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Datasheet for the decision of 17 March 2023

Case Number: T 0489/20 - 3.3.07

Application Number: 12826670.7

Publication Number: 2790685

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Language of the proceedings: EN

Title of invention:
TRANSDERMAL DELIVERY SYSTEM COMPRISING BUPRENORPHINE

Patent Proprietor:
LTS LOHMANN Therapie-Systeme AG

Opponents:
Luye Pharma Switzerland AG
Pajaro Limited
Hexal AG
Swindell & Pearson Limited

Headword:
Buprenorphine/LOHMANN

Relevant legal provisions:
RPBA 2020 Art. 15a(1), 13(2)
EPC Art. 83, 54, 56

Keyword:

Amendment after summons
Sufficiency of disclosure - (yes)
Novelty - (yes)
Inventive step - (yes)

Decisions cited:

T 2080/18, G 0001/21, T 0259/15

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Case Number: T 0489/20 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 17 March 2023

Appellant: (Patent Proprietor)	LTS LOHMANN Therapie-Systeme AG Lohmannstrasse 2 56626 Andernach (DE)
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Respondent: (Opponent 3)	Hexal AG Industriestrasse 25 83607 Holzkirchen (DE)
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Respondent: (Opponent 4)	Swindell & Pearson Limited 48 Friar Gate Derby Derbyshire DE1 1GY (GB)
Representative:	FRKelly 27 Clyde Road Dublin D04 F838 (IE)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 20 December 2019 revoking European patent No. 2790685 pursuant to Article 101(3)(b) EPC.**

Composition of the Board:

Chairman	A. Usuelli
Members:	M. Steendijk
	L. Basterreix

Summary of Facts and Submissions

I. European patent 2 790 685 ("the patent") was granted on the basis of twenty-one claims.

Independent claim 1 of the patent as granted defined the following subject-matter:

"Transdermal therapeutic system for the transdermal administration of buprenorphine, comprising a buprenorphine containing self-adhesive layer structure comprising

A) a buprenorphine-impermeable backing layer, and
B) a buprenorphine-containing pressure-sensitive adhesive layer on said buprenorphine-impermeable backing layer, the adhesive layer comprising

a) at least one polymer-based pressure-sensitive adhesive,
b) an analgesically effective amount of buprenorphine base or a pharmaceutically acceptable salt thereof,
and
c) a carboxylic acid selected from the group consisting of oleic acid, linoleic acid, linolenic acid, levulinic acid and mixtures thereof, in an amount sufficient so that said analgesically effective amount of buprenorphine is solubilized therein to form a mixture, and the carboxylic acid buprenorphine mixture forms dispersed deposits in the said pressure-sensitive adhesive,

wherein said buprenorphine-containing pressure-sensitive adhesive layer is the skin contact layer for use in a method of treating pain by applying a transdermal therapeutic system for 7 days on the skin of a patient."

Claim 20 as granted defined a method as follows:

"Method of manufacture of a transdermal therapeutic system for the transdermal administration of buprenorphine in accordance with any one of claims 1 to 19, comprising the steps of

1. providing a buprenorphine-containing adhesive mixture or solution comprising
   a) buprenorphine base or a pharmaceutically acceptable salt thereof
   b) a carboxylic acid,
   c) a polymer-based pressure-sensitive adhesive, and
   d) solvent
2. coating said buprenorphine-containing adhesive mixture or solution on a film in an amount to provide the desired coating dry weight,
3. drying said coated buprenorphine-containing adhesive mixture or solution to provide a buprenorphine-containing adhesive layer with the desired coating dry weight,
4. laminating said buprenorphine-containing adhesive layer to a backing layer to provide an buprenorphinecontaining self-adhesive layer structure,
5. punching the individual systems from the buprenorphine-containing self-adhesive layer structure with the desired area of release, and

6. optionally adhering to the individual systems an active-free self-adhesive layer structure comprising also a backing layer and an active agent-free pressure-sensitive adhesive layer and which is larger than the individual systems of buprenorphine-containing self-adhesive layer structure."

