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**Datasheet for the decision
of 13 November 2024**

Case Number: T 1238/22 - 3.3.07

Application Number: 09722278.0

Publication Number: 2265251

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A61K31/5575, A61K31/542,
A61K45/06, A61K31/215,
A61K31/216

Language of the proceedings: EN

Title of invention:
PHARMACEUTICAL COMPOSITIONS HAVING DESIRABLE BIOAVAILABILITY

Patent Proprietor:
Alcon Research, Ltd.

Opponents:
Pohlman, Sandra M.
Alfred E. Tiefenbacher (GmbH & Co. KG)
Generics [UK] Limited (trading as Mylan)

Headword:
Pharmaceutical Compositions having Desirable Bioavailability /
ALCON

Relevant legal provisions:

RPBA 2020 Art. 12(6)

EPC Art. 111(2), 56

Keyword:

Late-filed request - admitted (yes)

Inventive step - (no)

Decisions cited:

T 2431/17



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Case Number: T 1238/22 - 3.3.07

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

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Decision under appeal: **Decision of the Opposition Division of the
European Patent Office posted on 1 April 2022
revoking European patent No. 2265251 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. The appeal was filed by the patent proprietor (appellant) against the decision of the opposition division, dated 1 April 2022, to revoke the patent in suit.
- II. The proceedings leading to the appealed decision may be summarised as follows:

Three oppositions had been 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 application as filed.

The opposition division issued on 9 October 2017 a first, interlocutory decision finding that the patent in amended form met the requirements of the EPC.

All parties appealed this first decision. In the course of these first appeal proceedings (case T 2431/17), the opponents objected for the first time that the priority was invalid for lack of entitlement, and submitted accordingly documents A045 (WO 2008/052031) as prior art under Article 54(2) EPC and A049 (WO 2009/117242) as prior art under Article 54(3) EPC. In the ensuing decision T 2431/17, the Board decided as follows:

- (a) The patent did not validly claim priority. As a result, A049 anticipated the subject-matter of the (then pending) main request.
- (b) As to auxiliary request 1 filed on 4 July 2018, the case was remitted to the opposition division for

further prosecution in view of the essential outstanding issues not covered by the appealed decision, namely the question of novelty over A049 and inventive step taking into account A045.

III. Following remittal, the opposition division revoked the patent. This second decision of the opposition division, dated 1 April 2022, is the subject of the present appeal decision.

IV. This second decision of the opposition division was based on:

- as main request, auxiliary request 1 filed on 4 July 2018;
- auxiliary requests 1-7 filed by letter dated 6 December 2021; and
- new auxiliary request 6 filed by letter dated 8 February 2022.

V. Claim 1 of the main request pertained to:

"An aqueous ophthalmic pharmaceutical composition, comprising:

a pharmaceutical vehicle suitable for topical application to an eye;
an amount of therapeutic agent;
an effectively low amount of surfactant; and
polyquaternium-1 with a number average molecular weight between 2,000 to 30,000 as a preservative;
wherein the therapeutic agent includes prostaglandin therapeutic agent and the surfactant includes hydrogenated and/or ethoxylated vegetable oil surfactant;

wherein the amount of prostaglandin therapeutic agent is at least 0.00001 w/v % but is less than 5 w/v % of the composition;
wherein the effectively low amount of hydrogenated and/or ethoxylated vegetable oil surfactant is at least 0.005 w/v % but is less than 0.3 w/v % of the composition;
wherein the composition is free of benzalkonium chloride; and
wherein the prostaglandin therapeutic agent comprises travoprost."

Claim 1 of **auxiliary request 2** differed from claim 1 of the main request by the deletion of the feature regarding the molecular weight of polyquaternium-1 and by the addition of the following disclaimer:

"with the proviso that the compositions of Examples E, G, H, I, J, K, L, M, N, O, P, Q, R, S, T and U of WO2009/117242A2 are excluded".

Claim 1 of **auxiliary request 4** corresponded to claim 1 of auxiliary request 2 with the addition of the feature:

"wherein the surfactant is entirely or substantially entirely ethoxylated and/or hydrogenated vegetable oil".

- VI. In the appealed decision, the opposition division:
- found that the subject-matter of the main request lacked novelty over A049, and
 - did not admit any of the auxiliary requests into the proceedings.

