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**Datasheet for the decision
of 3 May 2016**

Case Number: T 0284/13 - 3.3.07

Application Number: 05771775.3

Publication Number: 1789025

IPC: A61K9/70

Language of the proceedings: EN

Title of invention:

DEVICE FOR TRANSDERMAL DELIVERY OF ACTIVE PRINCIPLES

Patent Proprietor:

LABORATORIO ITALIANO BIOCHIMICO
FARMACEUTICO LISAPHARMA S.P.A.

Opponent:

BEIERSDORF AG

Relevant legal provisions:

EPC Art. 56, 100(a)

Keyword:

Inventive step - (no)



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Case Number: T 0284/13 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 3 May 2016

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Decision under appeal: **Decision of the Opposition Division of the European Patent Office posted on 26 November 2012 rejecting the opposition filed against European patent No. 1789025 pursuant to Article 101(2) EPC.**

Composition of the Board:

Chairwoman P. Schmitz
Members: D. Semino
D. Boulois

Summary of Facts and Submissions

I. European patent number EP 1 789 025 was granted on the basis of 13 claims. Independent claim 1 read as follows:

"1. Two-layered patch for dermal or transdermal administration of active principles consisting of:

- a) a first layer having a homogeneous composition and consisting of
 - at least one active principle,
 - a water-soluble film-forming agent selected from the group consisting of carboxymethylcellulose, chitosan, aqueous dispersions of acrylic and methacrylic polymers and polyvinyl alcohol,
 - a hydrophilic adhesive polymer, chosen from the group consisting of polyvinylpyrrolidone, tragacanth gum, arabic gum, karaya gum, xanthan gum, pectin and, polyaminomethacrylate adhesives,
 - at least one substance acting as absorption promoter and/or humectant and/or plasticiser chosen from the group consisting of glycerine, ethyl alcohol, propylene glycol, polyethylene glycol of molecular weight between 400 and 6000, sorbitol, phospholipids, terpenes, soya lecithin, phosphatidylcholine, cholesterol, cyclodextrin, isopropyl myristate, oleic acid, polysorbate 80 and diethylene glycol monoethyl ether, said first layer (a) having a residual water content lower than 20%;
- b) a second layer joined in a permanent manner to the first and having a permeability to water vapour of less than 500 g/m² in 24 hours, provided that:
when said adhesive in said layer (a) is polyaminomethacrylate and it is butylmethacrylate/(2-dimethylaminoethyl)-methacrylate/methylmethacrylate

copolymer in which the ratio between the monomers is 1:2:1, said water-soluble film-forming agent must be different from carboxymethylcellulose."

II. A notice of opposition was filed in which revocation of the patent in its entirety was requested.

III. In the decision under appeal, the following documents were cited, *inter alia*:

D2: WO-A-99/15210

D3: EP-A-0 184 470

D5: WO-A-03/101360

D13: WO-A-02/30402

IV. The decision of the opposition division rejecting the opposition was announced at the oral proceedings on 18 October 2012. As far as relevant to the present decision, it can be summarised as follows:

The patch of claim 1 differed from the disclosure of document D13, which was the closest prior art, in the presence of a specific backing layer, which caused a prolonged and enhanced release of the active compound. The problem was the provision of a transdermal patch endowed with an improved release of the active agent and the solution was not obvious, since D2 did not unambiguously link a backing layer to an improvement of the release, which depended on many factors. Documents D3, D5 and D2 could not represent the closest prior art and could therefore not lead to a different result. In particular, D2 was not directed to improving the release of active principle, but rather to improving and prolonging the adhesiveness of the patch to the site of application and to the provision of a patch which

acquired adhesiveness after contact with wet skin, which was not an aim of the patent. Moreover, although application on the skin was occasionally mentioned in D2, the document was mainly related to the administration to a moist mucosa and was therefore in a different field of application than the opposed patent, which was solely directed to the administration to the skin.

- V. The opponent (appellant) lodged an appeal against that decision. With the statement setting out the grounds of appeal, the appellant contested the decision *inter alia* insofar as inventive step was concerned.

- VI. With the reply to the statement setting out the grounds of appeal, the patent proprietor (respondent) filed four sets of claims as first to fourth auxiliary requests.

Claim 1 of the first auxiliary request corresponded to granted claim 1 with the replacement of the term "active principle(s)" with "drug(s)". Claim 1 of the second auxiliary request corresponded to claim 1 of the first auxiliary request with the amendment of the condition on the water content to "water in a maximum quantity of 20%". This condition was amended to "water in a quantity of from 1 to 20%" and "water in a quantity of from 1 to 15%" in claim 1 according to the third and to the fourth auxiliary requests respectively.

