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Datasheet for the decision of 10 May 2012

Case Number: T 0236/08 - 3.3.02

Application Number: 95927856.5

Publication Number: 773781

IPC: A61K 9/16, A61K 9/22

Language of the proceedings: EN

Title of invention:
Solid delivery systems for controlled release of molecules incorporated therein and methods of making same

Patentee:
Quadrant Drug Delivery Limited

Opponents:
Boehringer Ingelheim Pharma GmbH & Co. KG
Nektar Therapeutics

Headword:
Solid delivery systems for administration by inhalation

Relevant legal provisions:
EPC Art. 123(2)

Relevant legal provisions (EPC 1973):
-

Keyword:
"All requests - Article 123(2) - no: selection out of multiple lists"

Decisions cited:
-

Catchword:
-

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BeschwerdekammernBoards of Appeal Chambres de recours

Case Number: T 0236/08 **-** 3.3.02

D E C I S I O N
of the Technical Board of Appeal 3.3.02
of 10 May 2012

Appellant: (Opponent 1)	Boehringer Ingelheim Pharma GmbH & Co. KG Birkendorfer Strasse 65 D-88397 Biberach an der Riss (DE)
Respondent: (Patent Proprietor)	Quadrant Drug Delivery Limited 1 Mere Way Ruddington Nottingham NG11 6JS (GB)
Representative:	Stevens, Ian Edward Potter Clarkson LLP Park View House 58 The Ropewalk Nottingham NG1 5DD (GB)
Party as of right: (Opponent 2)	Nektar Therapeutics 150 Industrial Road San Carlos California 94070-6256 (US)
Representative:	Vossius & Partner Siebertstrasse 4 D-81675 München (DE)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted 30 November 2007 concerning maintenance of European patent No. 773781 in amended form.**

Composition of the Board:

Chairman: U. Oswald
Members: D. Boulois
R. Cramer

Summary of Facts and Submissions

I. European patent No. 0 773 781 based on application No. 95927856.5, originating from international patent application PCT/GB95/01861, was granted on the basis of a set of 20 claims. Independent claim 1 read as follows:

"1. A particulate composition, for therapeutic use, suitable for administration by inhalation, wherein the particles consist of a solid solution comprising a therapeutic agent and a glass-forming carbohydrate, higher than a monosaccharide, and that is capable of stabilising the agent during spray-drying and storage, with the proviso that when the therapeutic agent is insulin, the solution does not comprise citrate."

II. An opposition was filed against the granted patent. The patent was opposed under Article 100(a) EPC for lack of novelty and inventive step, under Article 100(b) EPC for insufficiency of disclosure, and under Article 100(c) EPC for added subject-matter.

III. In the decision pronounced on 6 November 2007, the European patent was maintained in amended form on the basis of the main request filed during oral proceedings before the opposition division (Articles 102(3) and 106(3) EPC 1973).

As regards the main request, the opposition division considered the subject-matter of amended claims 1-17 to meet the requirements of Articles 123(2) EPC. In particular, the expression "suitable for administration by inhalation" could be based on page 4, line 25 - page 6, line 3 in the application as filed. The

expression "therapeutic agent" had a basis on page 10, lines 15-17 and on page 14, lines 9-13 and the combination with inhalation could be derived from page 5, line 6 - page 6, line 3. The expression "capable of stabilising the agent during spray-drying and storage" was based on the passage of page 17, line 34 - page 18, line 2.

The amended claim 1 did not infringe Article 123(3) EPC, since a composition without disclaimer could be based on claim 12 as granted.

The opposition division considered that the requirements of Article 83 EPC were met, as were the requirements of novelty under Article 54 EPC vis-à-vis the prior art. According to the opposition division, the requirements of Article 56 EPC were also met over the closest prior art.

The patentee's request for apportionment of costs was rejected, because the oral proceedings had been arranged not only at the requests of all parties, but also because the opposition division itself had needed further information on some points.

IV. Opponent 01 (appellant) filed an appeal against said decision.

V. With a letter dated 20 August 2008, the proprietor (respondent) filed a main request and auxiliary requests 1 to 7.

The main request corresponded to the main request as filed during oral proceedings before the opposition division. The new auxiliary request 1 corresponded to former auxiliary request 7 and auxiliary requests 2 to 4 corresponded to former auxiliary requests 4 to 6. Auxiliary requests 5 to 7 were new requests.

