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**Datasheet for the decision
of 5 December 2007**

Case Number: T 1399/06 - 3.3.02

Application Number: 88303918.2

Publication Number: 0289342

IPC: A61K 31/465

Language of the proceedings: EN

Title of invention:

Method for the treatment of withdrawal symptoms associated with smoking cessation and preparations for use in said method

Patentee:

Aveva Drug Delivery Systems, Inc.

Opponent:

LTS Lohmann Therapie-Systeme AG

Headword:

Use of nicotine in a method of treatment of withdrawal symptoms/AVEVA

Relevant legal provisions (EPC 1973):

EPC Art. 56, 111(2)

Keyword:

"Admissibility of the main request and first auxiliary request (no): the introduction of the broader product claims is not justified"

"Inventive step of second auxiliary request (no): the independent use claims lack an inventive step"

Decisions cited:

T 0074/03

Catchword:

-



Case Number: T 1399/06 - 3.3.02

D E C I S I O N
of the Technical Board of Appeal 3.3.02
of 5 December 2007

Appellant: LTS Lohmann Therapie-Systeme AG
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Decision under appeal: Interlocutory decision of the Opposition
Division of the European Patent Office posted
4 July 2006 concerning maintenance of European
patent No. 0289342 in amended form.

Composition of the Board:

Chairman: U. Oswald
Members: M. C. Ortega Plaza
P. Mühlens

Summary of facts and submissions

- I. European patent No. EP-0 289 342, based on application No. 88 303 918.2, was granted on the basis of 22 claims.

Independent claim 1 as granted read as follows:

"1. A preparation for the once-daily, percutaneous administration of nicotine, which comprises nicotine uniformly distributed in a solid, semi-solid or mucilaginous medium which can be placed in intimate contact with the skin, said solid, semi-solid or mucilaginous medium being formed by adding a given amount of nicotine to a solution of a solidifying or gel-forming agent or mixture thereof in a suitable solvent or mixture of solvents and mixing or heating the mixture thereby obtained so as to form said solid, semi-solid or mucilaginous medium, said medium further being effective to permit controlled release of nicotine to the skin and containing an amount of nicotine sufficient to achieve a plasma nicotine concentration in excess of 2 ng/ml within 1 hour after administration and to maintain such plasma nicotine concentration between 5 to 30 ng/ml over a period of from 1 to 24 hours."

Independent claim 11 as granted read as follows:

"11. A device for the once-daily administration of nicotine, comprising nicotine uniformly distributed in a solid, semi-solid or mucilaginous medium which can be placed in intimate contact with the skin, and said medium being effective to permit controlled release of nicotine to the skin and containing an amount of

nicotine sufficient to achieve a plasma nicotine concentration in excess of 2 ng/ml within 1 hour after administration and to maintain such plasma nicotine concentration between 5 to 30 ng/ml over a period of from 1 to 24 hours."

Independent claim 21 as granted read as follows:

"21. Use of nicotine for the manufacture of a medicament for use in the once-daily, percutaneous administration of nicotine in a method for the treatment of withdrawal symptoms associated with smoking cessation and in which the nicotine is administered in an amount sufficient to maintain plasma levels of nicotine substantially equivalent to trough plasma levels resulting from intermittent smoking."

Independent claim 22 as granted read as follows:

"22. Use of nicotine for the manufacture of a medicament for use in the once-daily, percutaneous administration of nicotine in a method for combating the psychological dependence that occurs through frequent smoking and in which the nicotine is administered in an amount sufficient to maintain plasma levels of nicotine substantially equivalent to trough plasma levels resulting from intermittent smoking."

- II. Opposition was filed and revocation of the patent in its entirety was requested pursuant to Article 100(a) EPC 1973 on the grounds of lack of novelty.
- III. Following previous appeals (patentee's and opponent's appeals) against a first interlocutory decision of the

opposition division, the case was decided by the same board 3.3.02 (although in another composition) under the number T 74/03 (date of decision 10 May 2005). The board decided to set aside the first-instance decision and to remit the case to the department of first instance for further prosecution on the basis of the 5th auxiliary request.

