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**Datasheet for the decision  
of 19 June 2012**

**Case Number:** T 1412/07 - 3.3.02

**Application Number:** 98966846.2

**Publication Number:** 1140021

**IPC:** A61K 9/127

**Language of the proceedings:** EN

**Title of invention:**

Improved formulation for topical non-invasive application in vivo

**Patent Proprietor:**

IDEA AG

**Opponent:**

MIKA Pharma Gesellschaft für die Entwicklung und Vermarktung pharmazeutischer Produkte mbH

**Headword:**

Formulation containing penetrants/IDEA

**Relevant legal provisions:**

EPC R. 131(2), 126(1)(2), 134(1)

**Relevant legal provisions (EPC 1973):**

EPC Art. 83

**Keyword:**

"Appeal admissible (yes), filed in due time"  
"Sufficiency of disclosure (no)"

**Decisions cited:**

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**Catchword:**

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Case Number: T 1412/07 - 3.3.02

**DECISION**  
of the Technical Board of Appeal 3.3.02  
of 19 June 2012

**Appellant I:**  
(Patent Proprietor)

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**Appellant II:**  
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**Decision under appeal:**

**Interlocutory decision of the Opposition  
Division of the European Patent Office posted  
22 June 2007 concerning maintenance of the  
European patent No. 1140021 in amended form.**

**Composition of the Board:**

**Chairman:** U. Oswald  
**Members:** H. Kellner  
L. Bühler

## Summary of Facts and Submissions

- I. European patent No. 1 140 021, based on international application PCT/EP1998/008421, published as WO 2000/038653 and having application No. 98 966 846.2 in the EPO, was granted with 49 claims.

Independent claim 1 as granted reads as follows:

"Formulation comprising penetrants being capable of penetrating the pores of a barrier, even when the average diameter of said pores is smaller than the average diameter of said penetrants, provided that the penetrants can transport agents or else enable agent permeation through the pores after penetrants have entered pores, the agents associated with said penetrants being corticosteroids, especially glucocorticoids or mineralocorticosteroids, characterized in that the relative content of corticosteroids is above 0.1 weight-%, relative to total dry mass of the formulation, and the formulation comprises at least one antioxidant in an amount that reduces the increase of oxidation index to less than 100 % per 6 months."

- II. The documents cited during the proceedings before the opposition division and the board of appeal included the following:

(A12) Klein, R.A., "The detection of oxidation in liposome preparations", *Biochim. Biophys. Acta*, 210, 1970, 486-489

- (A13) Lichtenberg, D., Barenholz, Y., "Methods of Biochemical Analysis" vol. 33, "Liposomes: Preparation, Characterization, and Preservation", 1988, pages 337, 359, 360
- (E27) Product information of Sigma, Saint Louis, Missouri, for the product L- $\alpha$ -phosphatidylcholine; RLG 8/03 (Art. 54(3))
- (E28) Tadolini, B. et al., "Iron (III) stimulation of lipid hydroperoxide-dependent lipid peroxidation", Free Rad. Res. 27(6), 1997, 563-576
- (E29) Babincová, M. et al., "Carboxymethylated Glucan inhibits lipid peroxidation in liposomes", Z. Naturforsch. 54c, 1999, 1084-1088 (Art. 54(3))

III. Opposition was filed against the granted patent under Article 100(a) EPC for lack of novelty and inventive step and Article 100(b) EPC for insufficiency of disclosure. Additionally, objections concerning Article 100(c) EPC were raised, on the grounds that the granted patent contained subject-matter which had not originally been disclosed.

The opposition division held that the contested patent as amended according to the second auxiliary request met the requirements of the Convention.

Amended claims 7, 9 and 11 of the main request were in breach of Article 123(2) (100(c)) EPC and claim 1 of the first auxiliary request did not meet the requirements of Article 83 (100(b)) EPC in view of the expression "at least one antioxidant in an amount that

reduces the increase of oxidation index to less than 100 % per 6 months".

