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**Datasheet for the decision
of 26 April 2012**

Case Number: T 1751/07 - 3.3.02

Application Number: 99950105.9

Publication Number: 1117384

IPC: A61K 9/26

Language of the proceedings: EN

Title of invention:

Controlled release nanoparticulate compositions

Applicant:

Elan Pharma International Limited

Headword:

Nanoparticulate compositions/ELAN PHARMA

Relevant legal provisions:

EPC Art. 84

EPC R. 22(1)(3)

Keyword:

"Transfer of application (no): no entry into register and no clear-cut evidence of transfer"

"Claims clarity (no)"

Decisions cited:

J 0026/95

Catchword:

-



Case Number: T 1751/07 - 3.3.02

D E C I S I O N
of the Technical Board of Appeal 3.3.02
of 26 April 2012

Appellant: Elan Pharma International Limited
(Applicant) Monksland
Athlone
Westmeath (IE)

Representative: Pohlman, Sandra M.
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Decision under appeal: Decision of the Examining Division of the
European Patent Office posted 4 April 2007
refusing European patent application
No. 99950105.9 pursuant to Article 97(1) EPC
1973.

Composition of the Board:

Chairman: U. Oswald
Members: H. Kellner
L. Bühler

Summary of Facts and Submissions

I. European patent application No. 99 950 105.9, filed as international application PCT/US99/22897 and published as WO 00/18374, was refused by a decision of the examining division on the basis of Article 97(1) EPC 1973.

II. Claim 1 of the main request before the examining division read as follows:

"A solid dose controlled release composition comprising:

- (a) a nanoparticulate drug composition comprising a poorly soluble nanoparticulate drug to be administered and at least one surface stabilizer, wherein the nanoparticulate drug has an effective average particle size of less than about 1000 nm, and
- (b) at least one pharmaceutically acceptable rate-controlling polymer, wherein:
 - (i) the rate-controlling polymer is integrated in a rate-controlling matrix with the nanoparticulate drug composition or coats the nanoparticulate drug composition, and
 - (ii) the controlled release composition provides controlled release of the nanoparticulate drug for a time period ranging from 2 to 24 hours."

III. The examining division held the subject-matter of the main request not to be new, that of the first auxiliary

request not to be clear and the subject-matter of the other requests not to involve an inventive step.

IV. The appellant lodged an appeal against the decision of the examining division and filed grounds of appeal repeating the five sets of claims the examining division had taken its decision on.

V. On 24 November 2011, a communication of the board was despatched, drawing the applicant's attention to various amendments that, as examples, appeared to contravene Article 123(2) EPC. In addition, it was indicated that the objections raised by the examining division during the proceedings appeared to be basically still valid and that the wording of current claims 1 appeared to be not clear in the sense of Article 84 EPC. Finally, concern with respect to Article 83 EPC was expressed.

Inter alia it was set out that with respect to the claimed functional feature "the composition provides controlled release of the agent for a time period ranging from about 2 to about 24 hours", two questions seemed to arise, the second of them being whether the full amount of the agent as administered had to be released within the time period ranging from about 2 to about 24 hours, or whether release might start before 2 hours, with an unknown but freely choosable "remainder" to be released within the period ranging from about 2 to about 24 hours, or anything else.

VI. As a response to the communication of the board, the appellant, with letter of 30 March 2012, filed a new main request and auxiliary request 1 together with two

lines of auxiliary requests 2 to 4, line A being derived from the main request and line B following auxiliary request 1.

The wording of claim 1 of the main request is as follows (amendments marked with respect to claim 1 of the main request as decided on):

"A dosage form in tablet form or multiparticulate form comprising a ~~solid dose~~-controlled release nanoparticulate composition comprising:

- (a) a ~~nanoparticulate drug composition~~ comprising a poorly soluble nanoparticulate drug to be administered and at least one surface stabilizer associated with the surface of the nanoparticulate drug, wherein ~~the nanoparticulate drug has an effective average~~ at least 70% of the drug particles, by weight, have a particle size of less than ~~about~~ 1000 nm when measured by light scattering, and
- (b) at least one pharmaceutically acceptable rate-controlling polymer, wherein
 - (i) the rate-controlling polymer ~~is integrated in a rate controlling matrix with the nanoparticulate drug composition or coats the dosage form~~ nanoparticulate drug composition, and
 - (ii) the ~~controlled release~~ composition provides controlled release of the nanoparticulate drug, ~~for a time period ranging from about 2 to about 24 hours~~

wherein controlled release refers to therapeutically effective release of the drug in a patient for a time period ranging from 2 to 24 hours."