- IV. The present appeal lies from the interlocutory decision of the opposition division dispatched on 4 July 2006 maintaining the patent in amended form on the basis of the second auxiliary request (previous 5th auxiliary request with minor amendments) filed during the oral proceedings which took place before the opposition division on 4 April 2006.

The independent use claims 18 and 19 of the second auxiliary request filed during the oral proceedings of 4 April 2006 are identical to the use claims 18 and 19 of the 5th auxiliary request which served as a basis for remittal decision T 74/03.

Independent claim 18 of the second auxiliary request reads as follows:

"18. Use of nicotine for the manufacture of a medicament for use in the once-daily, percutaneous administration of nicotine in a method for the treatment of withdrawal symptoms associated with smoking cessation and in which the nicotine is administered in an amount sufficient to maintain plasma levels of nicotine substantially equivalent to trough plasma levels resulting from intermittent smoking, wherein said nicotine is uniformly distributed in a

solid or semi-solid medium with a surface area in the range 2 to 15 cm², more especially 5 to 10 cm² and a thickness in the range 0.5 to 3 mm, more especially 1 to 2 mm which can be placed in intimate contact with the skin."

Independent claim 19 of the second auxiliary request reads as follows:

"19. Use of nicotine for the manufacture of a medicament for use in the once-daily, percutaneous administration of nicotine in a method for combating the psychological dependence that occurs through frequent smoking and in which the nicotine is administered in an amount sufficient to maintain plasma levels of nicotine substantially equivalent to trough plasma levels resulting from intermittent smoking, wherein said nicotine is uniformly distributed in a solid or semi-solid medium with a surface area in the range 2 to 15 cm², more especially 5 to 10 cm² and a thickness in the range 0.5 to 3 mm, more especially 1 to 2 mm which can be placed in intimate contact with the skin."

V. The following documents cited during the proceedings are relevant to the present decision:

(8) M. A. H. Russell, C. Feyerabend, P.V. Cole, British Medical Journal, 1043-1046, May 1976

(11) Japanese patent publication No. 61-251619 in its English translation.

VI. The opposition division considered that the main request and the first auxiliary request (filed as

auxiliary request 6) were admissible. However, according to the opposition division's findings neither request was allowable within the meaning of Article 123(2) EPC.

As regards the second auxiliary request (filed as amended auxiliary request 5), the opposition division considered that it met the requirements of Article 56 EPC.

In particular, the opposition division considered document (11) to be the closest prior art. The opposition division defined the problem to be solved as how to modify the known patches so as to obtain a patch having a prolonged duration of action which would allow therapeutic nicotine plasma levels for a period of 24 hrs.

- VII. Both patent proprietor and opponent filed appeals against the said decision and filed grounds of appeal.
- VIII. The board sent a communication on 5 April 2007 as an annex to the summons for oral proceedings to be held the 2 July 2007, conveying the board's position about the admissibility of the sets of claims of the main request and first auxiliary request.
- IX. The appellant-opponent announced in a letter sent by fax on Saturday 30 June 2007 that it could not attend the oral proceedings for serious reasons within the meaning of the Notice published in OJ EPO 2000, 456.
- X. Oral proceedings were held on Monday 2 July 2007, in the absence of the appellant-opponent, in which

postponement of the oral proceedings was discussed with the representative of the appellant-patentee. After deliberation by the board the chairman announced that the oral proceedings were postponed to a date to be decided.

XI. A communication sent by the board on 2 July 2007 informed the parties that, having regard to the circumstances which led to the postponement of the oral proceedings, the board did not intend to order an apportionment of costs not in line with the general rule that each party meets the costs he has incurred (Article 104(1) EPC 1973). The board also said that the cost of the interpreters was being borne by the European Patent Office.

XII. The appellant-patentee announced in its letter of 7 November 2007, that since the patent was due to expire shortly, it would not attend the oral proceedings scheduled for 5 December 2007. The appellant-patentee referred to its previously filed written submissions, in particular those made in its letter dated 30 March 2007, as well as to the expert report of Professor Jonathan Hadgraft dated 3 February 2006.