- VII. In the present appeal proceedings, the appellant initially defended their case on the basis of the same requests as those underlying the decision of the opposition division, namely the main request, auxiliary requests 1-7 and new auxiliary request 6, all re-filed with their statement setting out the grounds of appeal dated 11 August 2022.
- VIII. The Board set out its preliminary opinion in a communication under Article 15(1) RPBA.
- IX. By letter dated 11 September 2024, the appellant withdrew all requests but two, namely auxiliary requests 2 and 4 (see V. above)
- X. Oral proceedings took place before the Board in the presence of the appellant only.
- XI. The parties' final requests were the following:
- (a) The appellant requests that the decision under appeal be set aside and that the patent be maintained on the basis of the main request, or, alternatively, on the basis of auxiliary request 1, these requests corresponding respectively to former auxiliary requests 2 and 4 as enclosed with the statement of grounds of appeal dated 11 August 2022.
 - (b) The respondents (opponents 1, 2 and 3) request that the appeal be dismissed and that none of the auxiliary requests be admitted into the proceedings.
- XII. The appellant's arguments may be summarised as follows:

(a) Admittance of the main request and auxiliary request 1

These requests corresponded respectively to the main request "a" and main request "b" submitted in response to the opponents' filing of A045 and A049. The opposition division's decision not to admit any of the auxiliary requests was not reasonable, because it had denied the patentee the right to defend any of the requests filed in response to the new objections. Hence the main request and auxiliary request 1 were to be admitted.

(b) Main request, inventive step

A045 was not suitable as closest prior art because it was silent on the issue of improving ocular bioavailability. If A045 was nonetheless taken as starting point, the skilled person would not have considered adding polyquaternium-1 to one of these formulations, because A045 taught to combine 1-dodecyl-2-pyrrolidone only with a single extra preservative, and because examples V-X of A045 already fulfilled the required antimicrobial standards. There was no motivation in A045 for the skilled person to remove zinc chloride and replace it with polyquaternium-1. Hence the main request met the requirements of inventive step.

(c) Auxiliary request 1, inventive step

The further limitation that the surfactant was entirely or substantially entirely ethoxylated and/hydrogenated vegetable oil excluded the presence of the 2-pyrrolidone required by A045. Hence, auxiliary request 1 met the requirements of inventive step.

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

(a) Admittance of the main request and auxiliary request 1

The opposition division had properly exercised their discretion not to admit these requests. These requests did not converge with previous requests, were not immediately allowable and raised new issues. Under Article 12(6) RPBA, the requests were not to be admitted into the appeal proceedings either.

(b) Main request, inventive step

A045, prior art pursuant to Article 54(2) EPC, pertained to microbial preservation of ophthalmic, otic and nasal compositions, and related to the same purpose or effect as the patent in suit. A045 showed compositions comprising 0.004% travoprost, 0.1% HCO-40 and no benzalkonium chloride (BAC). The subject-matter of claim 1 only differed from the compositions of A045 by the presence of polyquaternium-1. The technical problem was the provision of a further BAC-free aqueous ophthalmic composition of travoprost. The claimed solution did not involve an inventive step because A045 suggested the addition of polyquaternium-1.

(c) Auxiliary request 1, inventive step

The amendment to claim 1 of auxiliary request 1 had no bearing on the relevance of A045 on obviousness. Thus, auxiliary request 1 lacked compliance with Article 56 EPC for analogous reasons to the main request.

Reasons for the Decision

1. Admittance of the main request and auxiliary request 1
 - 1.1 The main request and auxiliary request 1 correspond respectively to auxiliary requests 2 and 4 filed in the first instance proceedings on 6 December 2021. The opposition division did not admit these requests into the proceedings.

Under Article 12(6) RPBA, the Board shall not admit requests which were not admitted in the proceedings leading to the decision under appeal, unless the decision not to admit them suffered from an error in the use of discretion or unless the circumstances of the appeal case justify their admittance.

- 1.2 Before reviewing the opposition division's decision not to admit the requests at hand, it is useful to summarise the preceding course of events in opposition and appeal proceedings:
 - 1.2.1 In the course of the previous appeal proceedings (T 2431/17), the appellant (patent proprietor) had filed a main request on 6 February 2018, and auxiliary requests 1-18 by letter dated 4 July 2018.

The issue of invalidity of the priority for lack of entitlement, documents A049 and A045, and the objections of lack of novelty and inventive step based thereon were first submitted during these previous appeal proceedings on 2 May 2019 and 15 August 2019.

