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# Datasheet for the decision of 27 March 2014

**Case Number:** T 0580/10 - 3.3.07

**Application Number:** 02017756.4

**Publication Number:** 1374907

**IPC:** A61K47/48

**Language of the proceedings:** EN

**Title of invention:**
Drug transport and delivery system

**Applicant:**
Ghanem, Ghanem Elias,
c/o Institut Jules Bordet
Mehlem, Francesco

**Headword:**
Drug transport and delivery system/Ghanem, Ghanem Elias, Mehlem Francisco

**Relevant legal provisions:**
EPC Art. 54

**Keyword:**
Novelty - main request (no) - auxiliary request (no)

**Decisions cited:**

**Catchword:**

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**Case Number: T 0580/10 - 3.3.07**

# D E C I S I O N
## of Technical Board of Appeal 3.3.07
## of 27 March 2014

**Appellant:** (Applicant 1)
Ghanem, Ghanem Elias,
c/o Institut Jules Bordet
rue Héger-Bordet 1
1000 Bruxelles (BE)

**Appellant:** (Applicant 2)
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3048 Worblaufen (CH)

**Decision under appeal:** **Decision of the Examining Division of the European Patent Office posted on 28 October 2009 refusing European patent application No. 02017756.4 pursuant to Article 97(2) EPC.**

**Composition of the Board:**

**Chairman:** J. Riolo
**Members:** D. Boulois
D. T. Keeling

## Summary of Facts and Submissions

I. European patent application No. 02 017 756.4 was refused by a decision of the examining division posted on 28 October 2009 on the grounds of non-compliance with Articles 54, 56 and 84 EPC.

II. The decision was based on the main request and auxiliary request 1 filed with letter dated 2 September 2009.

Independent claim 1 of the main request read:

"1. A tripeptide or a tetrapeptide or an methyl or ethyl ester thereof comprising a proteolytic enzyme cleavable amino acid moiety that is connected to a drug suitable for the treatment of arthritis, invasive parasitic diseases, Paludism (malaria), AIDS, and tumours, said tripeptide or tetrapeptide being selected from the group consisting of Phe-Phe-Pro, Pro-Phe-Phe, Phe-Phe-Ser, Ser-Phe-Phe, Phe-Phe-Asn, Asn-Phe-Phe, Phe-Gly-Phe-Val (Seq. Id. No. 1), Val-Phe-Gly-Phe (Seq. Id. No. 2), Phe-Arg-Phe-His (Seq. Id. No. 3), His-Phe-Arg-Phe (Seq. Id. No. 4), Phe-Arg-Val, Val-Arg-Phe, or these peptides wherein the terminal Phe is para-fluoro subsituted, and said proteolytic enzyme cleavable amino acid moiety that is connected to a drug is not a terminal moiety."

Independent claim 1 of the auxiliary request was identical to claim 1 of the main request.

III. The documents cited during the examination proceedings included the following:
(1) WO 00/31119
(3) GB-A-1 329 869

(5) WO 99/02177,

(6) De Barbieri et al: "Effects of an antitumor multipeptide complex on immunocompetent and antigen-responsive cells", Bollettino dell'Istituto Sieroterapico Milanese, vol. 55, no. 3, 1976, pages 201-215".

(7) De Barbieri: "Research on antitumor alkylating peptides", Cancer Cytology, Vol. 17, no. 2, 1977.

IV. In the decision under appeal the examining division held that the main request did not meet the requirements of Article 54 EPC over documents (1), (3) (5) and (6).

Document (1) disclosed the preferred compound of the application, namely L-prolyl-L-m-sarcolysyl-l-fluorophenyl-alanine, and the alkylating group of the sarcolysine group was considered to be the pharmacologically active part.

Document (3) disclosed tripeptides carrying a m-di-(2-chloroethyl)amino-phenyl-L-alanine moiety. Among the peptides bearing this moiety, L-prolyl-m-(di(2-chloroethyl)-amino)-phenyl-L-alanyl-p-fluoro-L-phenylalanine was disclosed.

Document (5) disclosed pharmaceutical preparations for treating cancer comprising at least one tri- or tetra-peptide selected from L-seryl-L-p-fluorophenylalanyl-L-m-sarcolysine, L-prolyl-L-m-sarcolysyl-L-p-fluoropenyalanyl, L-p-fluorophenylalanyl-L-m-sarcolysyl-L-asparagine, wherein the alkylating group of the sarcolysine residue was considered to be the active part.

Document (6) related to tri-, tetra- and penta-peptides with a sarcolysine moiety, and to their anticancer activity.

Document (7) was seen as the closest prior art, especially for the subject-matter of dependent claim 7, and disclosed the use of alkylating groups instead of adriamycine. The problem was formulated as the provision of an alternative anticancer drug to be coupled to the tri-peptide of document (7). The use of Adriamycin as anticancer drug was not considered as conferring an inventive step.

As regards the auxiliary request, documents (1), (3), (5) and (6) were found to be still relevant for novelty.
Document (7) was considered as the closest prior art for the subject-matter of dependent claim 7, which was found to lack inventive step for the same reasons as the main request.

Additionally, the subject-matter of claims 1, 2, 9 and 10 of the main and auxiliary requests were found to not meet the requirements of Article 84 EPC, in view of the unclarity of the terms "*a drug suitable for the treatment of arthritis, … and tumours*", and "*a drug suitable for the treatment of cancer*".