XIII. In a communication sent by fax on 27 November 2007, the board drew the parties' attention to the fact that the independent use claims 18 and 19 had been formulated in a "Swiss-type form" and that the "medicament" mentioned in these claims did not contain all the features which characterise the products claimed in claims 1 and 9. In particular, the parties were made aware that the use claims lacked the definitions characterising the medium

as effective for controlled release of nicotine, as well as the attained plasma values for the period of 1 to 24 hours.

XIV. Oral proceedings were held on 5 December 2007 in the absence of the appellant-patentee.

XV. The arguments submitted in writing by the appellant-patentee, in so far as relevant to the present decision may be summarised as follows:

(a) As regards the admissibility of the new main request and first auxiliary request

The 5th auxiliary request was submitted during the oral proceedings before the board in the appeal case T 74/03 in response to arguments heard for the first time during the said oral proceedings. Having reflected upon the form of the claims of the 5th auxiliary request since the oral proceedings before the board, and considered them with its technical advisers, the appellant-patentee considered that the limitations imposed on the claimed subject-matter were unnecessarily strict. In particular, the appellant-patentee did not see any need to limit the claimed subject-matter by reference to both the surface area and the thickness of the nicotine-containing medium, but took the view that reference to one of these technical parameters was sufficient to satisfy the requirements identified by the board of appeal in T 74/03 and laid down in the EPC.

The form of the amended product claims of the new main request and first auxiliary request, which referred to

the surface area of the nicotine-containing medium, was compatible with the *ratio decidendi* of decision T 74/03, which simply required the claimed subject-matter to be correlated to a structural characterisation of the preparation in order to confer novelty vis-à-vis the prior art. Therefore, in the appellant-patentee's view, the requirements of Article 111(2) EPC were satisfied.

The appellant-patentee filed no further comments on the admissibility of the late-filed requests after receiving the board's communication sent on 5 April 2007 as an annex to the summons for oral proceedings scheduled for 2 July 2007.

(b) As regards the inventive step arguments submitted by the appellant-patentee which may be relevant to the use claims of the second auxiliary request

Most of the arguments submitted by the appellant-patentee were dedicated to the product claims. However, the appellant-patentee clearly stated in writing that the "Swiss-type form" claims related to a medicament for once-daily use. Furthermore, in the appellant-patentee's opinion the advantage of the invention lay in the provision of a preparation allowing once-daily transdermal administration of nicotine (which in the appellant-patentee's view meant 24-hours action) whilst maintaining particular plasma nicotine levels which were sufficient to suppress the urge to smoke.

The Japanese patent application (11) disclosed a 12-hours nicotine-containing patch with an acrylic polymer as its nicotine-containing medium. The diffusion profile achieved by the nicotine-containing

medium employed in document (11) would be too slow to be considered in the manufacture of a smaller patch capable of providing sustained-release delivery of nicotine over a 24-hours period, as in the invention according to the patent in suit.

The appellant-patentee submitted that the identification of the particular trough levels of plasma nicotine concentration was a significant step in the making of the "claimed invention". Furthermore, document (11) did not disclose any plasma levels and did not render obvious the plasma levels according to the patent in suit.

The appellant-patentee further referred to the expert opinion dated 3 February 2006 in which Prof Hadgraft had explained that at the priority date the state of the art was such that reliable plasma nicotine concentration measurements were extremely difficult to achieve, and that the levels of plasma nicotine concentration which resulted from smoking had not yet been well characterised. Furthermore, nicotine was an extremely toxic substance and overdosing of a patient could be highly dangerous. Hence, the recognition that smoking cessation could be achieved with a lower nicotine plasma profile than that which can be observed in smokers when smoking at regular intervals, was of considerable significance.

The appellant-patentee therefore submitted that the lack of disclosure in document (11), the identification of specific trough plasma levels, and the identification of those plasma levels as desirable in

smoking cessation therapy, constituted a step that required inventive skill.

