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**Datasheet for the decision
of 5 March 2010**

Case Number: T 1609/07 - 3.3.02

Application Number: 02001663.0

Publication Number: 1205180

IPC: A61K 9/48

Language of the proceedings: EN

Title of invention:

Delivery system for hydrophobic drugs

Applicant:

R.P. Scherer Technologies, Inc.

Opponent:

-

Headword:

Delivery System for Hydrophobic Drugs/R.P. SCHERER
TECHNOLOGIES, INC.

Relevant legal provisions:

EPC Art. 54, 83, 84, 111

Relevant legal provisions (EPC 1973):

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Keyword:

"Main request, auxiliary request 1 - novelty (no)"

"Auxiliary requests 2-5 - sufficiency (no): the tests in the original application, which allow to determine whether a given hydrophobic surfactant meets the functional definition as claimed, are only applicable to a preferred class of hydrophobic surfactants, but not to hydrophobic surfactants in their entirety"

"Auxiliary request 6 - clarity (no): percentages do not add up to 100%"

"Auxiliary request 7 - remittal (yes): undecided issues"

Decisions cited:

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Catchword:

-



Case Number: T 1609/07 - 3.3.02

D E C I S I O N
of the Technical Board of Appeal 3.3.02
of 5 March 2010

Appellant: R.P. Scherer Technologies, Inc.
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Decision under appeal: Decision of the Examining Division of the
European Patent Office posted 24 April 2007
refusing European patent application
No. 02001663.0 pursuant to Article 97(1) EPC
1973.

Composition of the Board:

Chairman: U. Oswald
Members: A. Lindner
J.-P. Seitz

Summary of Facts and Submissions

- I. European patent application No. 02 001 663.0 was refused by a decision of the examining division posted on 24 April 2007 on the basis of Article 97(1) EPC 1973 on the grounds that the subject-matter of claim 1 of the main request and of auxiliary requests 1 and 2 lacked novelty.
- II. The decision was based on claims 1-10 of the main request filed with letter of 15 September 2005, on claims 1-10 of auxiliary request 1 and on claims 1-9 of auxiliary request 2, both filed with letter of 4 October 2006.

Independent claim 1 of the main request before the examining division reads as follows:

"1. The use of a hydrophilic surfactant component in an oral pharmaceutical composition comprising a carrier system for a hydrophobic drug, said carrier system comprising a digestible oil which undergoes lipolysis in vivo and a pharmaceutically acceptable surfactant of which the hydrophilic surfactant component is a part for dispersing the oil in vivo, characterised in that the hydrophilic surfactant component is one which does not substantially inhibit the lipolysis of the digestible oil."

- III. The documents cited during the examination and appeal proceedings included the following:

(1) EP-A-0 370 481

IV. The arguments in the first-instance decision may be summarised as follows:

The present application dealt with the problem of bioavailability of hydrophobic drugs from carrier systems. The purpose of using a hydrophilic surfactant component in the carrier system was to enhance bioavailability of the drug. The characterising feature of claim 1 of the main request was seen as a mere explanation for the technical effect, which was the improved bioavailability of the drug. Document (1) also related to the improvement of bioavailability of drugs and taught that resorption-enhancing surfactant components like Labrasol improved bioavailability. The use of the hydrophilic surfactant component in a carrier system comprising a digestible oil (Witepsol H 15) was described in document (1) and thus considered to be known. Although the reaction mechanism of the hydrophilic surfactant component Labrasol in the oral dosage form was not disclosed in document (1), it was the inevitable result of the enhanced bioavailability. The previously described use of the surfactant inherently had the same technical effect as the claimed use. The mere naming or interpretation of a chemical reaction of the surfactant in the claim could not establish novelty, since the function, i.e. the technical effect, had already been made available to the public. As a consequence, the subject-matter of each claim 1 of the main request and of auxiliary requests 1 and 2 lacked novelty. Moreover, the examining division expressed doubts that the selection of further hydrophilic surfactants could be effected without undue burden.

V. The appellant (applicant) lodged an appeal against this decision.

VI. With the statement of the grounds of appeal dated 3 September 2007, the appellant filed auxiliary requests 1 to 5.

The sole independent claims 1 read as follows:

(a): Auxiliary request 1:

"1. The use of a hydrophilic surfactant component in an oral pharmaceutical composition comprising a carrier system for a hydrophobic drug, said carrier system comprising a digestible oil which undergoes lipolysis in vivo and a pharmaceutically acceptable surfactant of which the hydrophilic surfactant component is a part for dispersing the oil in vivo, characterised in that the hydrophilic surfactant component does not substantially inhibit the lipolysis of the digestible oil and is a transesterification product of polyethylene glycol with glycerol esters of capric and/or caprylic acids."