II. Four oppositions were filed against the grant of the patent on the grounds that its subject-matter lacked novelty and inventive step and that the claimed invention was not sufficiently disclosed.

The patent proprietor filed the appeal against the decision of the opposition division to revoke the patent. The decision was based on the patent as granted (main request), auxiliary requests I, II, III as filed on 23 August 2019 (corresponding to auxiliary requests requests III, I and II as filed on 5 October 2018) and auxiliary request IV as filed during the oral proceedings before the opposition division held on 23 October 2019.

In its decision the opposition division cited *inter alia* the following documents:

D1: US 2010/0119585 A1
D3: WO 98/36728
D11: US 2010/0112064 A1
D30: Tabular presentation of results of Examples 6 and 7 from the patent filed by opponent 3 during the oral proceedings on 23 October 2019.

The opposition division came to the following conclusions:

(a) The claimed subject-matter evidently concerned a TTS involving a biphasic structure which was sufficiently disclosed in the patent.

(b) Document D1 disclosed in claims 1 and 7 a TTS for administration of buprenorphine comprising a backing layer and a pressure-sensitive adhesive layer for application to the skin, wherein the adhesive layer comprises droplets of a buprenorphine/carboxylic acid solution and wherein the said carboxylic acid is selected from oleic acid, linoleic acid, linolenic acid and levulinic acid. Document D1 further described in paragraph [0027] various possible periods of time for the duration of administration, including administration during 168 hours (7 days).

The subject-matter of claims 1-4 as granted lacked novelty in view of document D1, as it merely resulted from the single selection of the 7 day duration of administration already described in document D1.

(c) Claim 1 of auxiliary request I defined with respect to granted claim 1 additionally that the adhesive layer contains more than 0.6 mg/cm^2 of buprenorphine base.

Document D1 represented the most promising starting point in the prior art. The only difference between the claimed subject-matter and this prior art concerned the definition of the buprenorphine concentration.

In the absence of evidence of any particular effect from the distinguishing feature, the problem to be

solved was seen in the provision of an alternative buprenorphine TTS suitable for pain treatment by application on the skin for 7 days.

Document D1 already suggested that the buprenorphine concentration and surface area of the described TTS can be adjusted to influence the release profile of the buprenorphine. Moreover, as acknowledged in the patent and described in document D3, available buprenorphine preparations for 7 day application were known to comprise 0.8 mg/cm^2 buprenorphine.

The claimed subject-matter was therefore obvious as solution to the identified objective technical problem.

(d) Auxiliary requests II and III did not meet the requirement of novelty in view of document D1.

(e) Auxiliary request IV was not admitted into the proceedings.

III. With the statement of grounds of appeal the appellant (patent proprietor) filed document D31, which provided an extended tabular presentation of results of Examples 6 and 7, and requested that the patent be maintained as granted (main request) or on the basis of one of auxiliary requests I, II, III or IV corresponding to auxiliary requests requests I, IV, II and III on which the decision under appeal was based.

IV. With the summons of 22 April 2022 the parties were invited to attend oral proceedings on 17 March 2023 on the premises of the European Patent Office.

In its communication pursuant to Article 15(1) RPBA the Board expressed *inter alia* the preliminary opinion that the decision under appeal did not involve any substantial procedural violation and that the patent as granted met the requirements of sufficiency of disclosure, novelty and inventive step.

V. In the letter of 17 January 2023 respondent-opponent 1 objected that the method of claim 20 was not characterized by the use in a dosage regimen as defined for the composition of claim 1.

VI. With the letter of 16 February 2023 the appellant filed auxiliary requests V to IX, which corresponded respectively to the main request and auxiliary requests I to IV, in which the claims directed to the method of manufacture (see claim 20 as granted) are deleted.

VII. In the letter of 16 February 2023 the appellant requested arrangement of a video link to allow the remote attendance to the oral proceedings by an accompanying person. In response the Board informed the parties with the communication of 23 February 2023 that it would consider the arrangement for the oral proceedings to take place by videoconference if all parties agreed to such format, but that the Board was not in the position to arrange a video link for the attendance of an individual participant.