Independent claim 1 and dependent claims 2, 7 and 10 of the main request read as follows:

(a) main request:

"1. A particulate composition, for therapeutic use, suitable for administration by inhalation, wherein the particles consist of a solid solution comprising a therapeutic agent and a glass-forming carbohydrate and that is capable of stabilising the agent during spray-drying and storage wherein the particles further comprise a physiologically acceptable carboxylate, nitrate, sulfate or bisulfate glass, and wherein the carbohydrate is selected from disaccharides, trisaccharides and oligosaccharides, the corresponding sugar alcohols, polysaccharides and chemically modified carbohydrates."

"2. A composition according to claim 1, wherein the carbohydrate is a non-reducing glycoside of a polyhydroxy compound selected from sugar alcohols and other straight chain polyalcohols."

"7. A composition according to any preceding claims, wherein the therapeutic agent is a protein or peptide, nucleotide, oligonucleotide or nucleic acid."

"10. A composition according to Claim 7, wherein the therapeutic agent is insulin."

Independent claim 1 and either dependent claims 2, 10 or 11 of the respective auxiliary requests read as follows:

(b) auxiliary request 1:

"1. A particulate composition, for therapeutic use, suitable for administration by inhalation, wherein the particles consist of a solid solution comprising a therapeutic agent and a glass-forming carbohydrate, higher than a monosaccharide, and that is capable of stabilising the agent during spray-drying and storage wherein the particles further comprise a physiologically acceptable carboxylate, nitrate, sulfate or bisulfate glass, and wherein the particles are 0.1 to 10 µm in size."

"10. A composition according to Claim 7, wherein the therapeutic agent is insulin."

(*c) auxiliary request 2:*

"1. A particulate composition, for therapeutic use, suitable for administration by inhalation, wherein the particles consist of a solid solution comprising a therapeutic agent and a glass-forming carbohydrate, higher than a monosaccharide, and that is capable of stabilising the agent during spray-drying and storage wherein the particles further comprise an inhibitor of the Maillard reaction."

"11. A composition according to Claim 7, wherein the therapeutic agent is insulin."

(d) auxiliary request 3:

"1. A particulate composition, for therapeutic use, suitable for administration by inhalation, wherein the particles consist of a solid solution comprising a therapeutic agent and a glass-forming carbohydrate that is capable of stabilising the agent during spray-drying

and storage, wherein the particles comprise a molecular water pump buffer and wherein the carbohydrate is selected from disaccharides, trisaccharides and oligosaccharides, the corresponding sugar alcohols, polysaccharides and chemically modified carbohydrates."

"10. A composition according to Claim 7, wherein the therapeutic agent is insulin."

(e) auxiliary request 4:

"1. A particulate composition, for therapeutic use, suitable for administration by inhalation, wherein the particles consist of a solid solution comprising a therapeutic agent and a glass-forming carbohydrate and that is capable of stabilising the agent during spray-drying and storage wherein the particles further comprise a physiologically acceptable carboxylate, nitrate, sulfate or bisulfate glass, and wherein the carbohydrate is selected from disaccharides, trisaccharides and oligosaccharides, the corresponding sugar alcohols, polysaccharides and chemically modified carbohydrates, wherein the therapeutic agent is a nucleotide, oligonucleotide, nucleic acid, an enzyme, a growth hormone, a growth factor, a monoclonal antibody, an interferon, an interleukin or a cytokine, cyclosporin A, estrogen, progesterone, testosterone, SH-135 or tamoxifen."

"2. A composition according to claim 1, wherein the carbohydrate is a non-reducing glycoside of a polyhydroxy compound selected from sugar alcohols and other straight chain polyalcohols."

(f) auxiliary request 5:

"1. A particulate composition, for therapeutic use, suitable for administration by inhalation, wherein the particles consist of a solid solution comprising a therapeutic agent and a glass-forming carbohydrate and that is capable of stabilising the agent during spray-drying and storage wherein the particles further comprise a physiologically acceptable carboxylate, nitrate, sulfate or bisulfate glass, and wherein the carbohydrate is selected from disaccharides, trisaccharides and oligosaccharides, the corresponding sugar alcohols, polysaccharides and chemically modified carbohydrates."