(b): Auxiliary request 2:

"1. The use of a hydrophilic surfactant component in an oral pharmaceutical composition comprising a carrier system for a hydrophobic drug, said carrier system comprising a digestible oil which undergoes lipolysis in vivo and a pharmaceutically acceptable surfactant comprising a lipophilic surfactant component and a hydrophilic surfactant component for dispersing the oil in vivo, characterised in that the hydrophilic surfactant component is one which does not

substantially inhibit the lipolysis of the digestible oil, the digestible oil comprising 20 to 60wt%, the hydrophilic surfactant comprising 25 to 50wt% and the lipophilic component comprising 20 to 45wt% of the carrier system."

(c): Auxiliary request 3:

"1. The use of a hydrophilic surfactant component in an oral pharmaceutical composition comprising a carrier system for a hydrophobic drug, said carrier system comprising a digestible oil which undergoes lipolysis in vivo and a pharmaceutically acceptable surfactant of which the hydrophilic surfactant component is a part for dispersing the oil in vivo, characterised in that the hydrophilic surfactant component is one which does not substantially inhibit the lipolysis of the digestible oil and in that (a) the digestible oil is selected from a vegetable oil, an animal oil or a triglyceride oil containing C₆ to C₁₂ fatty acids or (b) the carrier system includes a lipophilic surfactant which is a digestible oil, no further digestible oil being included in the carrier system."

(d): Auxiliary request 4:

"1. The use of a hydrophilic surfactant component in an oral pharmaceutical composition comprising a carrier system for a hydrophobic drug and the hydrophobic drug, said carrier system comprising a digestible oil which undergoes lipolysis in vivo and a pharmaceutically acceptable surfactant of which the hydrophilic surfactant component is a part for dispersing the oil in vivo, characterised in that the hydrophilic

surfactant component is one which does not substantially inhibit the lipolysis of the digestible oil and in that the hydrophobic drug has a logP >2."

(e): Auxiliary request 5:

"1. The use of a pharmaceutically acceptable hydrophilic surfactant in an oral pharmaceutical composition comprising a carrier system for a hydrophobic drug, said carrier system comprising a digestible oil which undergoes lipolysis in vivo and a hydrophilic surfactant for dispersing the oil in vivo, characterised in that the hydrophilic surfactant is one which does not substantially inhibit the lipolysis of the digestible oil and in that the pharmaceutical composition contains no lipophilic surfactant."

VII. In the communication annexed to the summons to oral proceedings of 16 December 2009, the board expressed its preliminary opinion with regard to the requests on file. Thus, the board concluded that the subject-matter of each claim 1 of the main request and of auxiliary request 1 appeared to lack novelty over document (1). As regards auxiliary requests 2 to 5, it appeared that the selection of the hydrophilic surfactant would be an undue burden for the skilled person.

VIII. In his reply of 17 February 2010, the appellant withdrew his request for oral proceedings and filed auxiliary requests 6 to 9, which sole independent claims 1 respectively read as follows:

(f): Auxiliary request 6:

"1. The use of a hydrophilic surfactant component in an oral pharmaceutical composition comprising a carrier system for a hydrophobic drug, said carrier system comprising a digestible oil which undergoes lipolysis in vivo and a pharmaceutically acceptable surfactant comprising a lipophilic surfactant component and a hydrophilic surfactant component for dispersing the oil in vivo, characterised in that the hydrophilic surfactant component is one which does not substantially inhibit the lipolysis of the digestible oil and is a trans-esterification product of polyethylene glycol with glycerol esters of capric and/or caprylic acids, the digestible oil comprising 20 to 60wt%, the hydrophilic surfactant comprising 25 to 50wt% and the lipophilic component comprising 20 to 45wt% of the carrier system."

(g): Auxiliary request 7:

"1 The use of a hydrophilic surfactant component in an oral pharmaceutical composition comprising a carrier system for a hydrophobic drug, said carrier system comprising a digestible oil which undergoes lipolysis in vivo and a pharmaceutically acceptable surfactant of which the hydrophilic surfactant component is a part for dispersing the oil in vivo, characterised in that the hydrophilic surfactant component is one which does not substantially inhibit the lipolysis of the digestible oil and is a trans-esterification product of polyethylene glycol with glycerol esters of capric and/or caprylic acids and in that (a) the digestible

oil is selected from a vegetable oil, an animal oil or a triglyceride oil containing C6 to C12 fatty acids or (b) the carrier system includes a lipophilic surfactant which is a digestible oil, no further digestible oil being included in the carrier system."

(h): Auxiliary request 8:

"1. The use of a hydrophilic surfactant component in an oral pharmaceutical composition comprising a carrier system for a hydrophobic drug and the hydrophobic drug, said carrier system comprising a digestible oil which undergoes lipolysis in vivo and a pharmaceutically acceptable surfactant of which the hydrophilic surfactant component is a part for dispersing the oil in vivo, characterised in that the hydrophilic surfactant component is one which does not substantially inhibit the lipolysis of the digestible oil and is a trans-esterification product of polyethylene glycol with glycerol esters of capric and/or caprylic acids and in that the hydrophobic drug has a $\log P > 2$."

