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Datasheet for the decision of 12 March 2018

Case Number: T 2397/12 - 3.3.01

Application Number: 06751251.7

Publication Number: 1877419

IPC: C07J41/00, A61P35/00, A61K31/575

Language of the proceedings: EN

Title of invention:
POLYMORPHIC AND AMORPHOUS SALT FORMS OF SQUALAMINE DILACTATE

Applicant:
GENAERA CORPORATION

Headword:
Crystalline Squalamine Dilactate/GENERA

Relevant legal provisions:
EPC Art. 54(2), 56

Keyword:
Inventive step - (yes)

Decisions cited:
T 0777/08

Europäisches Patentamt
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Beschwerdekammern

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Case Number: T 2397/12 - 3.3.01

D E C I S I O N
of Technical Board of Appeal 3.3.01
of 12 March 2018

Appellant: (Applicant)	GENAERA CORPORATION 5110 Campus Drive Plymouth Meeting, PA 19462 (US)
Representative:	Nederlandsch Octrooibureau P.O. Box 29720 2502 LS The Hague (NL)
Decision under appeal:	**Decision of the Examining Division of the European Patent Office posted on 27 April 2012 refusing European patent application No. 06751251.7 pursuant to Article 97(2) EPC**

Composition of the Board:

Chairman	A. Lindner
Members:	M. Pregetter
	L. Bühler

Summary of Facts and Submissions

I. The present appeal lies from the decision of the examining division refusing European patent application No. 06 751 251.7, published as WO2006/116309.

II. The following documents, cited during the examination and appeal proceedings, are referred to below:

(1) Herbst et al., Clinical Cancer Res. Vol. 9(11), pp. 4108-4115 (2003)

(2) Bhargava et al., Clinical Cancer Res. Vol. 7(12), pp. 3912-3919 (2001)

(3) Li et al., J. Pharm. Biomed. Anal. Vol. 32(1), pp. 85-96 (2003)

(4) WO-A-03/080027

(5) Genaera website; retrieved from the internet on 16 October 2006: URL: http://vvww.genaera.com/ARVO2004/images/slide02.gif>

(6) Website of the National Library of Medicine (National Institutes of Health); retrieved from the internet on 16 October 2006: URL: http://chem.sis.nlm.nih.gov/chemidplus/jsp/common/ChemFull.jsp?MW=718.0469> - last modified 9 September 2004

(10) Moriarty et al., Tetrahedron Lett. 1995, 36, 5139-5142

III. The decision under appeal was based on the main request and on auxiliary request 1, both filed during oral

proceedings before the examining division. While there were issues with admission, sufficiency of disclosure and clarity in respect of the main request, the independent claims of the auxiliary request were found not to involve an inventive step.

IV. With its statement of grounds of appeal, the appellant submitted a main request and an auxiliary request.

Claim 1 of the main request reads:

"A crystalline form of the dilactate salt of 3ß-(N-[3-aminopropyl]-1,4-butanediamine)-7α,24R-dihydroxy-5α-cholestane-24-sulfate."

V. Oral proceedings were held on 12 March 2018.

VI. The appellant's arguments, insofar as they are relevant to the present decision, may be summarised as follows:

Public availability of document (5)

Document (5) depicted one slide from a presentation. The slide included the date "2004", referring to a year. Nothing was known about the circumstances in which the presentation had been given. Furthermore it was not known when the slide had been put on the web page of the applicant's company. Due to internal problems because of financial difficulties resulting in a loss of documentation, it was not possible to provide any further information or evidence.

Inventive step

Documents (1) to (3) related to "MSI-1256F", a synonym for squalamine lactate. They provided no detailed

information on squalamine. They did not disclose squalamine dilactate and did not describe a crystalline form. Document (4) only mentioned squalamine lactate in a list on page 5. Neither squalamine dilactate nor a crystalline form was disclosed. The closest prior art was represented by document (6), which was the only document disclosing structural information. Most of the information in document (6) pointed towards the presence of a monolactate, see molecular weight and the molecular formula. Although water of hydration was mentioned, that did not necessarily imply that the squalamine lactate of document (6) was in a crystalline form. Document (6) did not mention a crystalline state. There were thus two differences between the subject-matter of claim 1 of the main request and the closest prior art, the type of squalamine salt and the crystalline form. The solution to the problem of providing a squalamine form with certain advantages (application as filed, paragraph bridging pages 1 and 2) was not obvious. There was no crystalline form of squalamine available, see e.g. document (10), note 4. Even though the skilled person aimed, without any doubt, at the provision of a crystalline form of squalamine, such a form was not achievable before the present invention. There was no teaching or guidance in the art on how to provide crystalline forms of squalamine. Consequently, an inventive step had to be acknowledged.