"10. A composition according to Claim 7, wherein the therapeutic agent is insulin."

(g) auxiliary request 6:

"1. A particulate composition, for therapeutic use, suitable for administration by inhalation, wherein the particles consist of a solid solution comprising a therapeutic agent and a glass-forming carbohydrate and that is capable of stabilising the agent during spray-drying and storage wherein the particles further comprise a physiologically acceptable carboxylate glass, and wherein the carbohydrate is selected from disaccharides, trisaccharides and oligosaccharides, the corresponding sugar alcohols, polysaccharides and chemically modified carbohydrates."

"10. A composition according to Claim 7, wherein the therapeutic agent is insulin."

(h) auxiliary request 7:

"1. A particulate composition, for therapeutic use, suitable for administration by inhalation, wherein the particles consist of a solid solution comprising a therapeutic agent and a glass-forming carbohydrate and that is capable of stabilising the agent during spray-drying and storage wherein the particles further comprise a physiologically acceptable carboxylate glass, and wherein the carbohydrate is selected from disaccharides, trisaccharides, oligosaccharides and their corresponding sugar alcohols."

"10. A composition according to Claim 7, wherein the therapeutic agent is insulin."

VI. The board sent the parties a communication pursuant to Article 15(1) RPBA as an annex to the summons to oral proceedings, expressing the preliminary opinion that none of the requests met the requirements of Article 123(2) EPC.

In particular, the combination of the feature "**suitable for administration by inhalation**" in claim 1 of the main request with the subject-matter of dependent claims 2,7, 9 and 10 was not disclosed directly and unambiguously in the originally filed application. Moreover, the feature of claim 1 "**that is capable of stabilising the agent during spray-drying and storage**" and the subject-matter of claims 15-17 of the main request had not basis in the application as originally filed.

Since these features and claims were present in all auxiliary requests, the objections raised against the

main request applied mutatis-mutandis to all auxiliary requests.

VII. Opponent 02 announced with a letter dated 29 February 2012 that it would not be attending the hearing planned for 10 May 2012.

VIII. The respondent announced with a fax dated 23 March 2012 that it would not be attending, or represented at the oral proceedings before the board of appeal.

IX. The appellant announced with a letter dated 26 March 2012 that he would not be attending the hearing.

X. Oral proceedings took place on 10 May 2012 in the absence of the parties.

XI. The appellant's arguments during the written phase of the appeal proceedings can be summarised as follows:

As regards Article 123(2) EPC, it objected to the following features of claim 1:
- "suitable for administration by inhalation": the application as originally filed did not show any preference for this particular way of administration. Moreover, several examples had a technical teaching inconsistent with the scope of the claims.
- "a therapeutic agent": the originally filed application related to "guest substances" whose substitution by a therapeutic agent" had no basis.
- "wherein the carbohydrate is selected from disaccharides, trisaccharides and oligosaccharides, the corresponding sugar alcohols, polysaccharides and

chemically modified carbohydrates": the basis for this feature was lacking in the original application.
- **"that is capable of stabilising the agent during spray-drying":** there is no basis for this feature in the originally filed application.

Further objections and arguments were also provided with regard to lack of disclosure (Article 83 EPC), and lack of novelty (Article 54 EPC) and inventive step (Article 56 EPC).

XII. The respondent's arguments during the written phase of the appeal proceedings can be summarised as follows:

As regards Article 123(2) EPC, the respondent considered that the opposition division had correctly understood that a basis for the feature **"suitable for administration by inhalation"** could be found for example on page 5, line 6 to page 6, line 3 in the originally filed application and that the combination with "**therapeutic agent**" was disclosed on, for example, page 14, lines 9 to 13 in addition to page 5, line 6 to page 6, line 3.
As regards the term **"wherein the carbohydrate is selected from disaccharides, trisaccharides and oligosaccharides, the corresponding sugar alcohols, polysaccharides and chemically modified carbohydrates",** it had a basis in original claim 4 or on page 17, lines 25 to 28.
In response to the objections made to the feature **"that is capable of stabilising the agent during spray-drying",** the respondent referred to the decision of the opposition division.