The amended claims of the second auxiliary request met the requirements of Article 83 (100(b)) EPC as the skilled person, with the critical expression in claim 1 of the first auxiliary request still present, now obtained a precise indication as to which antioxidant in which amount had to be used; the same held for the choice of the microbicide. It was assumed that thereby the "oxidation index" parameter was achieved automatically.

- IV. The patent proprietor and the opponent filed appeals against the decision of the opposition division.
- V. With its statement of grounds of appeal, the appellant (patent proprietor) submitted three sets of claims as main request and first and second auxiliary requests.

Claim 1 of the main request is identical to claim 1 as granted; there are some amendments in claims 25 and 26.

With respect to the claims as granted, the single amendment in claim 1 of the first auxiliary request is the introduction of part of the features of granted claim 13; this claim 1 reads as follows (amendments marked by the board):

"Formulation comprising penetrants suspended or dispersed in a polar liquid in the form of fluid droplets surrounded by a membrane-like coating of one or several layers, said coating comprising at least two kinds or forms of amphiphilic substances with a

tendency to aggregate, provided that said at least two substances differ by at least a factor of 10 in solubility in said liquid or else that said substances when in the form of homo-aggregates, for the more soluble substance, or of hetero-aggregates, for any combination of both said substances, have a ~~preferred~~ average diameter smaller than the diameter of the homo-aggregates containing merely the less soluble substance; ~~or else provided that the presence of the more soluble substance lowers the average elastic energy of the membrane-like coating in the vicinity of thermal energy,~~ said droplets being capable of penetrating the pores of a barrier, even when the average diameter of said pores is smaller than the average diameter of said penetrants, provided that the penetrants can transport agents or else enable agent permeation through the pores after penetrants have entered pores, the agents associated with said penetrants being corticosteroids, especially glucocorticoids or mineralocorticosteroids, characterized in that the relative content of corticosteroids is above 0.1 weight-%, relative to total dry mass of the formulation, and the formulation comprises at least one antioxidant in an amount that reduces the increase of oxidation index to less than 100 % per 6 months."

In claim 1 of the second auxiliary request part of the features of granted claim 9 is added at the end of claim 1 of the first auxiliary request:

"wherein the anti-oxidant is selected from the group consisting of between 0.0025 and 0.2 w-% of BHA or BHT, of between 0.001 and 2 w-% of TBHQ or PG, of between

0.005 and 5 w-% of tocopherols, of between 0.001 and 5 w-% of ascorbic acid esters, of between 0.001 and 5 w-% of ascorbic acid, of between 0.001 and 5 w-% of sodium bisulphite or sodium metabisulphite, of between 0.0001 and 2 w-% of thiourea, of between 0.01 and 5 w-% of cysteine, of between 0.01 and 5 w-% of monothioglycerol, of between 0.0005 and 2 w-% of NDGA, of between 0.005 and 5 w-% of glutathione, of between 0.001 and 5 w-% of EDTA, of between 0.001 and 5 w-% of citric acid."

VI. The appellant (patentee), in reply to the statement of grounds of appeal of the appellant (opponent) filed twelve further sets of claims.

Their claims 1 are all based on claim 1 of the first auxiliary request and all of them contain the feature

"the formulation comprises at least one antioxidant in an amount that reduces the increase of oxidation index to less than 100 % per 6 months."

Claims 1 of the auxiliary requests 2, 8 and 9 contain the same text with respect to particular antioxidants and their concentration to be contained in the formulation and further requests *inter alia* still more restricted lists of antioxidants to be contained in still narrower ranges of concentration.

VII. With fax of 6 January 2012 the appellant (opponent) requested an interlocutory decision on the admissibility of the patent proprietor's appeal.

