Internal distribution code:

(A) [-] Publication in OJ
(B) [-] To Chairmen and Members
(C) [-] To Chairmen
(D) [X] No distribution

Datasheet for the decision of 9 March 2023

Case Number: T 0063/20 - 3.3.07

Application Number: 08859677.0

Publication Number: 2217214

IPC: A61K9/20, A61K31/397

Language of the proceedings: EN

Title of invention:
PHARMACEUTICAL FORMULATION COMPRISING EZETIMIBE

Patent Proprietor:
ratiopharm GmbH

Opponents:
HGF Limited
Hoffmann Eitle
Bülle Dr., Jan
Wittkopp, Alexander

Headword:
Formulation comprising ezetimibe / RATIOPHARM

Relevant legal provisions:
RPBA 2020 Art. 12(4), 11
EPC Art. 123(2), 84, 111(1)
EPC R. 43(6)

Keyword:

Late-filed evidence - admitted (yes)
Amendments - main request - allowable (yes)
Claims - clarity - main request (yes)
Remittal - special reasons for remittal

Europäisches Patentamt
European Patent Office
Office européen des brevets

Beschwerdekammern

Boards of Appeal

Chambres de recours

Boards of Appeal of the
European Patent Office
Richard-Reitzner-Allee 8
85540 Haar
GERMANY
Tel. +49 (0)89 2399-0
Fax +49 (0)89 2399-4465

Case Number: T 0063/20 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 9 March 2023

Appellant: (Patent Proprietor)	ratiopharm GmbH Graf-Arco-Strasse 3 89079 Ulm (DE)
Representative:	Lederer & Keller Patentanwälte Partnerschaft mbB Unsöldstraße 2 80538 München (DE)
Respondent: (Opponent 1)	HGF Limited 1 City Walk Leeds Yorkshire LS11 9DX (GB)
Representative:	HGF HGF Limited 1 City Walk Leeds LS11 9DX (GB)
Respondent: (Opponent 2)	Hoffmann Eitle Patent- und Rechtsanwälte PartmbB Arabellastrasse 30 81925 München (DE)
Representative:	Hoffmann Eitle Patent- und Rechtsanwälte PartmbB Arabellastraße 30 81925 München (DE)
Respondent: (Opponent 3)	Bülle Dr., Jan c/o Kutzenberger Wolff & Partner Theodor-Heuss-Ring 23 50668 Köln (DE)
Representative:	Bülle, Jan Kutzenberger Wolff & Partner

Waidmarkt 11
50676 Köln (DE)

Respondent: (Opponent 4)
Wittkopp, Alexander
Jungfernstieg 38
20354 Hamburg (DE)

Representative:
Hamm&Wittkopp Patentanwälte PartmbB
Jungfernstieg 38
20354 Hamburg (DE)

Decision under appeal:
Decision of the Opposition Division of the European Patent Office posted on 11 November 2019 revoking European patent No. 2217214 pursuant to Article 101(3)(b) EPC.

Composition of the Board:

Chairman A. Usuelli
Members: J. Lécaillon
Y. Podbielski

Summary of Facts and Submissions

I. European patent 2 217 214 (hereinafter "the patent") was granted on the basis of 15 claims. The independent claims of the patent as granted read as follows:

"1. A pharmaceutical composition comprising:

5 to 20 wt-% ezetimibe,
50 to 85 wt-% diluent,
3 to 25 wt-% disintegrant,
2 to 5 wt-% solubility enhancer
1 to 10 wt-% binder, and
0.5 to 1 wt-% lubricant,

characterized in that the ezetimibe has a particle size distribution of d(0.9) of 9 µm to 20 µm and d(0.5) of 4 µm to 10 µm wherein the particle size is determined by laser diffraction using the "wet powder method"."

"13. A method for the preparation of a pharmaceutical composition comprising ezetimibe, the method comprising:

a) providing ezetimibe having a particle size distribution and a specific surface area as defined in claim 1 or 2;
b) preparing a blend comprising said ezetimibe and one or more pharmaceutically acceptable excipients,
c) optionally granulating the blend; and
d) processing the blend into a composition;

wherein the pharmaceutically acceptable excipients comprise

50 to 85 wt-% diluent,
3 to 25 wt-% disintegrant,
2 to 5 wt-% solubility enhancer
1 to 10 wt-% binder, and
0.5 to 1 wt-% lubricant."