Further objections and arguments were also provided with regard to lack of disclosure (Article 83 EPC), and lack of novelty (Article 54 EPC) and inventive step (Article 56 EPC).

XIII. Opponent 02 did not provide any comment or argument in the written phase of the appeal proceedings.

XIV. The following requests were on file:

The appellant (opponent 01) requested that the decision under appeal be set aside and that European patent No. 0 773 781 be revoked.

The respondent (patentee) requested that the appeal be dismissed and that the patent be maintained in the version as agreed by the opposition division (main request), or alternatively that the decision under appeal be set aside and that the patent be maintained according to one of the auxiliary requests 1-7 filed with the response to the grounds of appeal.

Reasons for the decision

1. The appeal is admissible.

2. *Article 123(2) EPC*

2.1 Main request

2.1.1 The feature "**suitable for administration by inhalation**" in claim 1 of the main request was not present in the claims as originally filed.

On pages 25 and 45 of the description, inhalation is described as a particular way of administration in connection with the use of a specific class of carbohydrates, namely the HDCs (hydrophobically derivatized carbohydrates). In view of the specificity of the embodiments disclosed on pages 25 and 45, these passages cannot serve as a basis for a generalisation to a particulate composition as claimed in claim 1.

The examples also cannot serve as a basis for the feature "**suitable for administration by inhalation**", as inhalation does not appear to be the sole or the preferred exemplified way of administration. Inhalation appears to be only one possible alternative among other ways of administration. Indeed, the sole examples showing compositions having inhalation as their purpose are example 2 and its corresponding Figure 1 as well as example 10. The other examples show compositions used for other purposes or having a size which renders them unsuitable for inhalation.

A basis for the feature "**suitable for administration by inhalation**" can however be found, as part of a list in several parts of the description of the application as originally filed. It appears from the following passages that inhalation is indeed one among several ways of administration disclosed in the description as originally filed:

- on pages 9 and 14 (see page 9, lines 15-17, and page 14, lines 9-13) the way of administration is presented as being either "mucosal, oral, topical, subcutaneous, intradermal, intramuscular, intravenous and by-inhalation".

- on page 42 (see lines 25-30) suitable delivery methods of guest substances of the present invention include "transdermal, transmucosal, oral, gastrointestinal, subcutaneous, ocular, intramuscular, intravenous and by-inhalation".

Consequently, the choice of the feature "**suitable for administration by inhalation**" in claim 1 of the main request has a basis in the application as originally filed and results from a choice among different possible ways of administration.
A further consequence is however that the combination of the subject-matter of claim 1 with the subject-matter of any dependent claim which also results from a selection among different possibilities would constitute an unallowable selection from multiple lists.

2.1.2 The subject-matter of dependent claim 10 restricts the composition of claim 1 to a composition "**wherein the therapeutic agent is insulin**".

Insulin was disclosed in the application as originally filed in original claim 22 and its corresponding part of the description (see page 30, line 32 to page 31, line 2) which read respectively "wherein the proteins are selected from the group consisting of enzymes, biopharmaceuticals, growth hormones, growth factors, **insulin**, monoclonal antibodies, interferons, interleukins and cytokines" and "include but are not limited to enzymes, biopharmaceuticals, growth hormones, growth factors, **insulin**, monoclonal antibodies, interferons, interleukins and cytokines".

Hence, the subject-matter of dependent claim 10 relates to a singling out from a list of possibilities concerning specifically the use of insulin. Its combination with the subject-matter of claim 1, which results similarly from a selection of possible ways of administration, constitutes a selection from multiple lists and has no basis in the application as originally filed.

2.1.3 The subject-matter of dependent claim 2 results also from a selection of possibilities, as regards the nature of the carbohydrate.
The feature "**non-reducing glycosides of polyhydroxy compounds selected from sugar alcohols, other straight chain polyalcohols"** constitutes a singling out from a list of carbohydrates on page 18 (see lines 12-16) and original claim 6.
The combination of the subject-matter of dependent claim 2 with the subject-matter of claim 1 of the main request results from a selection from multiple lists and is not disclosed directly and unambiguously in the originally filed application.

2.1.4 The respondent had not provided any argument to counter the objections raised by the board under Article 123(2) EPC in its preliminary opinion. However in the written proceedings, arguments regarding the existence of a support for the feature "**suitable for administration by inhalation**" on page 5, line 6 to page 6, line were given by the respondent.