As regards document (8), Prof Hadgraft's written opinion dated 3 February 2006 stated that it described a somewhat artificial smoking study carried out on a single individual who was required to smoke on a regular hourly basis. In contrast, the patent in suit disclosed levels reached under normal intermittent smoking conditions. The said written expert's opinion further stated that document (8) also disclosed a multi-participant clinical study in which plasma nicotine levels were measured in 15 smokers 2 minutes after the smoking of a cigarette under normal conditions. In Prof Hadgraft's view "(T)he results indicated that the plasma levels after smoking average in excess of 30ng/ml over the population of the study. The study provides no information regarding the variation of plasma levels as a function of time, and therefore it is impossible to tell from document (8) whether these levels are peak levels, trough levels or (most likely) somewhere in between" (point 24.1.5 of Prof Hadgraft's written opinion dated 3 February 2006).

The appellant-patentee did not file any comments on the board's communication sent by fax on 27 November 2007.

XVI. The appellant-opponent's arguments may be summarised as follows:

The new main request and first auxiliary request should not be considered admissible, since it was not possible to justify admitting broader product claims after the remittal order in decision T 74/03, which related to

further prosecution for assessment of inventive step on the basis of the 5th auxiliary request (which became the second auxiliary request) but did not allow a re-opening of the whole opposition procedure.

If the plasma levels over 24 hrs specified in the product claims were to be considered as a functional feature to be linked to the constitution of the patch, then such functional feature was lacking in the use claims.

The appellant-opponent acknowledged Prof Hadgraft's allegation that different materials to those disclosed in document (11) (as was the case with the gels in the examples in the patent in suit) would lead to different diffusion profiles, but it stressed that the chemical nature of the nicotine-containing medium was not defined in the claims.

One or the other plasma nicotine profile was not just the result of a particular geometry of the patch. Hence, the subject-matter claimed in the use claims could not be considered to involve an inventive step.

The use of the patches disclosed in document (11) related to the smoking cessation therapy, so document (11) remained the closest prior art.

The patches disclosed in document (11) for 12 hours fulfilled the condition of being suitable for use in the once-daily, percutaneous administration of nicotine.

Moreover, in the appellant-opponent's opinion many smokers did not smoke during the sleeping period at night.

The appellant-opponent also pointed to document (8) in connection with the plasma levels and stated that not only the peak levels but also the trough levels were known to be useful in the smoking cessation therapy.

XVII. The appellant-patentee had requested in writing that the decision under appeal be set aside and that the patent be maintained in amended form on the basis of the main request or on the basis of the first auxiliary request (both filed with the patentee's letter of 3 February 2006) or, alternatively, on the basis of the second auxiliary request filed at the oral proceedings before the opposition division held on 4 April 2006.

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

Reasons for the decision

1. *Admissibility*

1.1 Both appeals are admissible.

- 1.2 *Admissibility of the sets of claims filed after the order of remittal to the department of first instance in accordance with decision T 74/03*
- 1.2.1 The present appeals lie from an interlocutory decision of the opposition division maintaining the patent in amended form on the basis of the second auxiliary request filed during the oral proceedings held before the opposition division on 4 April 2006 (Articles 102(3) and 106(3) EPC 1973).
- 1.2.2 Following previous appeals (patentee's and opponent's appeals) against a first interlocutory decision of the opposition division, the case was decided by the same board 3.3.02 (although in another composition) under the number T 74/03 (date of decision 10 May 2005). In T 74/03 the board decided to set aside the first-instance decision and to remit the case to the department of first instance for further prosecution on the basis of the 5th auxiliary request (almost identical to the present second auxiliary request, the only difference being the introduction of the particle "or" between the words "solid" and "semi-solid" in the independent product claims).

The *ratio decidendi* of decision T 74/03 pursuant to Article 111(2) EPC is made clear in the reasons for the decision. In particular, auxiliary request 5 was a late-filed request admitted into the proceedings, in which the feature "with a surface area in the range 2 to 15 cm², more especially 5 to 10 cm² and a thickness in the range 0.5 to 3 mm, more especially 1 to 2 mm" was incorporated into independent product claims 1 and 9 (see granted claim 11). Claims 1 and 9 of said

request are product claims relating to a preparation and a device, respectively. This restriction concerning the constitution of the product claimed was undertaken by the patentee during the oral proceedings before the board in appeal case T 74/03 in order to overcome the objections raised pursuant to Article 54 EPC 1973 against the independent product claims of the main request and auxiliary requests 1 to 3.