"14. The use of ezetimibe as defined in claim 1 or 2 for the manufacture of a medicament having a dissolution profile as defined in claim 3."

"15. The use of corn starch paste for the manufacture of a pharmaceutical composition as defined in claim 1, wherein said corn starch paste contains at least 11 % by weight of corn starch."

II. Four 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 application as originally filed.

III. The opposition division took the decision to revoke the patent. The decision was based on the patent as granted as the main request, and on six auxiliary requests.

IV. The decision of the opposition division, posted on 11 November 2019, cited *inter alia* the following document:

D29: Presentation materials from Malvern: "Mastersizer S, Mastersizer 2000 and Mastersizer 3000: Method transfer - how to get the same results on all three systems"

V. The opposition division decided in particular as follows:

(a) The ground of opposition under Article 100(c) EPC prejudiced the maintenance of the patent according to the main request.
(b) Auxiliary requests 1 and 4 contravened Article 123(2) EPC.
(c) Auxiliary requests 2, 3, 5 and 6 did not meet the requirements of Article 84 EPC. Furthermore auxiliary requests 2 and 5 did not fulfill the requirements of Rule 43(6) EPC.

VI. The patent proprietor (appellant) lodged an appeal against the above decision of the opposition division.

VII. With its statement setting out the grounds of appeal, the appellant defended its case on the basis of patent as granted as the main request, and on the basis of auxiliary requests 1 to 6 filed therewith.

VIII. With letter dated 17 January 2023, the appellant withdrew its former main request and auxiliary requests 1 and 4. The former auxiliary requests 2, 3, 5 and 6 became the new main request and auxiliary requests 1 to 3, respectively.

Claim 1 of the main request filed on 17 January 2023 read as follows:

"1. A pharmaceutical composition comprising:

5 to 20 wt-% ezetimibe,
50 to 85 wt-% diluent,
3 to 25 wt-% disintegrant,
2 to 5 wt-% solubility enhancer,
1 to 10 wt-% binder, and
0.5 to 1 wt-% lubricant,

characterized in that the ezetimibe has a particle size distribution of d(0.9) of 9 µm to 20 µm and d(0.5) of 4 µm to 10 µm wherein the particle size is determined by laser diffraction using the "wet powder method" as described in Example 5 b)."

IX. The following items of evidence were filed by the appellant with its statement setting out the grounds of appeal (D36 and D37) and by opponent 1 (respondent 1) with its reply thereto (D38):

D36: Malvern Instruments, "Sample Suspension Unit" Manual, MAN 0177, Issue 1.1, August 1997
D37: EP 0 821 044 A2, page 5
D38: Pharmaceutical Technology Report, "Utility of Polyplasdone™ crospovidone as a Tablet Binder"

X. Oral proceedings were held before the Board on 9 March 2023.

XI. The appellant requested that the decision under appeal be set aside and that the patent be maintained on the basis of the main request or one of auxiliary requests 1-3, all filed with letter dated 17 January 2023.

The appellant further requested that the case be remitted to the opposition division for further prosecution should the main request be found to meet the requirements of Articles 123(2) EPC, or the objections raised by the opposition division to any auxiliary request be found not justified.

XII. Respondents 1, 2, 3, and 4 (opponents 1, 2, 3, and 4) requested that the appeal be dismissed.

Respondents 1, 3 and 4 further requested that the case be remitted to the opposition division for further prosecution should the Board not confirm the decision of the opposition division.

XIII. The arguments of the appellant, as far as relevant for the present decision, can be summarised as follows:

(a) Claim 1 of the main request fulfilled the requirements of Article 123(2) EPC. Its subject-matter corresponded to a combination of original claims 2 and 3 and the amended lower end-point of the range claimed for the particle size distribution of d(0.9) was based on the preferred embodiment disclosed on page 4, second paragraph lines 4-5 of the original application. The measurement method for the particle size was furthermore disclosed in the original description on page 4, penultimate paragraph.

(b) The objection of lack of clarity and the new argument of respondent 1 relating to the time for vortex agitation and sonication should not be admitted into the appeal proceedings.

