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Datasheet for the decision of 26 November 2009

Case Number: T 1638/06 - 3.3.02

Application Number: 00976217.0

Publication Number: 1239835

IPC: A61K 9/14

Language of the proceedings: EN

Title of invention:
Pharmaceutical compositions providing enhanced drug concentrations

Applicant:
BEND RESEARCH, INC.

Opponent:
-

Headword:
Enhanced drug concentration by polymer/BEND

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

Relevant legal provisions (EPC 1973):
-

Keyword:
"Main request - amendments - added subject-matter (yes); term used beyond own definition"
"Auxiliary request I: claims - clarity (no); undefined term"
"Auxiliary request II: claim - clarity (yes); definition of term not defined by common general knowledge to be found in description"

Decisions cited:
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Catchword:
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Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 1638/06 - 3.3.02

D E C I S I O N
of the Technical Board of Appeal 3.3.02
of 26 November 2009

Appellant: BEND RESEARCH, INC.
64550 Research Road
Bend, OR 97701-8599 (US)

Representative: Hiebl, Inge Elisabeth
Kraus & Weisert
Patent- und Rechtsanwälte
Thomas-Wimmer-Ring 15
D-80539 München (DE)

Decision under appeal: **Decision of the Examining Division of the European Patent Office posted 14 March 2006 refusing European application No. 00976217.0 pursuant to Article 97(1) EPC 1973.**

Composition of the Board:

Chairman: U. Oswald
Members: H. Kellner
J. Van Moer

Summary of Facts and Submissions

I. European patent application No. 00 976 217.0, filed as WO 01/47495 on the basis of international patent application PCT/IB00/01787, was refused for lack of clarity (Article 84 EPC) by a decision of the examining division in accordance with Article 97(1) EPC 1973.

The wording of claim 1 of the request before the examining division was:

"A pharmaceutical composition that is a simple physical mixture comprising;
(a) a drug in a pharmaceutically acceptable solubility-improved form, wherein said solubility-improved form provides at least one of
(i) increased solubility relative to the least soluble form of the drug, and
(ii) a dissolved drug concentration that is at least temporarily at least 1.25-fold the equilibrium concentration of said drug in a use environment;
and wherein when said drug is basic, said solubility-improved form provides improved dissolved drug concentration in a use environment relative to the free base and hydrochloride forms of said drug;
further wherein said solubility-improved form is
(1) a crystalline highly soluble salt form of the drug;
(2) a high-energy crystalline form of the drug;
(3) a hydrate or solvate crystalline form of a drug;
(4) an amorphous form of a drug (for a drug that may exist as either amorphous or crystalline); or
(5) a mixture of the drug (amorphous or crystalline) and a solubilizing agent; and

(b) a concentration-enhancing polymer, wherein said concentration-enhancing polymer is a cellulosic ionizable polymer that is soluble in a use environment when ionized;
characterized in that said concentration-enhancing polymer is present in an amount so that said composition provides, after introduction to a use environment, a maximum concentration of said drug in said use environment that is at least 1.25-fold an equilibrium concentration of said drug in said use environment and a concentration of said drug in said use environment that exceeds said equilibrium concentration for a longer time than the concentration of said drug in said use environment provided by a control composition exceeds said equilibrium concentration, wherein said control composition is free from said concentration-enhancing polymer and comprises an equivalent quantity of said drug in said solubility-improved form."

II. The applicant (appellant) lodged an appeal against the decision of the examining division and filed grounds of appeal together with a main request and an auxiliary request. With letter of 18 November 2009 the appellant filed a new set of claims as main request.

III. Oral proceedings took place on 26 November 2009.

During the oral proceedings, new auxiliary requests I and II were submitted in addition to the main request.