In clean version the claim reads:

"A dosage form in tablet form or multiparticulate form comprising a controlled release nanoparticulate composition comprising:

- (a) a poorly soluble nanoparticulate drug to be administered and at least one surface stabilizer associated with the surface of the nanoparticulate drug, wherein at least 70% of the drug particles, by weight, have a particle size of less than 1000 nm when measured by light scattering, and
- (b) at least one pharmaceutically acceptable rate-controlling polymer, wherein
 - (i) the rate-controlling polymer coats the dosage form, and
 - (ii) the composition provides controlled release of the nanoparticulate drug,

wherein controlled release refers to therapeutically effective release of the drug in a patient for a time period ranging from 2 to 24 hours."

The wording of claim 1 of auxiliary request 1 differs from claim 1 of the main request in that *in vitro* characteristics define the controlled release profile under section (b) of the claim, instead of the *in vivo* characteristics of the main request. This claim reads as follows:

"A dosage form in tablet form or multiparticulate form comprising a controlled release nanoparticulate composition comprising:

- (a) a poorly soluble nanoparticulate drug to be administered and at least one surface stabilizer associated with the surface of the nanoparticulate drug, wherein at least 70% of the drug particles, by weight, have a particle size of less than 1000 nm when measured by light scattering, and
- (b) at least one pharmaceutically acceptable rate-controlling polymer coating the dosage form, wherein the controlled release composition provides controlled release of the nanoparticulate drug for a time period ranging from 2 to 24 hours, the drug release being measured *in vitro* according to one of the following methods:

- (1) using a Distek Dissolution System with a Hewlett Packard Diode Array Spectrophotometer 8452A and a Hewlett Packard Flow Control device model 89092A at a temperature of 37°C, wherein a phosphate buffer at pH 7.4 is used as a testing medium,

- (2) using USP apparatus II (100 rpm) and a phosphate-citrate buffer, pH 6.8, containing 0.5% sodium lauryl sulphate, or

- (3) using USP apparatus I (100 rpm) and a KH_2PO_4 buffer, pH 7.5."

In claims 1 of auxiliary requests 2A and 3A based on the main request, additionally the rate controlling polymer is defined by a list of particular substances (2A) and further by indicating the percentage of the rate controlling polymer (3A). In claim 1 of auxiliary request 4A the listed examples of the rate controlling polymers were limited as compared to claim 1 of auxiliary request 3A.

Claims 1 of auxiliary requests 2B, 3B and 4B contain the same amendments, but based on auxiliary request 1.

- VII. With letter of 23 April 2012, received in the Office on the same day, the appellant requested a transfer of rights, i.e. that another company be registered as the proprietor of the application, instead of the company that had filed the application. A signed authorisation document was also filed, for the same attorney as the one already representing the applicant in the proceedings.
- VIII. Oral proceedings took place on 26 April 2012 in the presence of the representatives of the appellant, in particular the attorney who had acted during the proceedings before the examining division and during the written proceedings before the board.

As the result of a short discussion, it was established that the representative was speaking in the name of the company which had appealed and was still registered by the EPO as proprietor of the application on the day of the oral proceedings.

IX. The arguments of the appellant in both the written and oral proceedings may be summarised as follows:

With respect to Article 84 EPC, and relating to the wording "release ... for a time period ranging from 2 to 24 hours", the problem indicated in the communication was solved by restricting the subject-matter to *in vivo* release in claim 1 of the main request and to *in vitro* release in claim 1 of auxiliary request 1.

As could be seen from the numerous examples in the application and in particular figures 10 and 11, release could start before two hours after administration *in vivo* and then had to occur over a time period of at least two hours, and 24 hours at most. In the *in vitro* experiments the skilled person was instructed to perform one of three well-defined methods to investigate whether release occurred in a time period ranging from 2 to 24 hours, meaning that release had to occur for a minimum of 2 hours and for not longer than 24 hours, and thus he could decide whether the tested dosage form exhibited the features of the claim or not.

X. The appellant requested that the decision under appeal be set aside and that a patent be granted on the basis of the claims of the main request or, alternatively, on the basis of one of the auxiliary requests filed with letter of 30 March 2012.

Furthermore, it requested to correct obvious errors in the drawings (figures 10 and 11) as shown in the pages attached to the statement of grounds of appeal of 14 August 2007.

Reasons for the Decision

1. The appeal is admissible.

2. According to the jurisprudence of the boards of appeal, assessing whether there are documents satisfying the European Patent Office that a transfer has taken place in accordance with Rule 22(1) and (3) EPC and making the entry in the register is the responsibility of the relevant department of first instance. Accordingly, in appeal proceedings, substitution of another party for the original applicant is possible only once the relevant department of first instance has made the entry or where there is clear-cut evidence of a transfer (J 26/95, OJ 1999, 668, point 2 of the reasons).