- VII. In a communication sent in preparation of oral proceedings, the Board reviewed the submissions of the parties and in particular with regard to inventive step, expressed the preliminary opinion that "a document disclosing a two-layer patch (as the one claimed) should be taken as a starting point for the analysis of inventive step", that, in any case, "as all the

documents cited by the parties as closest prior art are reasonable starting points, inventive step can only be acknowledged, if the claimed patch is inventive with respect to any of them" and that this was "all the more valid for a document, such as D2, which discloses a two-layered patch developed for a similar purpose (topical administration of active agents with prolonged and/or multiple therapeutic effects, see last paragraph of page 3) and with a very similar composition to the claimed one" (point 3.1 in the communication).

- VIII. Oral proceedings were held on 3 May 2016 in the absence of the respondent as announced by letter of 2 March 2016.
- IX. The appellant's arguments, insofar as relevant to the present decision, can be summarised as follows:

Patent as granted - inventive step

The choice of document D13 as the closest prior art taken in the decision under appeal was a wrong one in view of the absence of the backing layer with all its related features and of the different problem stated therein, namely the preparation of patches in an easy and economic way without using organic solvents. Instead documents D2 or D4 should be taken as the closest prior art. D2, in particular, related to two-layer patches for dermal or transdermal administration of medicaments and disclosed in its example 23 a patch, from which the patch of granted claim 1 differed only in that as film-forming agent a component selected from carboxymethylcellulose, chitosan, aqueous dispersions of acrylic and methacrylic polymers and polyvinyl alcohol was used instead of ethylcellulose. As no effect was related to the choice of a different film-forming agent,

the problem was the provision of an alternative composition and the solution was not inventive *inter alia* in view of D2 itself, which disclosed carboxymethylcellulose and chitosan as suitable bioadhesive polymers in a list including also ethylcellulose.

Auxiliary requests - inventive step

The same arguments on inventive step applied to claim 1 according to the auxiliary requests, as the specification that the active agent was a drug did not constitute an additional difference (example 23 of D2 included insulin) and as a quantity of water below 20%, between 1 and 20% or between 1 and 15% did not provide any advantage over absence of water and D2 itself indicated that it was desirable to have a water quantity of less than 10% by weight.

- X. The respondent's arguments, insofar as relevant to the present decision, can be summarised as follows:

Patent as granted - inventive step

The opposition division was correct both with regard to the reasons why D2 should not be taken as the closest prior art and as to why this document did not provide the solution to the objective problem formulated when starting from document D13 as the closest prior art.

With regard to the auxiliary requests, no additional arguments on inventive step were provided by the respondent.

- XI. The appellant requested that the decision under appeal be set aside and the patent be revoked.

XII. The respondent requested that the appeal be dismissed, alternatively that the decision under appeal be set aside and the patent be maintained according to one of the four sets of claims filed as first to fourth auxiliary requests with the reply to the statement setting out the grounds of appeal.

Reasons for the Decision

Patent as granted - inventive step

1. The main point of disagreement between the parties concerned the choice of the closest prior art, whereby the appellant argued that document D2 (or alternatively D4) should be taken as starting point, while the respondent maintained the position in the decision under appeal that document D2 should not be considered as the closest prior art.
- 1.1 The patent in suit concerns devices for the delivery of active principles for dermal and transdermal application (field of the invention, paragraph [0001] of the patent) in particular in the form of two-layer patches (claim 1) and aims at avoiding drawbacks of the prior art products, including transport of active principle which is not maintained constant for long periods of time and dispersion of active principle into the environment or onto any clothes (paragraphs [0011] to [0013]).
- 1.2 Document D2 relates to bioadhesive compositions for topical administration of active agents (background of the invention, page 1, first paragraph), *inter alia* to bioadhesive compositions which achieve prolonged and/or multiple therapeutic effects (page 3, last paragraph) and serve as a pressure-sensitive adhesive suitable for

prolonged adherence to either wet/moist surfaces or dry surfaces, such as skin, for controlled release of an active agent therefrom (page 4, first paragraph). The compositions of D2 typically include a backing layer occlusive to water permeation to prevent loss of the active agent to the environment (page 66, last full paragraph).

- 1.3 In view of this, D2 cannot be considered as belonging to a different field of application than the opposed patent. On the contrary, it belongs to the same field of application and discloses two-layer patches similar to the ones claimed. On this basis, it is a promising candidate in the choice of the closest prior art and cannot be discarded in the analysis of inventive step.
- 1.4 Since inventive step can be acknowledged only if the claimed patch is inventive with respect to any reasonable starting point, including D2, the inventive step attack of the appellant starting from D2 must be evaluated. In this respect a discussion whether document D13, as chosen in the appealed decision, is closer than D2 to the claimed invention is, in view of the conclusion reached below (see point 1.11), purely academic, as it cannot change this conclusion.
- 1.5 Example 23 of D2 (table on page 79) discloses a composition consisting of 1% insulin (a drug), 25% polyvinylpyrrolidone (a hydrophilic adhesive polymer according to the list in granted claim 1), 14% ethyl cellulose (a film-forming agent) and 60% oleic acid (an additional substance according to the list in granted claim 1), the percentages indicating weight percent by dry weight of the total bioadhesive composition (page 73, first paragraph). The composition is prepared according to example 2 (page 72, last paragraph),

wherein the ingredients including a solvent (ethyl acetate for example 23) are mixed thoroughly until the mixture is completely homogeneous and thereafter the solvent is removed. A delivery system according to D2 is typically prepared (page 65, second full paragraph to page 66, last full paragraph) in a process including uniform mixing of the ingredients, coating the obtained composition on a release liner followed by solvent removal and bringing into contact with a backing layer, which is typically occlusive to water permeation, followed by winding into rolls.

