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Datasheet for the decision of 22 June 2016

Case Number: T 0455/13 - 3.3.01

Application Number: 08767427.1

Publication Number: 2146976

IPC: C07D295/108, A61K31/4453

Language of the proceedings: EN

Title of invention:
COMPOSITIONS OF TOLPERISONE

Applicant:
Sanochemia Pharmazeutika AG

Headword:
Tolperisone/Sanochemia

Relevant legal provisions:
EPC Art. 54

Keyword:
Novelty - (no)

Decisions cited:
T 0990/96

Catchword:

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Case Number: T 0455/13 - 3.3.01

D E C I S I O N
of Technical Board of Appeal 3.3.01
of 22 June 2016

Appellant: (Applicant)	Sanochemia Pharmazeutika AG Boltzmanngasse 11 1090 Wien (AT)
Representative:	Beer & Partner Patentanwälte KG Lindengasse 8 1070 Wien (AT)
Decision under appeal:	**Decision of the Examining Division of the European Patent Office posted on 1 August 2012 refusing European patent application No. 08767427.1 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 the European patent application No. 08 767 427.1, published as WO2008/133937.

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

(1) US 2006/0041141
(2) Technische Stellungnahme, Schuecker und Gerdes, Seiten 1-16 filed with the notice of appeal

III. The decision under appeal was based on the main request and on auxiliary request 1, both filed with letter of 27 June 2012.

The examining division considered that the subject-matter of claims 1, 2, 5 and 17 of the main request and of claims 1, 3 and 15 of auxiliary request 1 lacked novelty in view of document (1). The comparative examples 2 and 3 on pages 33 and 34 of the description as originally filed showed that tolperisone comprising the same levels of the impurity of 2-methyl-1-(4-methylphenyl)-propenone (4-MMPPO) as claimed in the independent compound claims of the main and auxiliary request 1 was obtained by the methods employed in document (1). Decision T 990/96 was cited in this context.

IV. With the statement of grounds of appeal, the appellant (applicant) re-submitted auxiliary request 1 of 27 June 2012 as its main request. The appellant also

filed document (2) and requested its exclusion from public file inspection.

V. Claim 1 of the main and only request reads as follows:

"Tolperisone comprising less than about 7 ppm 2-methyl-1-(4- methylphenyl)-propenone (4-MMPPO)".

VI. By letter dated 14 June 2016, the appellant withdrew its request for oral proceedings and asked for a decision according to the state of the file.

VII. Oral proceedings were held on 22 June 2016 in the absence of the appellant.

VIII. The appellant's arguments, in so far as they are relevant to the present decision, may be summarised as follows:
The request for exclusion of document (2) from public file inspection was substantiated by economic interests.
Making reference to the data of document (2), the appellant argued that it had shown that when using purification methods as known from document (1) the required purity could not be obtained. The appellant cited T 990/96 in this context.

IX. The appellant had requested in writing that the decision under appeal be set aside and that a patent be granted on the basis of the main request filed with the statement of grounds of appeal. It further requested exclusion of the document filed with the statement of grounds of appeal from file inspection.

X. At the end of the oral proceedings, the decision of the board was announced.

Reasons for the Decision

1. The appeal is admissible.

2. *Exclusion of document (2) from file inspection*

The data of document (2) as presented by the appellant in its statement of grounds of appeal have no influence on the assessment of novelty, cf. points 3.7 and 3.9 below. It is therefore not necessary to come to a decision on the exclusion of document (2) from file inspection.

3. *Novelty (Articles 52(1), 54 EPC)*

3.1 The subject-matter of claim 1 relates to the centrally-acting muscle relaxant tolperisone comprising less than about 7 ppm of the impurity 2-methyl-1-(4-methylphenyl)-propenone (4-MMPPO). In the context of the present application the term "tolperisone" includes isomers, salts, solvates and polymorphs (paragraph [0042]).

3.2 Toperisone and its hydrochloride are disclosed in prior art document (1). Document (1) defines a method for manufacturing pharmaceutically acceptable acid addition salts of tolperisone (claim 1). Document (1) recognises the presence of the impurity 4-MMPPO (paragraph [0019]) and provides the information that 4-MMPPO is present in a concentration of less than 500 ppm 4-MMPPO(<0.05% 4-MMPPO, as listed in the table in paragraph [0035] under the heading "Vinyl Ketone"). According to the appellant, the method of measurement used in document

(1) does not allow the actual content of 4-MMPPO to be determined. Document (1) thus discloses toplerisone comprising the impurity 4-MMPPO.