- VIII. On 19 January 2012, a communication of the board was despatched, expressing in particular the board's provisional opinion that the patent proprietor's appeal was submitted in time and therefore appeared admissible.
- IX. Appellant (opponent) filed a fax dated 15 May 2012 and appellant (patent proprietor) a letter dated 21 May 2012 each indicating that it would not be attending the oral proceedings. Oral proceedings took place on 19 June 2012 in the absence of the parties.
- X. The appellant (opponent) in its written submissions *inter alia* raised objections concerning Article 83 EPC 1973.

The teaching of the patent in suit could not be carried out by the skilled person because the term "oxidation index" was not part of the common general knowledge, was not defined or measured in the patent in suit and could at most (based on documents (A12) and (A13)) be measured for particular plant phospholipids while claim 1 of the patent in suit referred to penetrants in general and did not even mention phospholipids (pages 2 to 4 of the statement of the grounds for appeal, in particular the paragraph bridging pages 3 and 4).

It wasn't even possible to conduct comparative measurements because there was no enabling basis with respect to the conditions under which to carry out such experiments.

- XI. The appellant (patent proprietor)'s arguments in written form may be summarised as follows:



On the basis of the documents (A12) and (A13) and additionally taking account of documents (E27), (E28) and (E29), the "oxidation index" was a well-known parameter for the detection of the oxidation of phospholipids. Prepublished documents (A12) and (E28) indicated in particular that even the choice of the solvent for performing the measurement was no problem with regard to liposome preparations.

Thus, the measurement of the "oxidation index" in principle was no problem with respect to formulations containing phospholipids or liposome preparations and consequently also for the penetrants of the patent in suit.

In particular, the appellant (opponent) had merely made assertions, without having performed measurements and having demonstrated their failure.

XII. The appellant (patent proprietor) requested in writing that the decision under appeal be set aside and that the patent be maintained on the basis of the set of claims filed as main request or on the basis of one of the sets of claims of the first and second auxiliary requests, filed with letter of 24 October 2007, or on the basis of one of the sets of claims of the third to seventh auxiliary requests, all filed with letter of 30 April 2008. It further requested that the appeal of the appellant (opponent) be dismissed (eighth auxiliary request) or, in the alternative, that the patent be maintained on the basis of one of the sets of claims filed as ninth to fourteenth auxiliary requests filed with letter of 30 April 2008.

XIII. The appellant (opponent) requested in writing that the appeal of the patent proprietor be rejected as inadmissible. Further it requested that the decision under appeal be set aside and that the European patent No. 1 140 021 be revoked.

### **Reasons for the Decision**

1. Admissibility of the appeals

1.1 The opponent objected to the admissibility of the proprietor's appeal against the decision under appeal. It requested an interlocutory decision on this issue.

1.2 Regarding the calculation of the time limit for filing the notice of appeal, Rule 83(2) EPC 1973 (now Rule 131(2) EPC 2000) provides that where a procedural step is a notification, computation starts on the day following the receipt of the document notified, unless otherwise provided. Pursuant to Rule 78(2) EPC 1973 (now Rule 126(2) EPC 2000), in cases where notification is effected by registered letter such a letter is deemed to be delivered to the addressee on the tenth day following its posting, unless the letter has failed to reach the addressee or has reached him at a later date. If a period expires on a day on which one of the filing offices of the European Patent Office is not open for receipt of documents or on which mail is not delivered there, the period extends to the first day thereafter on which all the filing offices are open for receipt of documents and on which mail is delivered (Rule 85(1) EPC 1973, now Rule 134(1) EPC 2000).