- 1.6 The two-layer patch of granted claim 1 differs from the device of D2 in that a film-forming agent selected from the group consisting of carboxymethylcellulose, chitosan, aqueous dispersions of acrylic and methacrylic polymers and polyvinyl alcohol is used instead of ethyl cellulose.
- 1.7 In this respect it is noted that it was not disputed that an occlusive material is a material which meets the condition on permeability to water vapour in granted claim 1. Moreover, a residual water content lower than 20% indicates a quantity of water which can be arbitrarily small and up to 20%, which feature is implicitly fulfilled by the composition of example 23 of D2, which formally does not foresee the presence of water, but in which, as in any composition produced in the presence of ambient air, a total absence of water is not physically obtainable.
- 1.8 No data are present to show whether the use of any of the listed film-forming polymers provides any advantage or improvement over the composition of D2 containing ethylcellulose.

- 1.9 On that basis, the technical problem, starting from the device of D2, is the provision of a further two-layer patch for dermal administration of drugs.
- 1.10 Document D2 itself discloses ethylcellulose in a list of alternative polymers including also chitosan and carboxymethylcellulose (paragraph bridging pages 8 and 9), which are all disclosed as equally favourable ingredients. The skilled person, therefore, aiming at providing a further two-layer patch, would replace ethylcellulose with chitosan or carboxymethylcellulose as equally favourable polymers in view of the teaching of D2 without exercising any inventive activity.
- 1.11 On that basis, the two-layer patch of granted claim 1 does not involve an inventive step.

Auxiliary requests - inventive step

2. Claim 1 of the first auxiliary request corresponds to granted claim 1 with the replacement of the term "active principle(s)" with "drug(s)".
 - 2.1 As the composition of example 23 of D2 contains insulin, which is undisputedly a drug, the analysis of inventive step developed for granted claim 1 equally applies to claim 1 of the first auxiliary request, with the consequence that the two-layer patch of claim 1 of the first auxiliary request does not involve an inventive step.
3. Claim 1 of the second auxiliary request corresponds to claim 1 of the first auxiliary request with the amendment on the condition on the water content to "water in a maximum quantity of 20%".

- 3.1 The condition still means that water is present in the composition in a quantity which can be arbitrarily small and up to 20% and therefore does not change the analysis of inventive step developed for the main request (see in particular point 1.7, above) with the consequence that the two-layer patch of claim 1 of the second auxiliary request does not involve an inventive step for the same reasons as developed for the main and the first auxiliary requests.
4. The condition on the quantity of water is amended to "water in a quantity of from 1 to 20%" and "water in a quantity of from 1 to 15%" in claim 1 according to the third and to the fourth auxiliary requests respectively with respect to claim 1 according to the second auxiliary request.
- 4.1 While it is inevitable that the composition of example 23 of D2 contains an (arbitrarily) small quantity of water (see point 1.7, above), there are no reasons to assume that this quantity is above 1% as required by claim 1 according to the third and fourth auxiliary requests, so that it must be acknowledged that a further difference is present with respect to the disclosure in D2. However, no effect has been shown to be related to the presence of water in the claimed quantity, nor to the combination of the two distinguishing features, so that the technical problem remains the same as formulated for granted claim 1 (see point 1.9, above).
- 4.2 While the replacement of ethylcellulose is not inventive for the same reasons as detailed above (see point 1.10), also the presence of water in the specified range(s) is obvious still over document D2 itself, which discloses that its compositions are "substantially water-free", i.e. contain less than about 10% by weight water

(preferably less than 5% and most preferably less than 3%) prior to application (page 12, first paragraph). The skilled person, therefore, aiming at providing a further two-layer patch, would pick a quantity of water within the ranges in the claim without exercising any inventive activity.

- 4.3 For these reasons, the two-layer patch of claim 1 of the third and fourth auxiliary requests does not involve an inventive step.

Conclusion

5. As claim 1 according to all request on file does not involve an inventive step, there is no need to analyse any other objection and the patent is to be revoked.

Order

For these reasons it is decided that:

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

The Registrar:

The Chairwoman:



S. Fabiani

P. Schmitz

Decision electronically authenticated