(i): Auxiliary request 9:

"1. The use of a pharmaceutically acceptable hydrophilic surfactant in an oral pharmaceutical composition comprising a carrier system for a hydrophobic drug, said carrier system comprising a digestible oil which undergoes lipolysis in vivo and a hydrophilic surfactant for dispersing the oil in vivo, characterised in that the hydrophilic surfactant is one which does not substantially inhibit the lipolysis of the digestible oil and is a trans-esterification

product of polyethylene glycol with glycerol esters of capric and/or caprylic acids and in that the pharmaceutical composition contains no lipophilic surfactant."

IX. Oral proceedings were held on 5 March 2010 in the absence of the duly summoned appellant in accordance with Rule 115 EPC and Article 15(3) RPBA.

X. The appellant's submissions can essentially be summarised as follows:

As regards the main request, there was no disclosure in the prior art of selecting a hydrophilic surfactant that did not inhibit the lipolysis of a digestible oil. Document (1) did not constitute an enabling novelty-destroying disclosure as Whitesol was used as a simple carrier and as lipolysis was not mentioned. In fact, there was no teaching of any effect of the Labrasol on Whitesol. In connection with the alleged undue burden necessary for selecting further hydrophilic surfactants, it was held that a test was provided for the skilled person to establish whether or not a potential surfactant met the requirements of not inhibiting the lipolysis of the digestible oil.

XI. The appellant requested that the decision under appeal be set aside and that the novelty of claim 1 of either his main request filed on 15 September 2005 or one of auxiliary requests 1 to 5 filed on 3 September 2007 and 6 to 9 filed on 17 February 2010 be acknowledged, and that the case be then remitted to the examining division for further prosecution.

Reasons for the decision

1. The appeal is admissible.
2. Admissibility of auxiliary requests 6 to 9:

These requests were filed with letter of 17 February 2010 and therefore within the time limit set by the board in the official communication annexed to the summons to oral proceedings. Moreover, these requests were a reaction by the appellant to objections raised by the board in its communication. As a consequence, the board decided to admit auxiliary requests 6 to 9 into the proceedings (Article 13 RPBA).

3. Main request - novelty:
 - 3.1. Claim 1 of the main request is directed to the use of a hydrophilic surfactant in an oral composition. There are no additional elements in claim 1 which would further specify that use. All the features listed after the passage "in an oral pharmaceutical composition" serve to define the pharmaceutical composition in which the hydrophilic surfactant is used. Thus, the characterising part of claim 1 (the hydrophilic surfactant component is one which does not substantially inhibit lipolysis of the digestible oil) functionally defines the hydrophilic surfactant of the oral pharmaceutical composition, i.e. it excludes all those hydrophilic surfactant components which substantially inhibit the lipolysis of the digestible oil. It is, however, not related to the purpose or to the end for which the hydrophilic surfactant is added

to the composition. For the evaluation of novelty, the formulation "use of a hydrophilic surfactant in an oral pharmaceutical composition" only indicates that the surfactant is present in the composition, which is a mandatory property of each constituent of said composition. As a consequence, every known composition comprising all the features of the oral pharmaceutical composition according to claim 1 would destroy the novelty of the use as defined in said claim 1.

- 3.2. The table on page 11 of document (1) discloses the following oral composition:

Ceftriaxone sodium	300 mg
Labrasol	225 mg
Laureth-12	75 mg
Witepsol H15	380 mg

Labrasol is a transesterification product of polyoxyethylene glycol with glycerol esters of capric and caprylic esters which does not substantially inhibit the in vivo lipolysis of digestible oils (see page 16, lines 11-16 and page 17, lines 4-5 of the originally filed application). Accordingly, Labrasol is a specific embodiment of a hydrophilic surfactant as defined in claim 1 of the main request. Laureth-12 is a lipophilic surfactant and Witepsol H15 comprises hydrogenated coco-glycerides and therefore is a digestible oil which undergoes lipolysis in vivo. As a consequence, the above composition comprises all the features of the oral pharmaceutical composition according to present claim 1. In view of fact that the Labrasol is used in said composition (see point 3.1 above), the subject-matter of claim 1 of the main

request is not novel over document (1). The requirements of Article 54 EPC are therefore not met.