The documents produced with letter dated 23 April 2012 do not constitute clear-cut evidence of a transfer. They only created the obligation to assign rights, and did not constitute the assignment itself. The effective date of the assignment and possible conditions to be fulfilled before the assignment becomes effective cannot be inferred from the document produced.

Thus, the board was not in a position to replace the party shown in the register as proprietor of the application at the date on which the notice of appeal had been filed, and the representative therefore spoke in the name of that company.

3. The amended claims filed by the appellant with letter of 30 March 2012 represent an attempt to overcome the

objections raised in the communication of the board.
Consequently, they are admitted into the proceedings.

4. *Claim 1 of the main request; Article 84 EPC*

4.1 This claim relates to a dosage form comprising a controlled release nanoparticulate composition ... wherein ... the composition provides controlled release of the nanoparticulate drug, wherein controlled release refers to therapeutically effective release of the drug in a patient for a time period ranging from 2 to 24 hours.

4.2 Notwithstanding the fact that "release", which simply describes the step of the drug being freed from dosage form and entering the patient's body, cannot be "therapeutically effective" *per se*, but only makes it possible to achieve a therapeutically effective level of concentration of the drug within the body, the board accepts the explanation in the description (see page 20, lines 23 to 27 of the application: "providing a desired effect for a time period ranging from 2 to 24 hours") and the wording "therapeutically effective release" in current claim 1 of the main request is understood to mean further release activity after the therapeutically effective concentration of the drug in an appropriate body fluid has been reached.

4.3 In any case, the text

"the composition provides controlled release of the nanoparticulate drug, wherein controlled release refers to therapeutically effective release of the drug in a patient for a time period ranging from 2 to 24 hours"

on the one hand may indicate that a level of the drug's concentration producing the "desired effect" should be maintained over a period of at least two hours duration and of 24 hours at most, at whatever point on the time scale after the administration of the drug this level may have been reached to start this "period".

4.4 On the other hand, however, reading this text, a meaning at least cannot be excluded that the "therapeutically effective release" in the sense of the further release activity after the therapeutically effective concentration of the drug in an appropriate body fluid has been reached must - at least partly - occur in the "period" beginning at a time point 2 hours after administration and ending at a time point 24 hours after administration. This meaning is in line with the appellant's submission that release activity may begin before 2 hours after administration of the drug.

4.5 This substantive ambiguity renders the claim unclear in the sense of Article 84 EPC.

4.6 Article 84 EPC refers to the claims alone.

Nevertheless, the appellant referred to figures 10 and 11, both representing the profiles of *in vivo* plasma drug concentration over time, with respect to pairs of examples of the teaching of the application in the form of coated dosage forms and control compositions. However, in all of these profiles, plasma concentration starts to rise, which indicates release activity, two hours after application, while the

further extension of this activity over time with respect to example and control composition in both figures respectively is the same, even extending beyond 24 hours in figure 11 as originally filed.

This finding is in support of the meaning as indicated under point 4.4 of this decision and set out in the communication of the board as source of the question as to whether release of the drug may start before two hours after administration (point 2.2.2 of the communication of 24 November 2011).

4.7 Accordingly, even taking into account the submissions of the appellant with regard to the figures, the teaching of claim 1 of the main request is not clear in the sense of Article 84 EPC.

5. *Claim 1 of auxiliary request 1; Article 84 EPC*

5.1 This claim relates to

dosage forms, "wherein the controlled release composition provides controlled release of the nanoparticulate drug for a time period ranging from 2 to 24 hours, the drug release being measured *in vitro* according to one of the following methods: ...".

Again, the appellant stated that the meaning was clearly that release had to occur for a minimum of 2 hours and not longer than 24 hours.

Again, however, a meaning that release occurs in a time period ranging from 2 to 24 hours after start of the measurement cannot be excluded, 2 and 24 hours now

representing points of time on the time scale describing the release measurement. It is also possible that release begins before 2 hours, because there is no definition of what part of the available amount of the nanoparticulate drug is to be released between the start of the experiment and 2 hours on the time scale and how much after this time, an issue also addressed in the communication of the board (point 2.2.2 of the communication of 24 November 2011).

5.2 Accordingly, the teaching of claim 1 of auxiliary request 1 is in breach of Article 84 EPC.

6. *Auxiliary requests 2A, 3A, 4A and 2B, 3B and 4B*

All these auxiliary requests contain the same feature relating to the time period of release as do claims 1 of the main request or auxiliary request 1 respectively, and the considerations and conclusions of points 4 and 5 of this decision therefore apply *mutatis mutandis*.

7. In view of these arguments and considerations, there was no need to decide on the appellant's request for correction of figures 10 and 11.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar:

The Chairman:

N. Maslin

U. Oswald