Indeed, one essential point addressed by the board of appeal in decision T 74/03 concerns the functional feature "containing an amount of nicotine sufficient to achieve a plasma nicotine concentration in excess of 2 ng/ml within 1 hour after administration and to maintain such plasma nicotine concentration between 5 to 30 ng/ml over a period of from 1 to 24 hours", which appears in the independent product claims.

Decision T 74/03 states that "the surface area is one of the possible features mentioned by the appellant (opponent) necessary for correlating the constitution of the product with the plasma levels".

Indeed, **both together**, the surface area **and** the thickness of the solid or semi-solid medium, were found to characterise and define the transdermal products' **constitution** in view of which the claimed subject-matter was found to be novel vis-à-vis the prior art document (1).

- 1.2.3 An inspection of the file shows that after remittal of the case to the department of first instance the opposition division summoned the parties to oral proceedings. As a reaction to the summons to oral

proceedings, the patentee filed with its letter of 3 February 2006 a new main request and a new auxiliary request 6 (first auxiliary request in the present appeal proceedings) and maintained its previous auxiliary request 5 as second auxiliary request.

The opposition division considered the two new requests admissible (point 2 of the opposition division's decision) even though the independent product claims of the new main request and new first auxiliary request were broader than the product claims of the set of claims of the request allowed by the board in decision T 74/03 as "auxiliary request 5" (which corresponds to the second auxiliary request) and which served as basis for the remittal.

In accordance with Article 111(2) EPC the department of first instance was bound by the *ratio decidendi* of board of appeal decision T 74/03 in so far as the facts remained the same.

The facts remained the same in respect of novelty, and hence to admit the two new sets of claims with broader product claims, which would have re-opened the novelty discussion, was going beyond the discretionary power of the opposition division, since it contravened Article 111(2) EPC.

The reasons for the remittal in the first appeal proceedings were clearly expressed in point 8 of decision T 74/03. In particular, it was reasoned that, although a long time had elapsed since the priority date of the patent in suit (filing date 29 April 1988 and both claimed priority dates in 1987), the case was

to be remitted to the department of first instance for further prosecution because a patent could not be maintained in an amended form filed for the first time at oral proceedings during an appeal procedure without investigation of whether all the EPC requirements had been met. Furthermore, the appellant-patentee had not approved the introduction of new grounds of opposition concerning inventive step and the board had no power to examine the requirements of Article 56 EPC.

Filing new sets of claims before the department of first instance would have been possible in the present case as a direct response to objections re lack of inventive step and/or because of the filing of additional documents, i.e. in the event that the facts had not remained the same (Article 111(2) EPC). However, this was not the case.

1.2.4 Therefore, the filing of the new sets of claims of the main request and first auxiliary request containing broader product claims is not in accordance with Article 111(2) EPC.

1.2.5 Additionally, it has to be stressed that it is well established case law of the boards of appeal that the patentee's right to file amendments in the course of proceedings is not unlimited in time.

The filing of new sets of claims by the appellant-patentee with broader product claims than those found allowable by the board of appeal in its decision T 74/03 is not justified just by claiming, as the appellant-patentee has done, that "the limitations imposed on the claimed subject-matter were

unnecessarily strict", and that it (the patentee) did not consider it necessary "to limit the claimed subject-matter by reference to both the surface area and thickness of the nicotine-containing medium, but rather that reference to one of these technical parameters is sufficient to satisfy the requirements identified by the Board of Appeal and the EPC" (see "Background to the proceedings", last paragraph on page 2 of appellant-patentee's grounds of appeal).