(c) Claim 1 of the main request met the requirements of Article 84 EPC and Rule 43(6) EPC. In particular, the skilled person would know, as revealed by D36, that the sonication power level was to be chosen such that agglomerates are disintegrated without any breaking up of particles through visual inspection under the microscope. If admitted into the proceedings, the argument of respondent 1 regarding the time for vortex agitation and sonication remained speculative.

XIV. The arguments of the respondents, as far as relevant for the present decision, can be summarised as follows:

(a) Claim 1 of the main request did not fulfill the requirements of Article 123(2) EPC. In particular, the amended ranges of particle size distribution of d(0.9) and of d(0.5) were not originally disclosed in combination. Moreover, the method of example 5b had not been originally disclosed for the specific amended ranges of particle size distribution. The subject-matter of present claim 1 was thus not originally disclosed.

(b) The objection of lack of clarity and the argument of respondent 1 relating to the time for vortex agitation and sonication should be admitted into the appeal proceedings.

(c) Claim 1 of the main request did not meet the requirements of Article 84 EPC. The wet powder method of example 5b did indeed not specify the sonication power level to be used, which constituted an essential feature of the method on which the result of the measurement depended. It was furthermore not possible to adjust the sonication power level so as to provide good dispersion without breaking-up of the particles in the time frame for vortex agitation and sonication defined in the method of example 5b. This feature was thus neither defined in the method itself nor could it be determined by the skilled person. Finally the wet powder method described in example 5b could have been introduced in the claim wording without compromising the conciseness of the claim, so that claim 1 of the main request did not comply with Rule 43(6) EPC.

Reasons for the Decision

1. Admittance of the new item of evidence D36

There was no request on file against the admittance of D36. This document was filed to address the clarity issue raised in the impugned decision. Its content is not complex and its filing is not against procedural economy. The Board therefore admits this document in the appeal proceedings (Article 12(4) RPBA 2020).

Main request

2. Amendments - Article 123(2) EPC

2.1 Claim 1 of the main request corresponds to original claim 3 when depending on original claim 2 wherein:

(a) the lower end-point for the particle size distribution of d(0.9) was amended from 7 µm to 9 µm (*i.e.* the feature "d(0.9) of **7** µm to 20 µm" was amended to "d(0.9) of **9** µm to 20 µm"), and
(b) it was specified that the particle size is determined by laser diffraction using the "wet powder method" as described in Example 5 b)."

2.2 Modification (a)

2.2.1 A preferred range for the particle size distribution of d(0.9) of "at least 9 µm" is disclosed on original page 4, second paragraph. This range is disclosed independently of any range for the particle size distribution of d(0.5). The combination of a preferred, even if not most preferred, lower end-point with another disclosed upper end-point to restrict the range

is therefore directly and unambiguously derivable from the original application.

2.2.2 The respondents argued that both ranges of particle size distribution d(0.9) and d(0.5) are interrelated, so that the combination of the amended range for d(0.9) with the one of d(0.5) was not originally disclosed. The combination of the present ranges would require multiple selections from the original disclosure and would result in the definition of a new subgroup of pharmaceutical compositions not originally disclosed.

2.2.3 This argument is not convincing. It is not apparent which multiple selections would have to be done. Starting from the combination of original claims 1 to 3, which defines an embodiment of the invention, only the lower end-point of the range of d(0.9) was modified based on a preferred embodiment disclosed in the original description. Furthermore, the definition of the particle size distribution in present claim 1 is still generic, so that no singling out of individual pharmaceutical compositions results from the amendment.

2.2.4 Regarding the issue of interrelation of the ranges of particle size distribution, the Board agrees that both parameters are involved in the definition of the particle size distribution profile of the claimed compositions. However an interrelation of both ranges, in the sense that the modification of one range would inevitably require a modification of the other one, does not exist.

