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**Datasheet for the decision
of 14 May 2014**

Case Number: T 0128/12 - 3.3.01

Application Number: 02766645.2

Publication Number: 1390378

IPC: C07H19/06, A61K31/7072,
A61P25/00, A61P35/00

Language of the proceedings: EN

Title of invention:
PHARMACEUTICALLY ACTIVE URIDINE ESTERS

Patent Proprietor:
Trommsdorff GmbH & Co. KG Arzneimittel

Opponent:
Molling, Matheus, Catharina

Headword:
5'-acyl uridines/TROMMSDORFF

Relevant legal provisions:
EPC Art. 54
EPC R. 115(2)
RPBA Art. 15(3)

Keyword:
All requests: novelty - selection invention (no)

Decisions cited:

Catchword:



**Beschwerdekammern
Boards of Appeal
Chambres de recours**

European Patent Office
D-80298 MUNICH
GERMANY
Tel. +49 (0) 89 2399-0
Fax +49 (0) 89 2399-4465

Case Number: T 0128/12 - 3.3.01

D E C I S I O N
of Technical Board of Appeal 3.3.01
of 14 May 2014

Appellant: Molling, Matheus, Catharina
(Opponent) Sirtemastraat 232
2513 SV The Hague (NL)

Representative: Molling, Matheus, Catharina
V.O.
Johan de Wittlaan 7
2517 JR Den Haag (NL)

Respondent: Trommsdorff GmbH & Co. KG Arzneimittel
(Patent Proprietor) Trommsdorffstrasse 2-6
52475 Alsdorf (DE)

Representative: Arth, Hans-Lothar
ABK Patent Attorneys
Jasminweg 9
14052 Berlin (DE)

Decision under appeal: **Interlocutory decision of the Opposition
Division of the European Patent Office posted on
10 November 2011 concerning maintenance of the
European Patent No. 1390378 in amended form.**

Composition of the Board:

Chairman A. Lindner
Members: G. Seufert
O. Loizou

Summary of Facts and Submissions

I. The appellant (opponent) lodged an appeal against the interlocutory decision of the opposition division on the amended form in which the European patent No. 1 390 378 could be maintained.

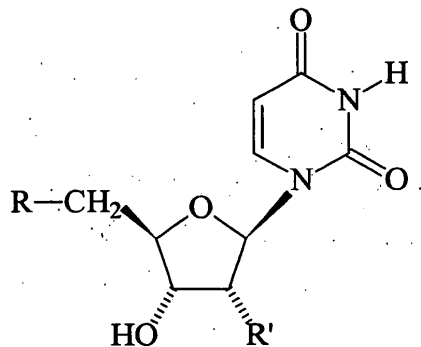
II. The present decision refers to the following documents:

- (1) US 5,470,838
- (5) J. Huang *et al.*, Synthetic Communication, Vol. 24, No. 4, 1997, pages 681 to 690

III. Notice of opposition was filed by the appellant requesting revocation of the patent in suit in its entirety on the grounds of lack of novelty and inventive step, exclusion from patentability under Article 53(c) EPC and insufficiency of disclosure (Article 100(a) and (b) EPC).

IV. The decision of the opposition division was based on the main request filed with letter of 24 August 2011. Independent claim 1 reads as follows:

"1. Compound having the general formula (I):



wherein

R represents R"-COO;

R' represents hydrogen or a hydroxy group;

R" represents, a monobranched or multibranched alkyl chain with 8 to 30 carbon atoms, a monoenoic alkyl chain with 8 to 30 carbon atoms, a monoenoic branched alkyl chain with 8 to 30 carbon atoms, a polyenoic alkyl chain with 8 to 30 carbon atoms, a polyenoic branched alkyl chain with 8 to 30 carbon atoms, a branched or unbranched alkyl chain with 8 to 30 carbon atoms containing a carbocyclic or heterocyclic ring, a monoinoic alkyl chain with 8 to 30 carbon atoms, a monoinoic branched alkyl chain with 8 to 30 carbon atoms, a polyinoic alkyl chain with 8 to 30 carbon atoms, a polyinoic branched alkyl chain with 8 to 30 carbon atoms, an alkyl chain with 8 to 30 carbon atoms containing at least one double and one triple bond, a branched alkyl chain with 8 to 30 carbon atoms containing at least one double and one triple bond, a hydroxy group or thiol group containing branched or unbranched and/or saturated or unsaturated alkyl chain with 8 to 30 carbon atoms, and pharmaceutically acceptable salts thereof."