VII. The appellant requested that the decision under appeal be set aside and that a patent be granted on the basis of the claims of the main request or, alternatively, the auxiliary request, both filed with the statement of grounds of appeal of 6 September 2012.

Reasons for the Decision

1. The appeal is admissible.

2. *Public availability of document (5)*

Document (5) depicts one slide of a presentation. It is not known when and in what circumstances the presentation was given. Presentations can be given internally, i.e. to a non-public audience, or to the public. There is furthermore no information as to whether the specific slide that forms document (5) has actually ever been presented. The board is thus unable to establish that document (5) has been publicly presented at a conference or on any other occasion.

Document (5) has been retrieved from the internet. Slide(s) making up the above-mentioned presentation have thus, at one point in time, been made public by publication on the internet. However, from document (5) itself it is not possible to derive the date on which any such publication took place.

The applicant has declared that, due to internal problems because of financial difficulties resulting in a loss of documentation, it is unable to provide any further information or evidence.

The board reaches the conclusion that there is not enough evidence on file to show that document (5) had been publicly available before the effective date of the European patent application.

Consequently, document (5) does not form part of the state of the art according to Article 54(2) EPC.

Main request

3. The subject-matter of claim 1 of the main request is based on claim 16 as originally filed and thus fulfils the requirements of Article 123(2) EPC

4. *Inventive step*

The present application aims at providing forms of squalamine that can be readily administered to patients, especially in the form of therapeutically active soluble salts that exhibit thermal stability upon storage and minimal toxicity and at providing economical methods for the manufacture of these salts (paragraph bridging pages 1 and 2 of the application as filed). The solution is found to be the crystalline form of a dilactate salt of squalamine, as defined in claim 1 of the main request.

The closest prior art is document (6), which is a database entry for squalamine lactate, disclosing its molecular weight, depicting its structure and mentioning the synonym "MSI 1256F", the CAS registry number and the molecular formula. From this molecular formula it can be clearly seen, from the letter "x" in front of the molecular formula fragment relating to the lactate, that it was not known which form of salt was present. Document (6), furthermore, does not disclose the presence of a crystalline form.

There are thus two differences between claim 1 of the main request and the closest prior art: the type of squalamine lactate salt and the crystalline form.

The problem can be seen as the provision of a stable form of squalamine suitable for use in pharmacy.

The problem has been solved (see examples 4, 5, 7 and 8 relating to the crystallisation of squalamine dilactate and example 6 relating to stability studies comparing amorphous and crystalline squalamine dilactate).

Two differences have been identified with regard to the closest prior art. In addition to finding suitable conditions, especially solvents, for crystallisation, the skilled person has to settle on a specific salt form of squalamine. Since squalamine dilactate is not disclosed in any of the documents comprised in the state of the art according to Article 54(2) EPC, it was not a compound that the skilled person would inevitably have selected when carrying out his routine tests for finding suitable crystallisation conditions. Consequently, the solution of the above-defined problem, i.e. the provision of crystalline squalamine dilactate, could not have been found by the skilled person following his routine approach.

The present case differs from the situation in T 777/08 in that there is no explicit disclosure in the prior art at hand of the compound to be crystallised.

The subject-matter of claim 1 of the main request involves an inventive step.

Independent claims 3 and 4 of the main request relate to the use of the crystalline form of squalamine dilactate as defined in claim 1 or claim 2 (which is dependent on claim 1) and consequently also involve an inventive step.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the examining division with the order to grant a patent on the basis of the following claims and a description to be adapted thereto:
   claims:
   1 to 7 of the main request filed with the statement of grounds of appeal.

The Registrar: The Chairman:

M. Schalow A. Lindner

Decision electronically authenticated