VIII. With their letters of 23 February 2023 and 2 March 2023 respondent-opponent 2 and respondent-opponent 3 informed the Board that they did not consent to the oral proceedings being held in the form of a videoconference. With the letter of 2 March 2023 respondent-opponent 4 announced not to attend the oral proceedings on 17 March 2023 if these oral proceedings

were held in person. In its communication of 8 March 2023 the Board informed the parties that the oral proceedings were to be held in person.

IX. During the oral proceedings held on 17 March 2023 the appellant withdrew its main request concerning the patent as granted and maintained auxiliary request V filed on 16 February 2023 as its new main request.

X. The arguments of the appellant relevant to the present decision are summarized as follows:

The decision under appeal was affected by procedural violations involving new reasons for denying novelty, the admittance of document D30 during the oral proceedings which precluded an adequate response from the appellant, unclear reasoning on inventive step and the wrong application of discretion in not admitting auxiliary request IV.

Document D31 provided a more comprehensive presentation of the results from examples 6 and 7 of the patent than document D30 and was to be admitted as a justified response to the filing of document D30 and the findings in the decision under appeal.

The deletion of the process claims in accordance with the new main request did not affect the considerations with respect to the remaining claims. The filing of the request was prompted by the argument from respondent-opponent 1 that the defined process was not characterized by the dosage regimen of claim 1.

In accordance with claim 1 of the main request the mixture of the carboxylic acid and the buprenorphine is dispersed and not dissolved in the adhesive. It was therefore evident to the skilled person that the defined TTS was based on a biphasic system. The patent provided sufficient instructions for the preparation of such systems.

Document D1 presented in claim 1 a generic disclosure of a TTS comprising droplets of buprenorphine dissolved in a carboxylic acid and dispersed in a matrix layer. This generic disclosure covered embodiments in which a buprenorphine containing matrix layer is for contact with the skin as well as embodiments in which an additional skin contact layer separates the buprenorphine containing matrix layer from the skin. This additional skin contact layer prevented according to document D1 premature exhaustion of the TTS. Document D1 further described that the transdermal therapeutic system can be modified and used for different durations of administration, including a longer duration of 7 days (168 hours). However, document D1 did not directly and unambiguously disclose which modification would allow the administration during 7 days.

The problem to be solved in view of document D1 was to be seen in the provision of a TTS with a biphasic structure for administration of buprenorphine in pain treatment by the prolonged application during 7 days. The experimental results reported in the patent as presented in document D31 demonstrated that this problem was indeed solved. Document D1 pointed to the problem of the premature exhaustion of the TTS due to excessively rapid

delivery of the active ingredient in case the delivery of the acid is too quick. According to document D1 such premature exhaustion could be prevented by including an additional polyacrylate based layer. The experimental results reported in document D1 indicated that the exemplified compositions of examples 1-4 already released practically all of the acid after 72 hours, even though each of these examples included an additional polyacrylate based skin contact layer. Document D1 provided no indication how a prolonged duration of 7 days could be achieved without the mentioned additional layer.

XI. The arguments of the respondents relevant to the present decision are summarized as follows:

Document D31 was not to be admitted for lack of relevance.

The objections against process claim 20 as granted had been maintained in the reply to the appeal by respondent-opponent 1. The late filing of the new main request was not justified by any exceptional circumstances.

According to the patent the dispersed deposits defined in the claims concerned distinguishable areas within the adhesive, such as visually distinguishable areas that could be identified microscopically. The patent failed to disclose how dispersed deposits which are not visually distinguishable could be distinguished and did therefore not sufficiently disclose the invention over the whole scope of the claims.

Document D1 disclosed a TTS for the administration of buprenorphine having the same structure as defined in claim 1 of the patent and mentioned different durations of administration, including the possible duration of 7 days. The definition in claim 1 of document D1 that the TTS comprised at least one pressure-sensitive adhesive matrix layer indicated a default structure with a single matrix layer for contact with the skin as represented in Figure 1 of document D1. The presence of an additional layer as illustrated by the embodiment of Figure 2 of document D1 was merely optional. Moreover, this additional layer could alternatively be located between the backing layer and the matrix layer, which also corresponded to a structure covered by claim 1 of the main request. The subject-matter of claim 1 of the main request thus resulted with respect to document D1 from a single selection regarding the administration duration and therefore lacked novelty.