Independent claims 4, 5, 16 and 17 are directed to the use of compounds of formula (I) for the manufacture of a medicament and their preparation and pharmaceutical compositions comprising them.

The opposition division held that the subject-matter of the main request

- was not excluded from patentability under Article 53(c) EPC,
- was sufficiently disclosed,

- was novel over the disclosure of documents (1) and (5) and
- involved an inventive step starting from either document (1) or (5) as the closest prior art.

V. With the statement of grounds of appeal the appellant maintained its objections of lack of novelty and inventive step and insufficiency of disclosure.

VI. In reply to the statement of grounds of appeal the respondent (patent proprietor) resubmitted the set of claims underlying the decision under appeal and filed amended pages 3 and 9 of the description. It also filed auxiliary requests I to III.

VII. Auxiliary request I differs from the main request in that the variable R" in formula (I) has been limited by deleting the definitions

- "a monobranched or multibranched alkyl chain with 8 to 30 carbon atom"
 - "a branched or monobranched alkyl chain with 8 to 30 carbon atoms containing a carbocyclic ring"
- from the independent claims. The dependent claims have been adapted accordingly.

In auxiliary request II the variable R" was further limited by also deleting the definitions

- a polyinoic alkyl chain with 8 to 30 carbon atoms,
- a polyinoic branched alkyl chain with 8 to 30 carbon atoms
- a hydroxy group containing branched or unbranched and/or saturated or unsaturated alkyl chain with 8 to 30 carbon atoms

from the independent claims. The dependent claims have been adapted accordingly.

In auxiliary request III the variable R" in formula (I) is defined as "a monoenoic alkyl chain with 8 to 30 carbon atoms, a polyenoic alkyl chain with 8 to 30 carbon atoms, a branched or unbranched alkyl chain with 8 to 30 carbon atoms containing a heterocyclic ring, a monoenoic alkyl chain with 8 to 30 carbon atoms, an alkyl chain with 8 to 30 carbon atoms containing at least one double and one triple bond, a thiol group containing an unbranched and saturated alkyl chain with 8 to 30 carbon atoms" in the independent claims. The dependent claims have been adapted accordingly.

- VIII. On 5 December 2013 the board issued summons to oral proceedings.
- IX. Right before the oral proceedings were opened, the registrar informed the board that the respondent had indicated by telephone some minutes ago that it would not be present at the proceedings. The oral proceedings took place as scheduled in the absence of the duly summoned respondent pursuant to Rule 115(2) EPC.
- X. The arguments of the appellant with respect to the decisive issues can be summarised as follows:

- Novelty

Example VI of document (1) disclosed 5'-acyl substituted uridines corresponding to compounds of formula (I) with R' equal to hydrogen or hydroxyl. The acyl residue was not defined in this specific part of document (1), but information as to its meaning was given in the description in the paragraph bridging columns 8/9. Document (1) also disclosed that an acyl residue derived from lipoic acid was a preferred acyl residue. Document (1), therefore, disclosed the

compound 5'-lipoyl uridine. Since example VI was specifically directed to 5'-acyl uridines there was no need to make multiple selections in order to arrive at the claimed subject-matter. Only one variable remained and its definition could be found in the paragraph bridging columns 8 and 9 of document (1). The acyl radical of lipoic acid was identical to the group R"CO of formula (I) of the patent with R" equal to 1,2-dithiolane-3-pentanyl, which was explicitly mentioned in claim 2 of the main request. Document (1) was therefore novelty destroying for the subject-matter of the main request.