On 31 December 2019, the appellant replied by submitting 16 new claim requests, namely the amended versions "a", "b", "c" and "d" of their previous main request and auxiliary requests 4, 8 and 12.

In decision T 2431/17, the Board found the priority to be invalid, rejected the (then) main request for lack of novelty over A049, and remitted the case to the opposition for further prosecution in view of the above new issues. Consequently, the Board neither took position on any of the lower ranking requests nor settled the question of admittance of the new a, b, c and d requests.

Upon remittal, the opposition division summoned the parties to oral proceedings and issued a preliminary opinion based solely on the request corresponding to auxiliary request 1 in T 2431/17.

The appellant submitted auxiliary requests 1-7 on 6 December 2021.

In the ensuing decision, the opposition division rejected the main request for lack of novelty, and did not admit any of the auxiliary requests.

- 1.2.2 According to the appealed decision (see §4), the auxiliary requests filed on 6 December 2021 were submitted late in the opposition procedure, and more than two years after the issues related to A049 first arose in the preceding appeal proceedings. None of these auxiliary requests had been expressly remitted to the opposition division with the Board's decision. These requests did not form part of a convergent development with respect to the higher-ranking requests, and resulted in the introduction of a number

of fresh issues of dispute at a very late stage in the opposition procedure. Accordingly, none of the auxiliary requests were admitted.

1.3 The Board's opinion is the following:

1.3.1 Auxiliary requests 2 and 4 were not filed for the first time on 6 December 2021, but were respectively identical to main request "a" and main request "b" filed during the first appeal proceedings on 31 December 2019. Accordingly, these requests were not submitted more than two years after the issues relating to A049 first arose in appeal proceedings, as reasoned by the opposition division, but after about four months only.

1.3.2 According to the appealed decision, none of these auxiliary requests had been expressly remitted to the opposition division with the Board's decision T 2431/17. However, in the Board's opinion, there was no reason to expect such express indication that these auxiliary requests should be considered upon remittal. The Board took the decision under Article 111(2) EPC to remit the case for further prosecution because of the new issues arising in appeal, namely the question of novelty over A049 and inventive step taking into account A045, and thus with the aim of having these issues examined at two levels of jurisdiction. Nothing in the *ratio decidendi* of T 2431/17 suggests that the auxiliary requests were to be excluded from examination upon remittal.

1.3.3 The admission of the opponents' submissions regarding priority, A045 and A049 in the first appeal proceedings justified that the appellant - patent proprietor be entitled to a fair and legitimate reaction. The Board

accepts that this turn of event did not give the appellant - patent proprietor "carte blanche" to file amended claim requests at this advanced stage of the overall opposition and appeal proceedings (namely on 31 December 2019) without limitation, e.g. regardless of their number, convergence, or new issues raised. However, while the admittance of these amendments was still subject to the opposition division's discretion, this discretion was to be applied in a balanced way considering that their filing was occasioned by the new objections. The opposition division's decision was not balanced in that it was based on the wrong assumption that the requests were filed for the first time on 6 December 2021, and it prevented the appellant - patent proprietor from defending any of the claim requests filed in response to the opponents' new objections and refiled after remittal. Thus the opposition division did not appreciate the actual date and the circumstances of their filing.

1.4 In addition, the Board considers that the circumstances of the present appeal case, namely the fact that the objection leading to the revocation of the patent was raised at a very late stage of the proceedings, and the withdrawal of all requests except the main request and auxiliary request 1, speak for their admittance.

1.5 Consequently, the Board decided to admit the main request and auxiliary request 1.

2. Main request, inventive step

2.1 According to the patent (see paragraph [0002]), the invention relates to ophthalmic compositions having relatively low concentrations of surfactant that promote the bioavailability of a therapeutic agent such

as travoprost. Further possible objectives are mentioned in the patent (see paragraphs [0003] and [0017]), including achieving a desired degree of stability as well as antimicrobial or preservation efficacy.