In as far as the claimed TTS was considered new over the disclosure in document D1 on the basis of a combined selection of a structure having a single adhesive matrix layer for contact with the skin and the duration of administration of 7 days, the objective technical problem in view of document D1 merely concerned the provision of an alternative TTS for the administration of buprenorphine for a duration of 7 days. Document D3 demonstrated that buprenorphine could indeed be effectively administered for the duration of 7 days with a TTS having its matrix layer comprising the buprenorphine in contact with the skin. Document D1 itself explained that the release profile of the buprenorphine could for instance be influenced by

the appropriate variation of the thickness of the matrix layer or the concentration of the buprenorphine in the matrix. The provision of an additional polyacrylate-based layer was optional and only described as required if the delivery of the acid would otherwise be too quick causing premature exhaustion of the TTS. Moreover, the additional layer could according to document D1 be located between the backing layer and the matrix layer. Such a structure was included by the definition of claim 1 of the main request. Following the considerations in T 259/15 the implementation and testing of a TTS with the structure of claim 1 of the main request would not involve particular technical difficulties. Accordingly, the skilled person had a reasonable expectation that by following the instructions in paragraph [0024] of document D1 a TTS for administration of buprenorphine during 7 days could be prepared without an additional skin contact layer. The TTS of claim 1 of the main request therefore represented in view of the prior art an obvious solution to the relevant objective technical problem.

The difference of the claimed subject-matter with the TTS described in document D3 concerned the structure involving the dispersed deposits in the adhesive layer. The objective technical problem in view of document D3 concerned the provision of an alternative TTS for the administration of buprenorphine. The TTS defined in claim 1 represented an obvious solution in view of document D1, which indicated that a TTS with a structure involving the dispersed deposits as defined in claim 1 of the main request could be used for

administration of buprenorphine for the duration of 7 days.

XII. The appellant requested that the decision under appeal be set aside and that the patent be maintained on the basis of its main request corresponding to auxiliary requests V filed on 16 February 2023.

The appellant further requested that document D31 be admitted in the appeal proceedings and that document D30 not be admitted.

XIII. The respondents requested that the appeal be dismissed.

The respondents further requested that document D31 not be admitted into the appeal proceedings.

Respondent-opponent 1 also requested that the new main request filed as auxiliary requests V on 16 February 2023 not be admitted.

Reasons for the Decision

1. Format of the oral proceedings

According to Article 15a(1) RPBA the board may decide to hold oral proceedings by videoconference if the board considers it appropriate to do so, either upon request by a party or of its own motion. In view of the disapproval to hold the oral proceedings by videoconference expressed by respondent-opponent 2 and respondent-opponent 3 and in the absence of any particular circumstances as mentioned in G 1/21 (see section 49) the Board did not consider it appropriate to hold the oral proceedings by videoconference.

According to Article 15a(2) RPBA a party, representative or accompanying person may, upon request, be allowed to attend by videoconference in case oral proceedings are scheduled to be held on the premises of the European Patent Office. As pointed out in the communication of 23 February 2023 the Board was not in a position to arrange a video link for the attendance of individual participants.

2. Alleged procedural violations

In its preliminary opinion expressed in the communication pursuant to Article 15(1) RPBA (see section 2.2) the Board indicated why it considered that the decision under appeal did not involve any procedural errors that could justify remittal or reimbursement of the appeal fee.

Subsequently the appellant relied on its previous written submissions. Accordingly, the Board confirms its opinion that the decision under appeal did not involve any procedural errors that could justify remittal or reimbursement of the appeal fee.

3. Admittance documents D30 and D31

3.1.1 The Board observed in its communication pursuant to Article 15(1) RPBA that the tabular presentation in documents D30 and D31 merely highlighted experimental results already reported in the patent itself and additionally only indicated percentages of released buprenorphine calculated from these results. This observation was not contested by any of the parties. The Board therefore considers that the content of documents D30 and D31 is part of the arguments

developed by the parties on the basis of existing evidence and does not represent new evidence. The Board does therefore not recognize any ground for excluding these documents from the appeal proceedings.