Document (1) was also enabling. The examples referred to in the respondent's letter support that the methods of example VI were suitable to prepare the 5'-acyl uridines, just not selectively. Moreover, it was well within the skilled person's common general knowledge to protect groups that should not be derivatised to improve selectivity. Furthermore, it was irrelevant for the assessment of novelty whether or not the prior art also allowed the selective production of the compound.

XI. The arguments of the respondent with respect to the decisive issues can be summarised as follows:

- Novelty

The claimed subject-matter was novel over the disclosure of document (1). Starting from this document, several selections had to be made in order to arrive at the claimed subject-matter, namely one for the uridine esters, one for the required substitution pattern and one for the required acyl substituent. The claimed compound class represented a novel selection from at least 120 different compound classes disclosed

in document (1). Furthermore, according to document (1) tri- and tetra acyl substituted derivatives, including N-acyl derivatives, were preferred. Document (1), therefore, taught away from the presently claimed subject-matter. With respect to example VI, it was pointed out that the reaction methods described therein did not work. As set out in detail in the submission of 24 August 2011, selective esterification of the 5'-position was not possible without first protecting the 2' and 3' hydroxyl groups. Document (1) was therefore not an enabling disclosure for 5'-acyl uridines.

- XII. The appellant requested that the decision under appeal be set aside and that the patent be revoked.
- XIII. The respondent requested in writing that the appeal be dismissed, or, alternatively that the patent be maintained on the basis of one of auxiliary requests I to III as filed with its reply to the grounds of appeal of 6 June 2012.
- XIV. At the end of the oral proceedings the decision of the board was announced.

Reasons for the Decision

1. The appeal is admissible.
2. Non-appearance at oral proceedings before the board
 - 2.1 The respondent was not present at the oral proceedings before the board to which it had been duly summoned (see point IX above).

- 2.2 According to Rule 115(2) EPC, oral proceedings may continue in the absence of a duly summoned party that does not appear. According to Article 15(3) of the Rules of Procedure of the Boards of Appeal (RPBA), the board is not obliged to delay any step in the proceedings, including its decision, by reasons only of the absence at the oral proceedings of any party duly summoned, which may then be treated as relying only on its written case. In deciding not to attend oral proceedings, the respondent chose not to avail itself of the opportunity to present its observations and comments orally.
- 2.3 The contentious issues were apparent from the decision under appeal, the statement of grounds of appeal and the reply thereto. The respondent must have expected that the board would decide on these issues at the oral proceedings. Hence, the board concludes that the respondent had opportunity to present its observations and comments on the grounds and evidence on which the board's decision, arrived at during oral proceedings, is based. The board was, therefore, despite the absence of the duly summoned respondent, in a position to take a final decision at the oral proceedings.

Main request

3. With its statement of grounds of appeal, the appellant had maintained its objection of insufficiency of disclosure with respect to the definition of several of the R"-groups in formula (I). At the oral proceedings before the board, the appellant was prepared to discuss novelty over document (1) based on the assumption that the skilled person would understand the meaning of these groups despite the unusual way in which they were defined. Since the main and auxiliary requests I to III

fail for other reasons (see point 4 and 5 below), the board sees no reason to conclude on the issue of sufficiency of disclosure.

4. Novelty

4.1 Claim 1 of the main request is directed to uridines and deoxyuridines which are esterified at the 5'-position of the ribose unit (see point IV above).

4.2 Document (1) discloses in example VI (see column 23, lines 35 to 67) the preparation of 5'-acyl uridines, i. e. a group of compounds esterified at the 5'-position group of the ribose unit. The term "acyl" is not further specified in this example. However, a definition of acyl in combination with uridines can be found in column 8, line 51 to column 9, line 17. This definition includes the acyl radical of lipoic acid (see column 9, line 9).

The acyl radical of lipoic acid (1,2-dithiolane-3-pentanoic acid) falls within the scope of the present claim 1, i. e. R' equal to hydroxy and R" equal to an alkyl chain including a heterocyclic ring, in particular 1,2-dithiolane-3-pentyl (see dependent claim 2, line 9). The subject-matter of the main request is therefore not novel over the disclosure of document (1).