The wording of claim 1 of the main request is:

" A solid composition being a simple dry physical mixture comprising

(a) a drug in a pharmaceutically acceptable solubility-improved form selected from a crystalline highly soluble salt form of the drug, a high-energy crystalline form of the drug, a hydrate or solvate crystalline form of the drug, an amorphous form of the drug, a mixture of the drug with a solubilizing agent; and

(b) a polymer selected from hydroxypropyl methyl cellulose acetate succinate, hydroxypropyl methyl cellulose phthalate, cellulose acetate phthalate and cellulose acetate trimellitate;

wherein the drug-to-polymer weight ratio is 0.01 to 5."

In claim 1 of auxiliary request I the words "being a simple dry physical mixture" are deleted.

After removing the words "solid" and "being a simple dry physical mixture" from claim 1 of the main request, and restricting its point (a) to "a crystalline highly soluble salt form of the drug", the single claim of auxiliary request II reads:

"A composition comprising

(a) a drug in a pharmaceutically acceptable solubility-improved form being a crystalline highly soluble salt form of the drug; and

(b) a polymer selected from hydroxypropyl methyl cellulose acetate succinate, hydroxypropyl methyl cellulose phthalate, cellulose acetate phthalate and cellulose acetate trimellitate;

wherein the drug-to-polymer weight ratio is 0.01 to 5."

IV. The two auxiliary requests were admitted into the proceedings.

V. The appellant's arguments, as set out in writing and during the oral proceedings, may be summarised as follows:

Concerning claim 1 of the main request, the provisions of Article 123(2) EPC were fulfilled, since the claimed solid composition being a simple dry physical mixture was disclosed in the description as originally filed, on page 11, lines 3 and 4. In addition, a solid composition had to be dry in any case so that its being a simple dry physical mixture could be derived from the content of the application as a whole.

Original disclosure of the auxiliary requests was also to be acknowledged.

The term "solubility-improved form" concerning the drug to be comprised in the composition as claimed was clear

under Article 84 EPC, because the skilled person knew how to improve the solubility of a drug and he also knew how to measure this improvement, from his common general knowledge. This reference to common general knowledge was supported *inter alia* by passages from two textbooks submitted with letter of 18 November 2009 as Annexes III and IV.

VI. The appellant requested that the decision under appeal be set aside and that the claims filed as main request with letter of 18 November 2009 or submitted during oral proceedings as auxiliary requests I or II be acknowledged under Articles 123(2) and 84 EPC and that the case be remitted to the department of first instance for further prosecution.

Reasons for the Decision

1. The appeal is admissible.

2. *Auxiliary requests I and II, admissibility*

The sets of claims which the appellant filed during the oral proceedings were admitted into the proceedings, since their wording is a simple and clear-cut amendment introduced in direct response to the objections of the board.

3. *Main request, Article 123(2) EPC*

In the application as originally filed, the term "simple dry physical mixture" is specifically defined as a particular alternative of the subject-matter of

the application in suit (page 11, lines 2 to 8 of the application as originally filed in the form of WO 01/47495). This definition includes the further features "wherein both the solubility-improved form and concentration-enhancing polymer are mixed in particulate form and wherein the particles of each, regardless of size, retain the same individual physical properties that they exhibit in bulk."

Introducing into claim 1 the term "simple dry physical mixture" without these further features in the form of the particular definition thus introduces subject-matter extending beyond the content of the application as filed.

4. *Auxiliary requests I and II, Article 123(2) EPC*

The features of claim 1 of auxiliary request I may be derived from page 10, lines 23 to 25, page 9, lines 19 to 26, and page 45, lines 1 to 5 of the description as originally filed together with the content of the original application as a whole, particularly the examples, in so far as the polymer (b) is to be selected from the group consisting of four particular polymers.

The citations above, in so far as defined in pages and lines, are all disclosed in a generalisable way to be valid for all the subject-matter of the application in suit.

With respect to the polymers (b), all the examples exclusively refer to exactly the same four particular

polymers as second component as are claimed in the compositions according to the current requests.