1.3 In the case under consideration, the decision of the opposition division was notified by registered mail with advice of delivery pursuant to Rule 78(1) EPC 1973 (now Rule 126(1) EPC 2000). It was posted on 22 June 2007. According to the advice of delivery, the decision was received by the proprietor's representative on 26 June 2007, i.e. within ten days following its posting. Therefore, the fiction of Rule 78(2) EPC 1973 (now Rule 126(2) EPC 2000) applies for the calculation of the starting day of the time limit and the decision is deemed to have been notified on the tenth day following its posting, i.e. on 2 July 2007. Pursuant to Rule 83(2) EPC 1973 (now Rule 131(2) EPC 2000), the two-month period for filing the notice of appeal ended on 2 September 2007, which however was a Sunday. Therefore, the time limit for filing the notice of appeal was extended pursuant to Rule 85(1) EPC 1973 (now Rule 134(1) EPC 2000) until Monday, 3 September 2007. Thus, the proprietor's notice of appeal of 3 September 2007 was filed in due time.

1.4 Since the remaining requirements for admissibility are also fulfilled, the proprietor's appeal is admissible. The opponent's appeal is likewise admissible.

1.5 The board was not bound to decide on the admissibility of the proprietor's appeal in advance of the oral proceedings to which the parties were summoned and did not consider it necessary, on the basis of the reasons advanced by the opponent, to issue an interlocutory decision on this issue.

2. *Requirements of Article 83 EPC 1973; all requests*

2.1 The subject-matter of claims 1 of all requests relates to formulations comprising penetrants, in some of the claims in the form of fluid droplets comprising amphiphilic substances in their coating, that enable corticosteroid permeation through the pores after penetrants have entered pores, the formulations being characterised by a content of corticosteroids and by a content of an amount of antioxidant that provides for stability of the formulation in terms of the increase of oxidation index to be less than 100 % per 6 months.

2.2 Claims 1 of all requests thus contain the characterising functional feature that the claimed formulation must comprise "at least one antioxidant in an amount that reduces the increase of oxidation index to less than 100 % per 6 months".

Consequently, in order to carry out the invention characterised by that parameter, the skilled person must be able to measure in a clear and complete way an "oxidation index" and, in its follow-up, the "reduction of the increase of oxidation index to less than 100 % per 6 months" in any one of the formulations he tries to produce according to the features set out in claims 1 of the requests.

2.3 However, the parameter "oxidation index" is not defined in the patent in suit, and in none of the examples is this parameter measured; no method of measuring is indicated in the patent in suit.

In addition, there is no indication whether "oxidation index" is to be measured for the overall formulation or for any ingredient it contains, be it a penetrant or any substance contained therein.

Under these circumstances, measuring the "oxidation index" under Article 83 EPC 1973 for the skilled person is only possible if he knows from his common general knowledge how to do that with respect to a formulation as claimed or to penetrants comprised in formulations according to the main request or to an amphiphilic substance which may be used to produce formulations according to claims 1 of one of the first to fourteenth auxiliary requests.

2.4 The appellant (patent proprietor) has submitted evidence to support the view that there was common general knowledge enabling the skilled person to carry out the invention.

2.4.1 However, the assessment of the mention of the term "oxidation index" in document (A12) and its repetition in the comprehensive book on liposomes (A13) and its mention in documents (E27), (E28) and (E29) reveals that the description of "oxidation index" is limited to phospholipid-containing liposomes.

Document (A12) relates to the screening of liposome preparations for autoxidation by measuring the change in absorbance at 233 nm. Based on the factual use of lecithin as the substance to be oxidised, an "oxidation index" was defined as the ratio of the absorption at 233 nm to the absorption at 215 nm (see document (A12), page 488, second and third paragraph).

Conditions for recording ultraviolet spectra of lecithin, or other phospholipid, as a liposome preparation were indicated (see document (A12), page 487, first paragraph, last sentence and the directly following first sentence of the next paragraph).

From this context it is clear that any mention of liposome preparations and measurement of autoxidation in this document relates to lecithin and at most to phospholipids, even if that is not repeated in every paragraph mentioning liposome preparations (for instance document (A12), page 487, first paragraph, last sentence and page 489, second paragraph as cited by the appellant (patent proprietor)).

