) EPC for the same reasons.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

B. Atienza Vivancos A. Usuelli

Decision electronically authenticated