Merely the resulting particle size distribution profile will be affected. The original claims (combination of claims 2 and 3) covered a great variety of particle size distribution profiles resulting from the

combinations of any claimed d(0.5) value with any claimed d(0.9) value. The restriction in present claim 1 of the range of d(0.9) has only the effect of restricting the scope of the claim to some of those many alternatives. Since the lower end-point of 9 µm for the d(0.9) value was originally disclosed as a preferred one independently of the d(0.5) value, this resulted in the definition of preferred subgroups of compositions having a d(0.9) of at least 9 µm and any d(0.5) value. This applies also to the specific d(0.5) range of original claim 3. As a consequence, the combination of both particle size distribution ranges is directly and unambiguously derivable from the original application.

2.3 Modification (b)

2.3.1 The respondents considered that the combination of the claimed method with the specific amended ranges of particle size distribution would not be originally disclosed.

In particular, respondent 1 argued during the oral proceedings that the skilled person would be aware that not all the methods disclosed in the penultimate paragraph on original page 4 would be applicable to any particle size range. Some methods such as sieves would indeed be unsuitable for narrow ranges. In view of the lack of specification of the sonication power level in the method of example 5b together with the very short time for vortex agitation (10 seconds) and sonication (30 seconds) defined therein, the method would not render possible the achievement of a good dispersion of the particles. In this context respondent 1 referred to D29, which would show that appropriate dispersion for the measurement of the d(0.9) particle size

distribution was achieved only after 300 seconds (see page 32). In the absence of an appropriate dispersion, the wet powder method would not provide good results (since agglomerates would actually be measured) and would thus not be appropriate for the amended narrow range of particle size distribution. It would therefore not be directly and unambiguously disclosed in the original application that the method of example 5b would be suitable for a narrow range as now claimed in amended claim 1.

2.3.2 This argument is not convincing.

In the original description, the particle size distribution ranges are not disclosed as being linked to any specific method. Furthermore, the methods mentioned on original page 4 penultimate paragraph are described in general for the measurement of the particle size. There is no indication in the original application that any of these methods would not be adapted for the measurement of the ranges defined therein. Moreover, the method of example 5b is defined as a preferred method in the original application (see page 4 penultimate paragraph last sentence) and was used in the examples (see *inter alia* example 5b sample 5). It is therefore directly and unambiguously derivable from the original application that this method is the most preferred one.

The argument of respondent 1 that the method of example 5b would not be appropriate for the measurement of the narrow range of particle size distribution of d(0.9) relies on technical considerations of the skilled person which go beyond what has to be considered when assessing the compliance with the requirements of Article 123(2) EPC, *i.e.* whether the original

application directly and unambiguously discloses the claimed subject-matter. Furthermore, in the present case, the results of sample 5 of example 5b, which confirm that the claimed method can be successfully employed for the measurement of the claimed particle size distribution range, would have cleared up any potential doubt the skilled person might have had regarding the suitability of the method of example 5b for said measurement.

2.3.3 In the written proceedings, respondent 4 also observed that the restriction in the particle size distribution resulted in excluding some embodiments of example 5b measured with the claimed wet powder method (see samples 1 and 2) while the particle size distribution of all the embodiments of example 5a, measured with the dry powder method, were still encompassed by the claimed range. This would therefore confirm that the original application did not disclose any link between the claimed particle size distribution and the claimed measuring method.

This argument is also not convincing. The results obtained when using the dry powder method of example 5a are indeed not relevant in the context of the wet method. Finally, the fact that the particle size distributions of samples 1 and 2 when measured with the method of example 5b do not fall under the scope of the amended claims does not mean that compositions having d(0.9) and d(0.5) values within the claimed ranges when measured by the method of example 5b were not originally contemplated. This is confirmed by sample 5 in example 5b, which actually falls within the scope of the claims.

2.4 As a result, claim 1 of the main request meets the requirements of Article 123(2) EPC.

3. Clarity

3.1 Article 84 EPC

3.1.1 The respondents argued that the sonication power level is critical for the obtained particle size distribution value. This essential feature is not specified in the method of example 5b. It would therefore not be possible for the skilled person to determine whether a given composition would fall within the scope the claims or not.

3.1.2 Furthermore, during the oral proceedings, respondent 1 additionally argued that the wet powder method of example 5b would not provide an appropriate dispersion of the particles due to the short duration of vortex agitation (10 seconds) and sonication (30 seconds). Hence no satisfactory particle size measurement could be performed since agglomerates would subsist. Contrary to the argument of the appellant, the skilled person would not be in a position to adapt the level of sonication power so as to obtain good dispersion with visual observation within these short times. According to respondent 1, the skilled person would thus not know how to perform the invention and whether it would be working within the scope of the claims or not.

