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**Datasheet for the decision
of 14 May 2008**

Case Number: T 0049/06 - 3.3.01

Application Number: 95928064.5

Publication Number: 0815113

IPC: C07D 491/22

Language of the proceedings: EN

Title of invention:

Water-soluble esters of camptothecin compounds

Applicant:

RESEARCH TRIANGLE INSTITUTE

Opponent:

-

Headword:

Esters of camptothecin/RESEARCH TRIANGLE INSTITUTE

Relevant legal provisions:

EPC Art. 84, 53(c)

Keyword:

"Clarity (no)"

"Treatment of human or animal bodies (not allowed)"

Decisions cited:

G 0005/83, G 0004/92

Catchword:

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Case Number: T 0049/06 - 3.3.01

D E C I S I O N
of the Technical Board of Appeal 3.3.01
of 14 May 2008

Appellant: RESEARCH TRIANGLE INSTITUTE
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Representative: Audier, Philippe André
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Decision under appeal: Decision of the Examining Division of the
European Patent Office posted 25 July 2005
refusing European application No. 95928064.5
pursuant to Article 97(1) EPC.

Composition of the Board:

Chairman: P. Ranguis
Members: J.-B. Ousset
C.-P. Brandt

Summary of Facts and Submissions

I. This appeal lies from the decision of the examining division to refuse the European patent application n° 95 928 064.5 published as WO-A-96/02546 (EP-A-0 815 113). The refusal was based on lack of novelty and lack of inventive step.

II. The examining division found that the subject-matters of claims 1-4 and 16 of the then pending set of claims were rendered not novel in view of the disclosures of documents (1) to (3).

(1) US-A-4 943 579

(2) J. Med. Chem. "Synthesis and structure activity of novel Camptothecin analogs", 1993, 36, 2689-2700.

(3) WO-A-95/10304

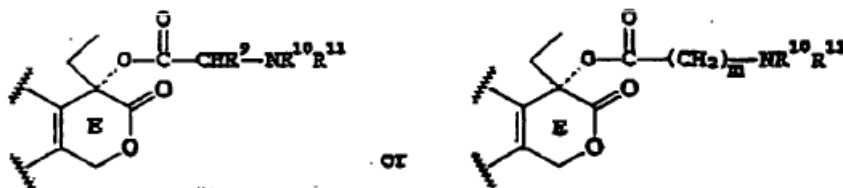
An inventive step was also denied on the basis of the teaching of document (2).

III. With the statement setting out the grounds of appeals, the appellant requested that a patent be granted on the basis of the set of eighteen claims refused by the examining division. This set of claims was submitted with a fax received on 16 January 2004. As an auxiliary request, oral proceedings were requested.

The independent claims 1,16,17 and 18 of this set of claims read as follows:

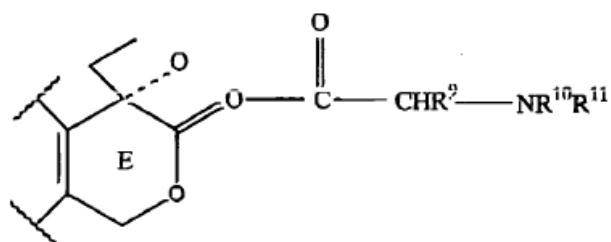
"1. A method for reducing the toxicity of a camptothecin compound, comprising esterifying the hydroxyl group at the 20-position of the E-ring of a

camptothecin compound to form a camptothecin compound in which the E-ring has the formula:

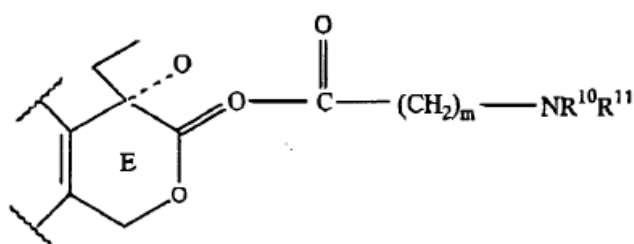


wherein $m = 1-6$, R^9 is the side chain of one of the naturally occurring alpha-amino acids, R^{10} and R^{11} are, independently, hydrogen or C_{1-8} alkyl, with the proviso that the camptothecin compound is not camptothecin or camptothecin substituted on the A-ring thereof with an alkyl group or with a substituted alkyl group as found in natural amino acids.

"16.A method for extending the in vivo systemic lifetime of a camptothecin compound in a mammal, comprising esterifying the hydroxyl group at the 20-position of the E-ring of a camptothecin compound to form a camptothecin ester compound in which the E-ring has the formula:



or



wherein $m = 1-6$, R^9 is the side chain of one of the naturally occurring alpha-amino acids, R^{10} and R^{11} are, independently, hydrogen or C_{1-8} alkyl, with the proviso that the camptothecin compound is not camptothecin or camptothecin substituted at the A-ring thereof with an alkyl or a substituted alkyl group as found in natural amino acids."

"17. A method for reducing the toxicity of a camptothecin compound, comprising esterifying the hydroxyl group at the 20-position of the E-ring of a camptothecin compound to form a camptothecin ester compound having the structure (I) or (II), wherein $n=2$, as shown in claim 5, and pharmaceutically acceptable salts thereof, and wherein said camptothecin compound has the structure (III), wherein $n=2$ as shown in claim 2, and pharmaceutically acceptable salts thereof."