Document (A13) refers to document (A12) and discloses nothing else; on the contrary, it is emphasised that the "index of oxidation" relates to peroxidation of egg yolk phosphatidylcholine. The major problem with the "index of oxidation" was that the absorption at 215 nm could not be used to quantitate phospholipids, since it was very sensitive to their exact molecular composition (see document (A13), page 360, second paragraph).

Documents (E27), (E28) and (E29) also relate to phosphatidylcholine or to phosphatidylcholine liposomes (see titles and abstracts) and not to liposomes in general, not even to phospholipid-containing liposomes in general.

Thus, by means of the cited documents the term "oxidation index" is defined for phosphatidylcholine

and for phosphatidylcholine-containing liposomes; it is set out that on its basis measuring methods could be derived for oxidation-phenomena of phospholipids and liposomes containing them.

2.4.2 However, phospholipids are only optional examples in their use to prepare formulations according to the patent in suit; they are not mentioned in claims 1 of the requests. Only in claim 18 of the patent in suit (and corresponding claims in the current requests) is it set out that "a lipid or a lipoid from a biological source or a corresponding synthetic lipid or any of its modifications, said lipid preferably belonging to the class of pure phospholipids with the chemical formula ...") may form an ingredient in the claimed formulation as a "lipid or lipid-like material" as one of multiple possibilities. Claim 19 of the patent in suit contains only a few examples concerning phospholipids in a very long list of other compounds.

Consequently, in the formulations of claims 1 as requested phospholipids represent only a very small section of the possible ingredients claimed.

Therefore, common general knowledge on the issue "oxidation index" is not available for the whole scope of the patent in suit and the teaching as claimed according to the current requests is not disclosed in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art.

2.5 Under these circumstances, the introduction into the claims of particular antioxidants and ranges for their concentration to be applied does not help.

2.5.1 On the one hand, the feature "the formulation comprises at least one antioxidant in an amount that reduces the increase of oxidation index to less than 100 % per 6 months" is still contained in the claims. It must still be fulfilled when carrying out its teaching and, consequently, the skilled person must be able to measure it, to be sure that this feature is met by the produced formulation.

2.5.2 Basically, however, nowhere in the patent in suit is any suggestion to be found that the use of any particular antioxidant in a particular concentration would make sure that the feature "the formulation comprises at least one antioxidant in an amount that reduces the increase of oxidation index to less than 100 % per 6 months" was fulfilled automatically or mandatorily. In the absence of any disclosure of a factually performed measurement of this feature, there is also no support of such a situation to be found in the patent in suit.

The assumption of the opposition division that, based on particular lists of antioxidants together with ranges of concentration, it could be seen for sure that the "oxidation index"-feature was fulfilled, is an unfounded assertion; even the patent proprietor avoided making it during the proceedings (see for instance page 20 of its letter of 30 April 2008, fourth paragraph: "... containing the particularly narrow ranges for antioxidants or microbicides respectively, to ensure that in this respect there should be no further doubt on the "probability" of carrying out the teaching").



Therefore, this assumption cannot be the basis for a decision in favour of maintenance of the patent in suit or any amended version of it as long as the "oxidation index"-feature is present.

- 2.6 In the circumstances of the case, the further argument of the appellant (patent proprietor) with respect to Article 83 EPC 1973 cannot succeed:

Requesting the appellant (opponent) to perform experiments to show that the teaching of the patent in suit cannot be carried out is not appropriate where, as in the patent in suit, the method to be performed is missing.

- 2.7 Therefore, no method for measuring the "oxidation index"-parameter of claims 1 of all requests which would have enabled the skilled person to carry out the invention within the full scope of the claims was disclosed in the patent or known in the art at the filing date.

3. Consequently, amended claims 1 of the main request and of the first to fourteenth auxiliary requests do not disclose the invention in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art (Article 83 EPC 1973) over the whole of the broad field claimed.

**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:

N. Maslin

U. Oswald