- 2.2 A045 generally pertains to microbial preservation of ophthalmic, otic and nasal compositions. A045 shows in particular (see page 30, formulations U-X) several compositions comprising 0.004% Travoprost, 0.1% HCO-40 (a hydrogenated and ethoxylated vegetable oil surfactant) and no benzalkonium chloride (BAC). These compositions additionally contain 1-dodecyl-2-pyrrolidone (DDP) and zinc chloride.
- 2.3 The appellant contests that A045 is a suitable starting point for the assessment of inventive step, because A045 does not relate to bioavailability, and because the exemplified compositions of A045 are not clearly ophthalmic compositions. The Board does not concur. The presence of travoprost in the exemplified composition indicates that these compositions are for ophthalmic use. In addition, the patent and A045 both address the problem of antimicrobial or preservation efficacy. Thus, A045 relates to the same purpose or effect as the patent in suit and represents a realistic starting point.
- 2.4 The subject-matter of claim 1 only differs from the compositions of A045 by the presence of polyquaternium-1. No effect is shown or alleged to result from the presence of polyquaternium-1. Accordingly, the technical problem is the provision of a further BAC-free aqueous ophthalmic composition of travoprost.

2.5 A045 generally aims at meeting the antimicrobial preservation criteria of the Pharmacopoeia, and to this end provides compositions comprising, as preservatives, DDP "in combination with benzalkonium chloride, benzadodecinium bromide, a zinc salt, polyquaternium-1, or N-octyl-2-pyrrolidone" (see page 4, line 1-11). The combination of DDP with polyquaternium-1 in particular is emphasised in claim 20 of A045. The skilled person, starting from one of the compositions U-X of A045, and seeking alternative BAC-free aqueous ophthalmic composition of travoprost, would consider either adding polyquaternium-1 to this composition, or replace the zinc salt component of the composition with the alternative polyquaternium-1 which is explicitly suggested in A045.

2.5.1 The appellant contends that the skilled person would not start from formulation U of A045 in view of its inferior preservative properties (see page 30, line 8 to page 31, line 8). In the Board's view, formulation U of A045 remains a realistic starting point for the reasons given above (see 2.3), and the skilled person would all the more consider adding polyquaternium-1 as a further preservative considering the shortfall in antimicrobial efficacy of formulation U. In this respect, the Board does not share the appellant's view that A045 teaches to combine DDP with only one single extra preservative (here, either zinc chloride or polyquaternium-1). The skilled person would not read the passage on page 4 (lines 1-11. "comprising 5-(R1)-N-(R2)-2-pyrrolidone in combination with benzalkonium chloride, benzadodecinium bromide, a zinc salt, polyquaternium-1, or N-octyl-2-pyrrolidone") as being exclusive.

2.5.2 Conversely, the appellant submits that formulations V-X already fulfil the required antimicrobial standards, and that the skilled person would not replace the zinc chloride in these formulations V-X with polyquaternium-1 without any idea of the effect on ocular bioavailability. This argument is however not convincing, because A045 generally presents polyquaternium-1 and zinc chloride as equally suitable alternatives. In addition, considering that no evidence was adduced to show that the claimed formulations are in this respect any better or worse than the formulations of A045, and that the problem is accordingly the provision of an alternative, the skilled person needs no specific motivation to consider this exchange.

2.6 For these reasons, the Board concludes that the main request does not meet the requirements of inventive step.

3. Auxiliary request 1, inventive step

Claim 1 of auxiliary request 1 differs from the main request in that it additionally requires that "the surfactant is entirely or substantially entirely ethoxylated and/or hydrogenated vegetable oil".

Formulations U and V of A045 contain not only 0.1 w/v % of the ethoxylated and/or hydrogenated vegetable oil surfactant HCO-40 but also DDP in amounts of respectively 0.001 and 0.01 w/v %. During the oral proceedings, the appellant referred specifically to page 8, line 10-11 of A045, according to which DDP, which is an essential component of the formulations in A045, would be a surfactant.

However, the limitation introduced in claim 1 of auxiliary request 1 does not entirely exclude the presence of an additional surfactant altogether, but merely requires HCO-40 to be "substantially entirely" the only surfactant. Claim 1 thus allows for the presence of an ill-defined minor amount of additional surfactant. In A045, DDP is explicitly used for the preservation of the formulations (see page 8, line 25). But even if the possible additional role of DDP as a surfactant was taken into account, its presence in formulations U and V in amounts which are ten or a hundred times lower than that of HCO-40 is not excluded by claim 1.

It follows that claim 1 of auxiliary request 1 does not contain any additional differentiating feature over A045, such that its subject-matter lacks an inventive step for the same reasons as for the main request.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar:

The Chairman:



A. Vottner

A. Uselli

Decision electronically authenticated