"18. A method for extending the in vivo systemic lifetime of a camptothecin compound in a mammal, comprising esterifying the hydroxyl group at the 20-position of the E-ring of a camptothecin compound to form a camptothecin ester compound having the structure (I) or (II), wherein $n=2$, as shown in claim 5, and pharmaceutically acceptable salts thereof, and wherein said camptothecin compound has the structure (III), wherein $n=2$, as shown in claim 2, and pharmaceutically acceptable salts thereof."

- IV. The board annexed to the summons to oral proceedings a communication.

The board was of the preliminary opinion that claims 1 and 16-18 were contravening the requirements of Article 53 c) EPC, because the wording of these claims also embraced treatments of human and animal bodies. Moreover, the board objected to the lack of clarity of claims 1 and 17 due to the presence of the expression "..reducing the toxicity..", since the wording of the claims did not mention the reference to which said reduction was to be assessed. Furthermore, the presence of the expression "..extending the in vivo systemic lifetime.." in claims 16 and 18 rendered them also unclear due to the absence of reference to which said extension was to be assessed.

- V. The appellant requested in its letter of 11 April 2008 the postponement of oral proceedings, given that in the annex of the summons to oral proceedings, the board introduced objections, which were not raised during the procedure before the first instance. A two and a half-month period to answer these objections and to draft an

amended set of claims were considered by the appellant as "serious and substantive reasons" according the notice of the Vice-Presidents dated of 1 September 2000 (OJ EPO 2000, 456) to allow such a request.

- VI. With a fax of 14 April 2008, the board informed the appellant that its request of postponement of oral proceedings was rejected. The board pointed out that according to Article 15(1) of the RPBA, a communication was sent as an annex to the summons to oral proceedings and that the invitation to oral proceedings was made according to the requirements of Rule 132(2) EPC. It was further added that the board did not see any reasons to postpone oral proceedings according to Article 15(2) of the RPBA (see OJ EPO 2007, 536). The board also added that the requirements of Article 113(1) EPC were not infringed in view of the matters to be discussed as recited in the communication annexed to the summons to oral proceedings. It was then concluded that the oral proceedings scheduled on 14 May 2008 were maintained.
- VII. Oral proceedings took place on 14 May 2008. The board was informed by a fax of 7 May 2008 that the appellant would not attend these oral proceedings. They were thus held in the absence of the duly summoned appellant in accordance with Rule 115(2) EPC.
- VIII. The appellant requested with its written statement setting out the grounds of appeal that the decision under appeal be set aside and a patent be granted on the basis of the set of eighteen claims submitted with fax received on 16 January 2004.

IX. At the end of these proceedings, the decision of the board was announced.

Reasons for the Decision

1. The appeal is admissible.

2. *Procedural matters*

The appellant has been informed in due time by the communication of the board of the objections based on Articles 53 c) and 84 EPC. Since the appellant had an opportunity to present his arguments in respect thereof, the requirements of Article 113(1) EPC are fulfilled. Although the appellant did not appear to oral proceedings, the board is therefore empowered to decide on these matters (see G 4/92, OJ EPO 1994, 149, Order 1; rule 115(2) EPC and Article 15(3) of the RPBA).

3. *Amendments*

Since the present application has to be refused for other reasons, the board considers that it is not necessary to examine whether the amendments fulfil the requirements of Article 123(2) EPC.

4. *Therapeutic treatment of human and/or animal bodies*

4.1 The wordings of claims 1 and 16-18 embrace the treatment of human and animal bodies. This is in contradiction with the requirements of Article 53 c) EPC (previous Article 52(4) EPC 1973). Although present

claims 1, 16 to 18 refer either to a "method for reducing the toxicity" or a "method to extending the in vivo lifetime", the difference with the usual wording "method of treatment" is only of form and does not change the subject-matter embraced by them. These claims are therefore in conflict with the requirements of Article 53 c) EPC (previous Article 52(4) EPC 1973) (see G 5/83, OJ EPO 1985, 64, point 13 mentioning Article 52(4) of the EPC 1973, which corresponds in the EPC 2000, applicable since 13 December 2007, to Article 53 c) EPC).

4.2 Since the appellant did not take the opportunity to comment on this point, the board does not see any reasons to depart from its previous preliminary opinion expressed in its communication annexed to the summons to oral proceedings.

4.3 Claims 1 and 16 to 18 contravene therefore the requirements of Article 53 c) EPC.

5. *Lack of clarity*

5.1 In the communication annexed to the summons to oral proceedings, the board made it clear that the presence of the expression "..reducing the toxicity.." in claims 1 and 17 and the presence of the expression "..extending the in vivo lifetime.." in claims 16 and 18 rendered these claims unclear, because the corresponding reference to which the reduction mentioned in claims 1 and 17 and the extension mentioned in claim 16 and 18 were to be assessed were missing in the wording of these claims.

5.2 Since the appellant did not take the opportunity to comment on this point, the board does not see any reasons to depart from its previous preliminary opinion expressed in its communication annexed to the summons to oral proceedings.

5.3 Claims 1 and 16 to 18 contravene therefore the requirements of Article 84 EPC.

6. For the reasons set out above, the main request is to be rejected.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar

The Chairman

M. Schalow

P. Ranguis