The board does not contest that the feature "**suitable for administration by inhalation**" has a basis in the application as originally filed, although the passage

cited by the respondent relates to the background of the invention and not to the invention itself, and does not form a valid basis for this amendment. Inhalation is indeed disclosed on page 6 (see line 27) under "Background of the Invention" and presented in various forms, such as topical, transdermal, subdermal, ballistic forms and implantable therapeutic systems.
Further passages mentioning this way of administration and forming a valid basis for an amendment were cited under point 2.1.1 above.

The board does not contest that the subject-matter of claim 1 alone meets the requirements of Article 123(2) EPC, since the feature "**suitable for administration by inhalation**" is a single selection among multiple possibilities.
However, a combination of the subject-matter of claim 1 with the subject-matter of a dependent claim which also results from a selection among different possibilities infringes Article 123(2) EPC.

2.1.5 Consequently, the combination of the subject-matter of claim 1 of the main request with at least the subject-matter of dependent claims 2 or 10 constitutes a selection from multiple lists and has no basis in the application as originally filed. Therefore, the main request infringes Article 123(2) EPC.

2.2 Auxiliary request 1

The feature "**suitable for administration by inhalation**" is present in claim 1 of auxiliary request 1 as well as

the feature "**wherein the therapeutic agent is insulin**" in dependent claim 10.
As in the case of the main request, the combination of the subject-matter of claim 1 of auxiliary request 1 with the subject-matter of dependent claim 10 results from a selection from multiple lists and has no basis in the application as originally filed.
Hence, auxiliary request 1 does not meet the requirements of Article 123(2) EPC.

2.3 Auxiliary request 2

The feature "**suitable for administration by inhalation**" is present in claim 1 of auxiliary request 2 and the feature "**wherein the therapeutic agent is insulin**" is present in dependent claim 11.
The objections raised against the main request and auxiliary request 1 apply also to auxiliary request 2.
Auxiliary request 2 does not meet the requirements of Article 123(2) EPC, since the combination of the subject-matter of claim 1 with the subject-matter of dependent claim 11 results from a selection from multiple lists and has no basis in the application as originally filed.

2.4 Auxiliary request 3

The feature "**suitable for administration by inhalation**" is present in claim 1 of auxiliary request 3 and the feature "**wherein the therapeutic agent is insulin**" is present in dependent claim 10.
The objections raised above against the main request apply *mutatis mutandis* to auxiliary request 3, which

for that reason does not meet the requirements of Article 123(2) EPC.

2.5 Auxiliary request 4

The feature "**suitable for administration by inhalation**" is present in claim 1 of auxiliary request 4 and the feature "**non-reducing glycosides of polyhydroxy compounds selected from sugar alcohols, other straight chain polyalcohols"** is present in dependent claim 2. Both features represent a selection from distinct lists, which results in a combination that is not disclosed directly and unambiguously in the application as originally filed.
Hence, auxiliary request 4 infringes Article 123(2) EPC.

2.6 Auxiliary request 5

The combination of the subject-matter of claim 1 of auxiliary request 5, which comprises the feature "**suitable for administration by inhalation**", with the subject-matter of dependent claim 10, which relates to compositions "**wherein the therapeutic agent is insulin**", constitutes, like the main request, a selection from multiple lists which is not disclosed directly and unambiguously in the originally filed application.
Accordingly, auxiliary request 5 fails to meet the requirements of Article 123(2) EPC.

2.7 Auxiliary request 6

Since the features "**suitable for administration by inhalation**" and "**wherein the therapeutic agent is insulin**" are present in claims 1 and 10 for this reason.
of auxiliary request 6, the objections raised for the main request apply *mutatis mutandis* to auxiliary request 6, which therefore also fails to meet the requirements of Article 123(2) EPC.

2.8 Auxiliary request 7

As in the case of auxiliary request 6, the features "**suitable for administration by inhalation**" and "**wherein the therapeutic agent is insulin**" are present in claims 1 and 10 respectively of auxiliary request 7, which therefore also fails to meet the requirements of Article 123(2) EPC.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The European patent No. 0 773 781 is revoked.

The Registrar: The Chairman:

N. Maslin U. Oswald