4.3 In the decision under appeal the opposition division held that the claimed subject-matter was novel over document (1) because multiple selections with respect to compounds of formula (I) or (II) were required to arrive at the claimed subject-matter. Even starting from example VI of document (1) a further selection from the general teaching of the description was

necessary. The respondent concurred with the opposition division's findings. It argued that to arrive at the claimed subject-matter a first selection had to be made between uridine and cytidine esters. With respect to the variables R_1 , R_2 , R_3 and R_4 in the uridine esters of document (1), a second selection had to be made within 15 different substitution patterns (i. e. either one, two or three of the variables R_1 , R_2 , R_3 and R_4 was/were hydrogen, while the remaining were/was not hydrogen, or none of the variables R_1 , R_2 , R_3 and R_4 was hydrogen). In addition, if the variables R_1 , R_2 , R_3 and R_4 were not hydrogen, each of them was independently selected from groups (a) to (d) according to column 8, line 67 to column 9, line 11. Thus, a third selection within those groups (a) to (d) and even a selection within group (d) had to be made.

- 4.4 The board does not agree. As explained in point 4.2 above, document (1) already discloses explicitly 5'-acyl uridines as a subclass. With respect to this subclass, the first and second selections, namely the selection of uridine esters with R_2 , R_3 , R_4 equal to hydrogen and R_1 equal to acyl (substitution pattern (13) according to the respondent's letter dated 6 June 2012) are already made. Starting from example VI, the only selection required is the selection of the acyl radical, which is defined in column 8, line 67 to column 9, line 11 as deriving from a list of specific carboxylic acids. Although divided into "different lists" (a) to (d), these "different lists" in fact represent a single list of equivalent alternative acyl radical, including lipoic acid. Following the established jurisprudence of the boards of appeal according to which, the selection of one item from a list of equivalent alternatives does not confer

novelty, document (1) unambiguously discloses lipoyl uridine, a compound which falls within the scope of the claims of the main request. Contrary to the findings of the opposition division, the board also sees no reasons as to why the skilled person reading example VI, which discloses a general reaction method for the preparation of 5'-acyl uridines and therefore does not further specify the acyl residue, would not consider the general disclosure of document (1), in particular those parts relating to uridine esters, for further information on the meaning of this residue and combine it with the disclosure of example VI.

- 4.5 The respondent also put forward that, according to document (1), tri- or tetra-substitution was preferred over di- or mono-substitution and that document (1) therefore taught away from the claimed compounds.
- 4.6 The board does not accept this argument. The fact that document (1) describes certain tri- or tetra-substituted compounds as preferred cannot detract from the fact that mono-substituted 5'-acyl uridines, whether they are preferred or not, are explicitly disclosed in example VI.
- 4.7 The respondent further argued that document (1) was a non enabling disclosure, because the 5'-acyl uridines could not be obtained by the skilled person following the reaction methods described in example VI. According to comparative examples carried out by the respondent, selective esterification with lipoic and lauric acid without first protecting the 2'- and 3'- hydroxyl groups was not possible. As non enabling disclosure, document (1) could not take away the novelty of the claimed subject-matter. In support of its assertions,

the respondent referred to its detailed submission of 24 August 2011.

4.8 The board notes that the respondent only argues that **selective** esterification is not possible. It was not denied that by following the reaction methods of document (1) 5-lipoyl and lauryl uridines were in fact obtained, but not in pure form (see also respondent's letter of 24 August 2011, page 7, first complete paragraph). Moreover, selectivity or purity are not features of the present claim 1 and therefore cannot be used to distinguish the claimed subject-matter from the prior art. Hence, the respondent's arguments with respect to an allegedly non enabling disclosure of document (1) cannot succeed.

4.9 In view of the above, the board concludes that the main request must be refused for lack novelty within the meaning of Article 54 EPC.

Auxiliary requests I to III

5. Claim 1 of each of the auxiliary requests I to III includes the compound 5'-lipoyl uridine. Hence, the same observations and conclusion as in point 4 above apply with the consequence that these requests must also be refused for lack of novelty.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.
2. The patent is revoked.

The Registrar:

The Chairman:



M. Schalow

A. Lindner

Decision electronically authenticated