V. The applicant (appellant) filed an appeal against the first instance decision.

VI. A communication expressing the board's preliminary opinion of the board was sent to the applicant.

The Board's opinion was that the main request did not meet the requirements of Article 53(c) EPC, since the subject-matter of claims 9, 10, 13 of said request related to a use or a method which involved directly or indirectly a method of treatment.

Moreover, the subject-matter of claims 1-6, 8-14 of the main request appeared to be not novel at least over the prior art documents (1), (5) and (6).
The subject-matter of claim 13 of the auxiliary request also embraced a method of treatment. Thus, the auxiliary request did not meet the requirements of Article 53(c) EPC.
As no changes had been made to the claims of the auxiliary request in comparison to the main request, apart from a reformulation of claim 9, the objections of lack of novelty applied *mutatis mutandis* to the auxiliary request.

VII. Oral proceedings before the board of appeal took place on 27 March 2013 in the absence of the appellant.

VIII. The appellant's written arguments can be summarised as follows:

The application had been restricted to drugs coupled to a peptide transport and delivery system. The difference between the term "*drug*" and the terms "*pharmacologically active site*" or "*pharmacologically active group*" was clearly outlined in the description of the application.
The description indeed specified that the present invention also included systems where part of a substance known to be a drug was also part of the transport and delivery system. This could be the case when the drug comprised itself a proteolytic enzyme cleavable amino acid. Thus, if the transport and delivery system was drug loaded, then the cleavable amino acid, in particular the pharmacologically active group or site substituted phenylalanine moiety, could not only be substituted by the drug but be the drug. In such cases, but also if only part of a drug was needed

to get the desired pharmaceutical effect, the transport and delivery system was described as coupled to or carrying a pharmacologically active site or a pharmacologically active group (see page 2, line 36 to page 3, line 11).

There was thus a difference between a drug and a pharmacologically active site or a pharmacologically active group. None of the cited prior art related to a peptide coupled with a drug.

The lack of novelty based on document (5) was merely based on the presence of an alkylating group, which could not be considered as a drug.

IX. The appellant requested that the first instance decision be set aside and a patent be granted on the basis of the main request or alternatively of the auxiliary request as filed with the letter dated 2 September 2009 before the examining division.

## Reasons for the Decision

1. The appeal is admissible

2. Main request- Novelty

2.1 The subject-matter of Claim 1 of the main request relates to a tripeptide or a tetrapeptide, as well as the ethyl or methyl ester thereof, connected to a drug suitable for the treatment of arthritis, invasive parasitic diseases, paludism (malaria), AIDS, or tumours. The amino acid moiety that is connected to said drug is not a terminal moiety. The said tripeptide might *inter alia* consist of the sequence Pro-Phe-Phe,or

the same tripeptide wherein the terminal Phenylalanine is para-fluoro substituted.

2.2 Document (5) discloses pharmaceutical compositions suitable for use in cancer chemotherapy, in particular against melanoma. The composition comprises at least one peptide as active agent, among which one of the preferred peptides is L-prolyl-m-sarcolysyl-L-p-fluorophenylalanine and its ethyl or methyl ester (see page 1, lines 1-24 and line 26; page 3, line 2; claim 1). This specific preferred compound is a tripeptide with the sequence of Pro-Phe-Phe, which terminal phenylalanine is fluorinated and esterified with an ethyl and which bears an alkylating agent loaded on the non-terminal phenylalanine moiety, namely a bis(2-chloroethyl)amine group.
Claim 1 of the main request thus lacks novelty over document (5).

2.3 According to the appellant, a difference must be made between a drug and a pharmacologically active group or pharmacologically active site. The compound disclosed in document (5) is constituted by a tripeptide linked with an alkylating group as active part. Accordingly, this alkylating group is not a drug.

The Board could however not follow this argumentation. The term "*drug*" is to be understood and interpreted in its broadest meaning, namely in the present case any chemical substance which has or might have a medical effect. The claimed "*drug*" cannot be restricted to any listed or even less any marketed chemical substances.

Moreover, it is not conceivable that in a general and systematic way, an isolated pharmacologically active group or pharmacologically active site might not be

able to have a pharmacological effect and act as a drug. The statement that a distinction must be made between a drug and a pharmacologically active group or pharmacologically active site is thus generally not plausible and is not supported by any evidence.
As regards in particular alkylating agents, this statement is particularly not credible, since the bis(2-chloroethyl)amine group disclosed in the peptide of document (5), has obvious intrinsic alkylating properties, even isolated from its phenylalanine ligand.

Furthermore, the appellant's argumentation is contradicted by the teaching of example 1 of the description, which discloses the same tripeptide as in document (5), namely L-proly-m-sarcolysyl-p-fluoro-phenylalanine ethyl ester, thus constituted by the sequence proline-phenylalanine-fluoro phenylalanine ethyl ester with the same alkylating agent loaded on the non-terminal phenylalanine moiety, namely a bis(2-chloroethyl)amine group. The text of example 1 further specifies that "*said alkylating group is assumed to be the pharmacologically active part of the such substituted phenylalanine moiety or, in other words, the* ***drug*** *loaded on the phenylalanine moeity*".

2.4 The main request does not meet the requirements of Article 54 EPC.

2.5 In view of these conclusions, there is no need to consider further documents taken into account by the first instance.

3. Auxiliary request - Novelty

The subject-matter of claim 1 of the auxiliary request 1 is identical to claim 1 of the main request. Hence the same conclusions apply *mutatis mutandis*.

The auxiliary request does not meet the requirements of Article 54 EPC.

**Order**

**For these reasons it is decided that:**

The appeal is dismissed.

The Registrar: The Chairman:

L. Fernández Gómez J. Riolo

Decision electronically authenticated