Main request (filed as auxiliary request V on 16 February 2023)

4. Admittance main request

The new main request was filed with the appellant's letter of 16 February 2023 after respondent-opponent 1 objected in its letter of 17 January 2023 for the first time explicitly that the method of claim 20 as granted was not characterized by the use in a dosage regimen defined for the composition of claim 1.

The set of claims of the new main request differs from the set of claims as granted by the deletion of the process claims.

The deletion of claims in the new main request merely sets aside the objection of lack of inventive step against the process as defined in claim 20 as granted without affecting the issues, submissions and conclusions with regard to the remaining claims, which had always been the principal focus of the opposition and appeal proceedings.

Under these circumstances the Board considered that in as far as the new main request represented an amendment to the appellant's case, this amendment was to be admitted under Article 13(2) RPBA (compare T 2080/18, sections 5.1.4-5.1.6).

5. Sufficiency

Claim 1 of the main request defines that the buprenorphine is solubilized in the carboxylic acid and that the carboxylic acid buprenorphine mixture forms deposits which are dispersed in the pressure-sensitive adhesive. The claimed subject-matter thus involves an adhesive layer in the form of a biphasic dispersion as opposed to a solution. In this context the patent explains in paragraph [0025] that the term "deposit" refers to distinguishable, e.g. visually distinguishable, areas within the pressure-sensitive adhesive, such as droplets which may be identified by use of a microscope. The patent further provides detailed instructions (see paragraph [0116]) for the preparation of the defined TTS, which are further illustrated by the subsequently described examples. As the skilled person is well aware of the distinction between a biphasic dispersion and a solution the Board considers that the circumstance that the patent does not disclose how dispersed deposits which are not visually distinguishable could be identified does not cast serious doubts on the reproducibility of the claimed subject-matter.

Accordingly, the Board concludes that the patent sufficiently discloses the invention claimed in accordance with the main request.

6. Novelty

6.1.1 Document D1 discloses a TTS for the treatment of pain (see paragraph [0001]) comprising a backing layer and at least one pressure-sensitive adhesive matrix layer based on polysiloxanes or polyisobutylene wherein droplets of a buprenorphine/carboxylic acid solution

are dispersed (see claim 1), wherein the carboxylic acid is selected from the group consisting of oleic acid, levulinic acid, linoleic acid and linolenic acid (see claim 7). According to document D1 (see paragraph [0017]) this structure allows for the maintenance of the thermodynamic activity of the buprenorphine in the system during the delivery of the buprenorphine due to the concomitant skin absorption of the carboxylic acid.

Document D1 presents in Figure 1 a schematic design of a TTS with a backing layer and a matrix layer covered by a protecting layer to be removed before application of the matrix layer to the skin. Figure 2 presents a TTS additionally comprising a polyacrylate skin contact layer between the matrix layer and the protecting layer. This embodiment involving a polyacrylate skin contact layer is specifically defined in dependent claim 10 and corresponds to the examples of document D1 (see paragraphs [0029]-[0034]).

Document D1 further provides in paragraphs [0018], [0024] and [0027] the following information:

[0018] "A further aspect of the invention concerns the effect that in systems of this kind, if the delivery of the acid is too quick, the rise in the thermodynamic activity can lead to an excessive increase in the permeation rate following application. The consequence is that the TTS becomes prematurely exhausted as a result of excessively rapid delivery of active ingredient. It has now been found that this kind of effect is prevented by addition of a further layer based on polyacrylates. This layer is located preferably between the polymer matrix layer, containing active ingredient, and the skin, or else between matrix

layer and backing layer. This additional layer is preferably embodied as a self-adhesive skin contact layer."