3.3 Achieving a higher degree of purity has been the subject of several decisions of the boards of appeal (Case Law, 7th edition 2013, I.C.5.1.4). The disclosure of a low molecular compound is considered to make it available at all levels of purity, unless there is evidence that hitherto all attempts at purification by conventional techniques have failed (cf. T 990/96, OJ 1998, 489, point 7 of the Reasons).

3.4 The purification of tolperisone by conventional techniques is disclosed in document (1):
example 5 of document (1) relates to the "Industrial Production of Tolperisone Hydrochloride" and describes the synthesis of tolperisone hydrochloride. It is noted that the same reaction scheme is disclosed in the present application in paragraph [0059], which incidentally makes reference to document (1).
Example 6 of document (1) describes the "Industrial Recrystallization of Tolperisone Hydrochloride". The tolperisone obtained from example 5 is heated under reflux in a mixture of 2-butanone and isopropanol. An optional hot filtration is foreseen. After cooling, separating the liquid and drying, a product of colourless crystals is isolated.

3.5 The present application describes a conventional recrystallisation process, under the heading: "Standard Recrystallization of Tolperisone". "Crude" tolperisone is refluxed in a mixture of 2-butanone and isopropanol, filtered while hot, cooled, the liquid separated, and dried (example 2).

3.6 The disclosure of document (1) and the present application are thus in general agreement. "Crude" tolperisone may be synthesised by the same reaction and recrystallised using the same solvent system and very similar temperature conditions. In conclusion, the recrystallization of tolperisone of example 2 of the application is indeed to be considered to represent the "Standard Recrystallization of Tolperisone" as known from the prior art. This has not been contested by the appellant.

3.7 The standard recrystallisation process of example 2 of the application is carried out in example 3 of the application in the form of repeated recrystallisations leading to a multiple-stage process. The respective concentrations of the 4-MMPPO are given in table 4.

Table 4 provides information on two batches:

Table 4: 4-MMPPO Content Following Repeated Recrystallizations, Non-Acifidified Solvent

Batch	[4-MMPPO], ppm Crude Tolperisone	[4-MMPPO], ppm After 1st Recryst.	[4-MMPPO], ppm After 2nd Recryst.	[4-MMPPO], ppm After 3rd Recryst.
1	107/51.1 before/after drying	<6.6	8.3	<6.6
2	7/<6.6	7.3	6.2	-

It can be clearly seen from these results that the prior art method, as described in document (1), when carried out one to three times, already leads to values of less than about 7 ppm of 4-MMPPO. In particular, the value of 6.2 ppm of batch 2 after the second recrystallisation discloses directly and unambiguously a value of 4-MMPPO of less than 7 ppm.

It is noted that said value of 6.2 ppm has not been

contested by the appellant either in the statement of the grounds of appeal, or in its document (2). Consequently, tolperisone having the required levels of purity is obtainable by using conventional methods.

3.8 The application as originally filed shows in example 3 and table 4 that standard, i.e. conventional, purification processes succeed in providing higher degrees of purity such as defined in claim 1 of the main request.

Document (1) thus anticipates the subject-matter of claim 1 of the main and only request.

Claim 1 of the main request is not novel (Art. 54 EPC).

3.9 The appellant has cited T 990/96, point 8 of the Reasons. In T 990/96 the board stated that a high purity could impart novelty to a low molecular compound, if it were proved on the balance of probabilities that all prior attempts to achieve a particular degree of purity by conventional purification processes had failed. The burden of proving the existence of such an extraordinary situation lies with the party alleging its existence. The appellant has not discharged this burden. On the contrary: as already outlined in point 3.8 above, it has demonstrated in the application as filed that the claimed purity can be achieved by using conventional purification processes. Neither in this letter nor elsewhere has the applicant shown why the values of further test series differ from the values disclosed in table 4 of the present application.

Consequently, the exceptional situation foreseen in

T990/96 does not apply in the present case.

3.10 The appellant has further argued that the addition of an acid during the recrystallization can reduce the concentration of 4-MMPPO considerably. The appellant's attention is drawn to the fact that claim 1 of the main request allows for the presence of the impurity 4-MMPPO in concentrations of up to but less than 7 ppm. Extremely low concentrations of 4-MMPPO are therefore not relevant for the assessment of novelty of a claim defining amounts of 4-MMPPO up to 7 ppm.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

M. Schalow A.Lindner

Decision electronically authenticated