3.1.3 It was undisputed that the sonication power level is critical for the measurement of the particle size distribution and to determine whether a given composition falls within the scope of the claims or not.

3.1.4 As argued by the appellant, the skilled person is aware that the sonication level has to be chosen such that agglomerates are dispersed but without any breaking up of the particles as determined by microscopic observation before and after sonication. This is apparent from the Malvern laser diffraction instrument handbook including the apparatus used in example 5b of the patent (see D36 page 7.2). Contrary to the opinion of respondent 4, this method does *a priori* not require to know the particle size of the starting material since microscopic observation is done before and after sonication.

3.1.5 In this context, the argument of respondent 1 that determining the sonication power level would not be possible due to the vortex agitation and sonication times remains unsubstantiated. The reference to the 300 seconds required for good dispersion based on page 32 of D29 is not meaningful because D29 does not provide experimental details in particular regarding the starting agglomerated sample. There is no evidence that an ezetimibe sample according to the invention would be in such an agglomerated state requiring such a long sonication time. Respondent 1 has not provided any experimental evidence that no appropriate dispersion could be obtained within the time defined in the wet powder method of example 5b for an ezetimib sample. Moreover, the method was actually successfully applied to sample 5 in example 5b. Finally the Board observes that the issue of whether the skilled person is able to carry out the claimed invention is an issue of sufficiency of disclosure and not of clarity.

3.1.6 In its written submission, respondent 1 also argued that the teaching of D36 would not apply to the present case because the samples described in D36 are much

larger and different from the present ezetimibe compositions. The Board sees no reason why the same issue with sonication would not occur with the present compositions and be the reason for the observed difference in particle size distribution depending on the sonication power level. The microscopic observation suggested in D36 could thus be applied in any case.

3.1.7 Hence, in the absence of any substantiated evidence of the contrary, it is credible that by performing the microscopic observation suggested in D36, the sonication power level allowing dispersion of agglomerates while avoiding particle break up in the method of example 5b can be determined. The Board is therefore of the opinion that the skilled person would apply this sonication power level in the claimed method and would thus know how to perform said wet powder method in a reliable manner. As a result the method defined in claim 1 is clear.

3.1.8 Accordingly, claim 1 of the main request fulfills the requirements of Article 84 EPC.

3.2 Since the objection of lack of clarity is not convincing, no decision on the admittance of this objection and of the new argument provided by respondent 1 during the oral proceedings in relation to the time for sonication and vortex agitation is required.

3.3 Rule 43(6) EPC

3.3.1 The Board observes that the issue of whether a method of measurement would be such that it may impair the conciseness of a claim is to be assessed on a case by case basis and is not merely an issue of word count. In

the present case, the Board is of the opinion that a reference to the description is necessary to preserve the conciseness of the concerned claims.

3.3.2 Hence, claim 1 of the main request complies with Rule 43(6) EPC.

4. Remittal

4.1 Under Article 11 of the Rules of Procedure of the Boards of Appeal (RPBA) 2020 (OJ EPO 2019, A63), which applies in the present case according to Article 25(1) RPBA 2020, the Board may remit the case to the department whose decision was appealed if there are special reasons for doing so.

4.2 In the present case, the appealed decision does not address the grounds for opposition under Articles 100(a) and 100(b) EPC. As recalled in Article 12(2) RPBA 2020, the primary object of the appeal proceedings is to review the decision under appeal in a judicial manner. This principle would not be respected if the Board were to conduct a complete examination of the all the grounds of opposition. Consequently, under these circumstances, the Board considers that special reasons for remitting the case to the opposition division exist. Therefore, the Board considers it appropriate to accede to the requests of the appellant as well as respondents 1, 3 and 4 for a remittal (Article 111(1) EPC).

Order

For these reasons it is decided that:

The decision under appeal is set aside.

The case is remitted to the opposition division for further prosecution.

The Registrar: The Chairman:

B. Atienza Vivancos A. Usuelli

Decision electronically authenticated