The features of the single claim of auxiliary request II are originally disclosed on page 7, lines 14 to 16, page 9, lines 19 to 26, and page 45, lines 1 to 5 of the description as originally filed.

In this claim, all forms of solubility-improved drugs but one are removed from the list of possible components (a) of the composition. This removal amounts to the restriction of the subject-matter as claimed to one single embodiment out of a plurality of originally equally disclosed embodiments (*ibid*, page 9, lines 19 to 26) and as such is allowable.

5. *Auxiliary request I, Article 84 EPC*

Having regard to the written submissions on file and the outcome of the oral proceedings, there is no evidence that the person skilled in the art per se would know **which level** of solubility-improvement a drug has to fulfil to be classified "solubility-improved". This lack of evidence in particular applies to a hydrate or solvate crystalline form of the drug or to an amorphous form of the drug, and is also relevant with respect to the question as to when a crystalline soluble salt is to be called a crystalline **highly** soluble salt.

Consequently, the skilled reader of the application in suit is bound to particular definitions within this application in order to be able to clarify the subject-

matter of solubility-improved drugs or "crystalline **highly** soluble salt" forms.

The application in suit contains an effort to give an exact definition on page 31, lines 20 to 25. "Preferred highly soluble salt forms" are defined as "those salt forms that have aqueous solubility at least 1.25-fold, preferably at least 2-fold, and more preferably at least 5-fold, the aqueous solubility of the more soluble of the crystalline free base and the crystalline hydrochloride salt forms". But as the facts on file stand, this attempt to define the term "solubility-improved" relates only to particular cases not referred to in the current requests and therefore is of no general use.

With respect to a hydrate or solvate crystalline form as contained in auxiliary request I, there is no definition to be found at all, while as far as "an amorphous form of the drug" is concerned, the skilled person finds that he has to compare in at least an in vitro test medium a maximum concentration of the drug to the equilibrium concentration of the drug provided by the drug in crystalline form. However, in this case it is not clear what crystalline form is meant; it could be exactly the purely crystalline form of the same salt as the amorphous form that is tested, or the crystalline form of the lowest solubility form of the drug itself, whether salt or not or anything else.

Consequently, with the definition either missing altogether or based on a comparison to an undefined reference with respect to a hydrate or solvate crystalline form of the drug or to an amorphous form of

the drug, the feature of the solubility-improved drug form has to be regarded as unclear under Article 84 EPC in auxiliary request I.

6. *Auxiliary request II, Article 84 EPC*

In the case of "crystalline **highly** soluble salts" there is a definition in the description that tells the skilled person to compare in at least one in vitro test medium the maximum concentration of the drug to the equilibrium concentration provided by the lowest solubility form of the drug (page 30, lines 23 to 30) which may be measured as indicated in the examples given.

He can work this out in the framework of reproducibility or repeatability of measurements, even if he will find that this condition is met by nearly all forms of a drug except the only one that is the lowest solubility form. The term "lowest solubility form of the drug" is to be understood with respect to the state of the art at the priority date of the application (see in this context also page 9, lines 4 to 11 of the description as originally filed).

Thus, this feature is the basis for a very broad claim, but it is at least clear under Article 84 EPC.

7. Although the EPC does not guarantee the parties an absolute right to have all the issues in the case considered at two instances, it is recognised that any party may be given an opportunity for two readings of the important elements of a case.

In the present case, the features of the single claim of auxiliary request II as now amended are to be found valid under Articles 123(2) and 84 EPC, whereas the examining division's decision was restricted to the clarity of to the former claims. Thus, a new situation has been created with respect to the new claim, which should now be examined on its own merits.

The board has therefore decided to exercise its discretion under Article 111 EPC and to remit the case to the first instance for further prosecution on the basis of auxiliary request II.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the first instance for further prosecution on the basis of auxiliary request II submitted during the oral proceedings.

The Registrar: The Chairman:

N. Maslin U. Oswald