[0024] "The transdermal therapeutic systems of the invention can be provided with different release profiles and in different dose strengths. As already described above, for example, the active ingredient release profile can be influenced by means, for example, of appropriate variation to the layer thickness of the active-ingredient-containing matrix and/or the skin contact layer, or by altering the concentration of active ingredient in the matrix. The dose strength of the TTS of the invention can be modified, for example, by varying the surface area of the active-ingredient-containing matrix, while keeping the composition and layer thickness of the matrix and skin contact layer the same, in order thus to obtain different dose strengths."

[0027] "The transdermal therapeutic systems of the invention can be modified and used for different durations of administration. The TTS of the invention can for example each be applied for at least 12 h or 24 h. With preference, however, the individual TTS of the invention can also be used over a respective application duration of at least 72 h, 84 h or 96 h. Longer application durations, however, are also possible, such as 120 h, 144 h or 168 h, for example."

6.1.2 Claim 1 of the main request defines a TTS structure having the buprenorphine containing adhesive layer (B) located on the backing layer (A) and wherein said buprenorphine containing layer is the skin contact layer. The wording "on the backing layer" clearly indicates that layer (B) is in contact with layer (A).

Accordingly, contrary to the respondents' argument this definition does not allow for a possible further layer in between the backing layer (A) and the buprenorphine containing adhesive layer (B).

Claim 1 of the main request, which is formulated in the format of Article 54(5) EPC, further defines the feature that the TTS is for use in a method of treating pain by applying the TTS for 7 days on the skin of a patient.

6.1.3 The Board observes that document D1 presents in claim 1 a generic disclosure requiring the TTS to comprise at least one matrix layer without individualizing a TTS structure in which the matrix layer is located on the backing layer and represents the layer for contact to the skin. This generic definition covers the embodiment of Figure 1 of document D1, in which the matrix layer is for contact with the skin as also required in claim 1 of the main request, as well as the embodiment of Figure 2 and claim 10 of document D1, in which the TTS comprises a separating skin contact layer which distinguishes it from the structure defined in claim 1 of the main request.

Paragraph [0027] of document D1 states in its opening phrase that the transdermal therapeutic systems of the invention can be modified and used for different durations of administration before presenting a list of durations, including a preferred duration of 72 h, 84 h or 96 h and possible longer durations such as 120 h, 144 h or 168 h.

Document D1 mentions in paragraphs [0018] and [0024] various modifications which influence the release profile of the TTS. In this context paragraph [0018]

specifically mentions that the early exhaustion of the TTS in case of disproportionate delivery of the carboxylic acid can be prevented by an additional layer based on polyacrylates, which is preferably located between the buprenorphine containing matrix layer and the skin. Paragraph [0024] further teaches that the release profile can for instance be influenced by appropriate variation of the layer thickness of the active-ingredient-containing matrix or the skin contact layer, or by altering the concentration of active ingredient in the matrix. However, document D1 does thereby not specifically disclose which modification allows for an administration duration of 7 days.

The Board therefore considers that document D1 does not directly and unambiguously disclose the utility of a TTS with a structure as defined in claim 1 of the main request for the defined application duration of 7 days.

6.1.4 Accordingly, the Board concludes that the subject-matter of claim 1 of the main request is new in view of document D1.

7. Inventive step

7.1 Closest prior art

7.1.1 The parties agreed that document D1 qualifies as a suitable starting point in the prior art.

7.1.2 Respondent-opponent 2 additionally relied on documents D3 and D11 as alternative starting points in the prior art.

Document D3 describes a TTS for the administration of buprenorphine for the duration of 7 days which is

prepared from a polyacrylate solution including buprenorphine and levulinic acid (see D3, pages 42-43, Example 1). In view of the prolonged administration duration of 7 days described for the TTS in document D3 the Board considers that document D3 represents a suitable alternative starting point in the prior art.

Document D11 relates to a TTS comprising at least a polysiloxane polymere base material comprising microreservoirs containing the active ingredient and an additive (see D11, paragraph [0009] and claim 1), wherein the active agent may be buprenorphine and the additive may be a fatty acid such as levulinic acid (see D11 paragraph [0011] and claim 6). The Board considers document D11 less pertinent than document D1, because document D11 describes a TTS with similar structure as document D1, but does not mention a 7 day application duration and does not focus on pain treatment with buprenorphine.

