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Datasheet for the decision of 31 January 2017

Case Number: T 2108/14 - 3.3.07

Application Number: 03752490.7

Publication Number: 1551372

IPC: A61K9/14, A61K9/16, A61K9/20, A61K9/28, A61K9/50

Language of the proceedings: EN

Title of invention:
SEQUESTERING SUBUNIT AND RELATED COMPOSITIONS AND METHODS

Applicant:
Alpharma Pharmaceuticals LLC

Relevant legal provisions:
EPC Art. 123(2), 84, 54, 111(1)

Keyword:
Amendments - allowable (yes)
Claims - clarity - main request and first auxiliary request (no) - second auxiliary request (yes)
Novelty - (yes)
Appeal decision - remittal to the department of first instance (yes)

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Case Number: T 2108/14 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 31 January 2017

Appellant: (Applicant)	Alpharma Pharmaceuticals LLC 400 Crossing Boulevard Bridgewater, New Jersey 08807 (US)
Representative:	Pfizer European Patent Department 23-25 avenue du Docteur Lannelongue 75668 Paris Cedex 14 (FR)
Decision under appeal:	**Decision of the Examining Division of the European Patent Office posted on 10 June 2014 refusing European patent application No. 03752490.7 pursuant to Article 97(2) EPC.**

Composition of the Board:

Chairman	A. Usuelli
Members:	R. Hauss
	P. Schmitz

Summary of Facts and Submissions

I. The appeal lies from the decision of the examining division, announced on 31 March 2014 and posted on 10 June 2014, refusing European patent application No. 03 752 490.7.

II. The following documents were cited in the course of the examination proceedings:

D1: US 5 639 476 A

D2: WO 01/58447 A1

D3: USP 26 (2003), Chapter <711>: Dissolution

III. The decision under appeal was based on a single request. The examining division found that the subject-matter of claim 1, directed to a composition, lacked novelty in view of the disclosure of documents D1 and D2. The subject-matter of independent claim 37, directed to a sequestering subunit, lacked novelty in view of the disclosure of document D2.

IV. The applicant (appellant) lodged an appeal against that decision. With the statement setting out the grounds of appeal the appellant also submitted an amended set of claims, replacing the claims considered in the decision under appeal. In a further submission dated 19 December 2016, the appellant suggested that remittal would be appropriate if the board agreed to set aside the decision under appeal.

V. In a communication issued in preparation for oral proceedings and advising the appellant of the board's preliminary opinion, the board raised objections to the amended claims under Articles 84 and 123(2) EPC. In the context of Article 84 EPC, the board observed *inter alia* that, since dissolution testing according

to USP26 Chapter <711> (referred to in claim 1) left some scope for varying the test conditions, it could not be excluded that different results might be obtained depending on the specific test conditions chosen.

The board observed further that novelty had not been conclusively established relative to the disclosure of document D2.

Furthermore, document **D4** (WO 01/58451 A1), cited in the application, also appeared to be highly relevant; *inter alia*, several example formulations described in document D4 anticipated the subject-matter of claim 1.

Should it be established that a request on file met the requirements of Articles 123(2), 84 and 54 EPC, it would be decided whether a remittal of the case to the examining division was appropriate.

VI. With letter of 20 January 2017, the appellant withdrew the set of claims filed with the statement setting out the grounds of appeal and submitted three new sets of claims designated as the main request, first auxiliary request and second auxiliary request.

The independent claims of the **main request** read as follows:

"1. A pharmaceutical composition in the form of a bead, pellet, granule or spheroid comprising

a subunit comprising an opioid antagonist in sequestered form,

which subunit is coated with a opioid agonist in releasable form,

wherein the subunit comprising the opioid antagonist in sequestered form further comprises a core and a material that is impermeable to the opioid antagonist

configured to prevent release of at least 90% of the opioid antagonist in the gastrointestinal tract for a time period that is greater than 24 hours, as determined by dissolution testing according to USP26 Chapter <711> opioid antagonist.

20. A capsule suitable for oral administration comprising a plurality of the beads, pellets, granules or spheroids of claim 1."

Independent claims 1 and 20 of the **first auxiliary request** are identical to the corresponding claims of the main request, except that claim 1 of the first auxiliary request, after the passage *"as determined by dissolution testing according to USP26 Chapter <711>"* continues as follows:

", for example by (i) using Apparatus 2 (paddle)- placing the composition in 900 ml of 0.1N HCl at 37° C using USP paddle method 2, at 75 rpm, or (ii) using Apparatus 1 (baskets) at 50 rpm, 500ml water at 37°C, and taking samples to test for the presence of the opioid antagonist."

Independent claims 1 and 20 of the **second auxiliary request** are identical to the corresponding claims of the main request, except that claim 1 of the second auxiliary request, after the passage *"as determined by dissolution testing according to USP26 Chapter <711>"*, continues as follows:

", using Apparatus 1 (baskets) at 50 rpm, 500ml water at 37°C, and taking samples to test for the presence of the opioid antagonist."

VII. Oral proceedings before the board took place on 31 January 2017. In the course of the oral proceedings, the appellant replaced the **main request** by an amended

version in which the term *"opioid antagonist"* at the end of claim 1 (present due to a clerical error) was deleted, the requests being otherwise identical.