4. Auxiliary request 1 - novelty:

Claim 1 of auxiliary request 1 differs from claim 1 of the main request in that the hydrophilic surfactant component is limited to transesterification products of polyethylene glycol with glycerol esters of capric and/or caprylic acids. In view of the fact that the Labrasol used in document (1) is also a transesterification product of polyethylene glycol with glycerol esters of capric and/or caprylic acids, this limitation cannot impart novelty to claim 1 of auxiliary request 1. As a consequence, the requirements of Article 54 EPC are not met for the same reasons as outlined in points 3.1 and 3.2 above.

5. Auxiliary request 2 - sufficiency:

5.1. In its decision, the examining division argued that the selection of further suitable hydrophilic surfactants might cause an undue burden. In view of the fact that the claims lacked novelty, the examining division did finally not decide on this issue. The objection in connection with the possible undue burden was raised under Article 84 EPC. The board is of the opinion that this point is a question of sufficiency, which is a requirement of Article 83 EPC.

5.2. In claim 1 of auxiliary request 2, the hydrophilic surfactant is defined by its function (it must not substantially inhibit the lipolysis of the digestible oil). In order to determine whether a given hydrophilic

surfactant does or does not fall within this functional definition, the skilled person must be able to rely on information found in the original application, normally in the form of tests, which allows him to verify this, unless such information belongs to his general knowledge, for which, however, there is no indication at all in the present case. The original application (see pages 30 to 35) does indeed comprise an in-vitro test for determining the suitability of hydrophilic and lipophilic surfactants. However, regarding hydrophilic surfactants, the suitability of this test is limited to a certain class of surfactants, i.e. the transesterification products of polyoxyethylene glycol with glycerol esters of capric and caprylic acids. Reference is made to page 16, lines 11-16 of the original application, where it is stated that this class of hydrophilic surfactants does not substantially inhibit the in vivo lipolysis of digestible oils. On page 17, lines 4-6, Labrasol and Softigen 767 are listed as preferred hydrophilic surfactants. Then, in lines 10-12 of the same page, it is stated that the "suitability for this invention of other hydrophilic surfactants **of this class** can readily be determined by the in vitro test described hereafter" [emphasis by the board]. In view of the fact that the "surfactants of this class" refer to the transesterification products of polyoxyethylene glycol with glycerol esters of capric and caprylic acids mentioned above, the said in vitro test is only applicable to such surfactants. As regards hydrophilic surfactants which do not belong to the class of transesterification products of polyoxyethylene glycol with glycerol esters of capric and caprylic acids, the skilled person has no means of verifying whether they do not substantially inhibit the

lipolysis of the digestible oil and thus fall within the definition of present claim 1. As a consequence, the subject-matter of claim 1 of auxiliary request 2 is not sufficiently disclosed as required by Article 83 EPC.

6. Auxiliary request 3 to 5 - sufficiency:

In view of the fact that the hydrophilic surfactants defined in each claim 1 of auxiliary requests 3 to 5 are likewise not limited to the transesterification products of polyoxyethylene glycol with glycerol esters of capric and caprylic acids, the reasoning of point 5.2 above applies *mutatis mutandis* to these claims. As a consequence, the requirements of Article 83 EPC are not met.

7. Auxiliary request 6 - clarity:

In claim 1 the carrier system for the hydrophobic drug comprises 20-60 wt% of a digestible oil, 25-50 wt% of the hydrophilic surfactant and 20-45 wt% of the lipophilic component. Clarity, as regards claims comprising a mixture, demands that the proportions given for each constituent must add up to 100 %. This is not the case for 60 wt% of the digestible oil, which, when combined with the minimum amounts of the hydrophilic surfactant and the lipophilic component (25 wt% and 20 wt%, respectively), adds up to 105 wt%. As a consequence, the subject-matter of claim 1 of auxiliary request 6 is not clear (Article 84 EPC).

8. Auxiliary request 7:

8.1. Sufficiency:

As the hydrophilic surfactant of claim 1 is now limited to the transesterification products of polyoxyethylene glycol with glycerol esters of capric and caprylic acids, the test described on pages 30-35 of the original application is now applicable to all the hydrophilic surfactants claimed. As a consequence, the requirements of Article 83 EPC are met.

8.2. Remittal to the first instance:

Although Article 111(1) EPC does not guarantee an absolute right to have all the issues in the case considered by two instances, it is well recognised that any party should where appropriate be given the opportunity to have two readings of the important elements of the case. Hence, a case is normally referred back if essential questions regarding the patentability of the claimed subject-matter have not yet been examined and decided by the department of first instance.

In view of the fact that the examining division only decided on novelty and in view of the appellant's requests (see point XI above), the board has reached the conclusion that, in the circumstances of the present case, the case should be remitted to the examining division for further prosecution on the basis of auxiliary requests 7 to 9 filed on 17 February 2010.

Order

For these reasons it is decided that:

The case is remitted to the examining division for further prosecution on the basis of auxiliary requests 7 to 9 filed on 17 February 2010.

The Registrar:

The Chairman

N. Maslin

U. Oswald