7.2 Problem to be solved

7.2.1 As indicated in section 6.1.3 above, the difference between the subject-matter of claim 1 of the main request with the teaching in document D1 concerns the combination of the feature defining the structure of the TTS in which the buprenorphine containing adhesive layer is on the backing layer and serves as the skin contact layer with the feature of the purpose of the pain treatment by an application duration of 7 days.

The difference between the subject-matter of claim 1 of the main request with the teaching in document D3 concerns the biphasic structure of the buprenorphine containing adhesive layer.

7.2.2 The results reported in examples 6 and 7 of the patent and summarized in document D31 indicate that the defined structure of the TTS allows to achieve delivery of buprenorphine for effective pain treatment over the duration of 7 days.

Starting from document D1 the problem to be solved may in view of these results be formulated as the provision of a TTS with a biphasic structure for administration of buprenorphine in pain treatment by the prolonged application during 7 days.

Starting from document D3 the problem to be solved may be formulated as the provision of an alternative TTS for administration of buprenorphine in pain treatment.

7.3 Assessment of the solution

The assessment whether the subject-matter defined in claim 1 of the main request was obvious to the skilled person as solution to the objective technical problem in view document D1 or document D3 critically depends on whether in view of the prior art the skilled person had a reasonable expectation of success that a TTS in which a biphasic buprenorphine containing adhesive layer is located on the backing layer and serves as the skin contact layer could provide for effective pain treatment for the duration of 7 days.

The only available prior art mentioning a TTS with a biphasic buprenorphine containing adhesive layer and a possible prolonged administration duration of 7 days is document D1.

Document D1 explains that the particular biphasic structure of the buprenorphine containing adhesive

layer allows for increased thermodynamic activity of the active ingredient buprenorphine and that a decrease in thermodynamic activity due to the delivery of the buprenorphine is compensated by the concomitant delivery of the carboxylic acid (see D1, paragraph [0017].

Document D1 further indicates (see paragraph [0027]) that the described compositions can be modified and used for different durations of administration, including longer application durations such as 168 h.

As mentioned in section 6.1.3 above, document D1 describes various modifications which influence the release profile of the TTS. Document D1 indicates that the release profile can be influenced by appropriate variation of the thickness of the buprenorphine matrix layer, the skin contact layer and the buprenorphine (see D1, paragraph [0024]). Document D1 further informs that early exhaustion of the TTS in case of disproportionate delivery of the carboxylic acid can be prevented by an additional layer based on polyacrylates which is preferably located between the buprenorphine containing matrix layer and the skin (see paragraph [0018]).

However, the results in Table 3 of document D1 demonstrate that when using the exemplified compositions of document D1 more than 90% of the carboxylic acid is already delivered after 3 days, which apparently leaves the compositions practically depleted well before the 7 days defined in claim 1 of the main request. These exemplified compositions of document D1 actually include the additional layer described in paragraph [0018] for preventing possible premature exhaustion of the TTS. In this context the

information in paragraph [0024] merely indicates that the release profile of the exemplified compositions could be influenced by adjusting the thickness of the matrix or the additional skin contact layer, but this provides the skilled person with no reasonable expectation that the prolonged application duration of 7 days could be achieved with a TTS in which the additional layer is omitted.

The apparent depletion of the exemplified compositions after 3 days described in document D1 distinguishes the present case from the circumstances in T 259/15. In T 259/15 the testing of an available TTS for its possible suitability for a prolonged application duration was not considered to involve particular technical difficulties (see T 259/15, section 1.3.6). In the present case the exemplified compositions of document D1 had been tested and appeared not suitable for administration for 7 days.

7.4 Accordingly, the Board concludes that the subject-matter of claim 1 of main request involves 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 opposition division with the order to maintain the patent on the basis of the claims of the main request, filed as auxiliary request V with the letter dated 16 February 2023, and a description to be adapted.

The Registrar: The Chairman:

B. Atienza Vivancos A. Usuelli

Decision electronically authenticated