VIII. The appellant's arguments, as far as relevant to the present decision, may be summarised as follows:

Clarity (main request and first auxiliary request)

While the USP standard (document D3) allowed for some variation in methodology, dissolution testing was clearly meant to provide information which was useful for understanding the behaviour of the dosage form in the gastrointestinal tract, and it could thus be expected that methods which were adequate for that purpose would not provide grossly different results. The person skilled in the art would furthermore know, in each specific case, to choose test conditions (such as the pH of the dissolution medium) which most closely modelled the expected *in vivo* behaviour of the sample. In any case, minimal variations could matter only at the edge of the scope claimed, if at all.

Clarity (second auxiliary request)

In case the board was of the view that specific parameters must be associated with the test, the second auxiliary request defined a single method for dissolution testing.

Remittal

The examining division had neither taken a decision nor provided a detailed opinion on the issue of inventive step. Moreover, the claims had been substantially amended in the course of the appeal proceedings. Under those circumstances, remittal of the case to the examining division was justified, all the more so as

the board had not yet disclosed its stance on inventive step.

IX. The appellant requested that the decision under appeal be set aside and that the case be remitted to the department of first instance for further consideration, based on the main request filed during the oral proceedings before the board, or one of auxiliary requests 1 or 2, filed with letter of 20 January 2017.

Reasons for the Decision

1. Clarity - main request

1.1 Claim 1 specifies that the release of the opioid antagonist in the gastrointestinal tract is to be assessed by *in vitro* dissolution testing according to USP26 Chapter <711>.

1.2 The referenced USP26 Chapter <711> (see document D3) describes types of apparatus for dissolution testing but, as conceded by the appellant, leaves some scope for varying the test conditions.

1.3 Hence, it cannot be excluded that different results may be obtained depending on the specific test conditions chosen, such as the pH value of the dissolution medium. As a consequence, some doubt may arise as to when the criterion for prevention of release of at least 90% of the opioid antagonist should be considered to be met, especially in borderline cases in which about 90% of the opioid antagonist will have been released after a time of about 24 hours. In the absence of more precise instructions, the person skilled in the art may thus be unable to establish in every case for a given formulation whether or not its composition and

structure meet the criterion of claim 1 of preventing the release of at least 90% of the opioid antagonist for a time period of greater than 24 hours.

1.4 For this reason, the board has arrived at the conclusion that claim 1 of the main request does not meet the requirements of Article 84 EPC.

2. Clarity - first auxiliary request

2.1 The scope defined by claim 1 of the first auxiliary request (see point VI above) is the same as that of claim 1 of the main request, since claim 1 of the first auxiliary request mentions additional conditions for dissolution testing only by way of example and thus, not as mandatory and limiting technical features.

2.2 Hence, claim 1 of the first auxiliary request does not meet the requirements of Article 84 EPC, for the same reason as claim 1 of the main request.

3. Clarity - second auxiliary request

3.1 Claim 1 of the second auxiliary request defines specific test conditions for dissolution testing, requiring a particular combination of apparatus, medium and stirring rate (see point VI above).

3.2 Hence, the board considers that the objection discussed above in the context of the main request and first auxiliary request has been overcome and that claim 1 of the second auxiliary request meets the requirements of Article 84 EPC.

4. Amendments - second auxiliary request

4.1 Claims 1 and 20 of the second auxiliary request are based on claim 28 (see also paragraphs [0013]

and [0075]) of the application as published (WO 2004/026283), relating to composite subunits comprising a sequestering subunit coated with a therapeutic agent in releasable form. That embodiment is combined with definitions of technical features which are more specific than the functional terms originally used in the claims, and which are generally disclosed, and recognisably preferred, in the application in paragraphs [0039], [0106], [0051] (opioid and opioid antagonist), [0023] (particulate forms), [0024] (core and impermeable material), [0018], [0019], [0020] and [0134] (dissolution properties).

4.2 Hence, the board finds that the subject-matter of independent claims 1 and 20 of the second auxiliary request does not extend beyond the content of the application as filed (Article 123(2) EPC).

5. Novelty - second auxiliary request

5.1 Claim 1 relates to a pharmaceutical composition in the form of beads, pellets, granules or spheroids, comprising a sequestered form of an opioid antagonist. That sequestered form (designated in the claim as a "subunit") is coated with an opioid agonist in releasable form. Those technical features are also mandatory in independent claim 20, due to the reference in that claim to the beads, pellets, granules or spheroids of claim 1.

5.2 The technical feature of particulate sequestered forms of opioid antagonists being coated with an opioid agonist is not disclosed in any of prior-art documents D1, D2 or D4.

5.3 Hence, the subject-matter defined in the present claims is novel relative to the disclosure of documents D1, D2 and D4 (Article 54(2) EPC).

6. Remittal

6.1 The examining division has not taken a decision on inventive step and has not considered document D4 (see paragraph V above).

D4 concerns tamper-resistant oral opioid agonist formulations comprising an opioid antagonist in a sequestered form, and is therefore regarded by the board as a relevant prior-art disclosure, since it relates to the same teaching and general type of formulation as the present application.

6.2 After substantial amendment, the present claims focus on the concept of a particulate composition which is coated with an opioid agonist in releasable form, and capsules containing such particles. Thus the composite structure of the particles may become relevant in the assessment of inventive step. In that context, further investigation may be required, since the documents cited in the proceedings so far do not provide any information regarding such galenic forms or the common general knowledge on that account.

6.3 Under these circumstances, and in conformity with the appellant's request, the board deems it appropriate to remit the case to the examining division for further prosecution (Article 111(1) EPC).

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the department of first instance for further prosecution.

The Registrar: The Chairman:

K. Boelicke A. Usuelli

Decision electronically authenticated