As regards the appellant-patentee's first argument, suffice it to say that the set of claims of auxiliary request 5 was filed exclusively on the responsibility of the appellant patentee's official representative during the oral proceedings before the board in the appeal proceedings T 74/03. Moreover, the features incorporated into claims 1 and 9 (previous claim 11), concerning the surface area and the thickness, appeared **both together** in claim 3 as granted (claim 2 as granted did not define the constitution of the nicotine medium) and claim 12 (directly dependent on independent product claim 11 in the granted version), respectively. It is quite normal procedure during opposition appeal proceedings to incorporate a dependent claim (in the present case the next possible) into an independent claim in order to overcome objections. Furthermore, none of the granted claims related solely to the surface area as the preferred feature.

The appellant-patentee's second argument does not stand up to scrutiny when considered in the light of Article 111(2) EPC and the *ratio decidendi* of decision T 74/03, which had settled the issues of novelty and sufficiency of disclosure (Article 83 EPC).

Hence, the appellant-patentee's **perception** that in the present case the remittal to the department of first instance allowed him a further opportunity for filing broader claims than those already examined and decided upon by the board in decision T 74/03 is not correct.

- 1.2.6 Additionally, the opposition division's opinion that the new sets of claims were not against the *ratio decidendi* of decision T 74/03 since the board had not stated in its decision whether or not the surface area alone would suffice as a novelty bringing feature is not correct.

This approach by the opposition division ignores the actual *ratio decidendi* of decision T 74/03 in which the board decided on the basis of sets of claims which were admissible and formally allowable. Indeed, the fact that in T 74/03 the board did not decide on the novelty of hypothetical claim's wording (for instance of a claim relating to a transdermal preparation whose constitution had been characterised only by the surface area) cannot be taken by the opposition division as an invitation to find admissible broader product claims than those found to be novel by the board in T 74/03.

Furthermore, since the new sets of claims had been filed extremely late (i.e. after the remittal), they should have been found to be clearly allowable in order to be considered admissible. However, this was not the case since the opposition division expressed the view that both sets of claims (main request and first auxiliary request) were not allowable within the meaning of Article 123(2) EPC.

Hence, the opposition division's argument in favour of the admissibility of the late filed sets of claims of the main request and first auxiliary request on the grounds that the claims would be easy to handle (page 9, point 2.1 of the opposition division's decision) is in conflict with the more important condition at such a late stage of the procedure (namely after the remittal for further prosecution) which requires the claims to be "clearly allowable".

Furthermore, it could not be assumed that the handling of the new sets of claims would be "easy" unless there were a presumption that both sets of claims were immediately to be rejected as not allowable under Article 123(2) EPC. However, as stated above, clearly unallowable sets of claims should have been immediately rejected by the opposition division as filed too late.

Finally, it has to be stressed that, if the new sets of claims had been allowable, then a full re-examination of the case in respect of the requirements of Articles 84, 83 and 54 EPC would have been necessary, contrary to the requirements of Article 111(2) EPC.

1.2.7 Accordingly, the opposition division's decision to admit the late-filed sets of claims of the main request and the first auxiliary request into the proceedings was not correct.

1.2.8 In conclusion, the sets of claims of the main request and the first auxiliary request are not admissible.

1.2.9 The set of claims of the second auxiliary request was correctly admitted into the proceedings by the opposition division since it is almost identical to the set of claims of the previous "auxiliary request 5", with only a minor amendment (introduction of the particle "or" between the words "solid" and "semi-solid" in the independent product claims).

The appellant-opponent has not disputed the admissibility of this set of claims.

2. *Second auxiliary request, use claims*

2.1 Claims 18 and 19 of the second auxiliary request are independent claims. They are identical to claims 18 and 19 of the 5th auxiliary request dealt with by the board of appeal in respect of the requirements of Articles 123, 84, 83 and 54 EPC in decision T 74/03.

2.2 Both claims 18 and 19 of the second auxiliary request are formulated as "Swiss-type" claims and relate to the use of nicotine for the manufacture of a medicament "for use in the once-daily, percutaneous administration of nicotine".

The medical indication of nicotine claimed in claim 18 concerns the treatment of withdrawal symptoms associated with smoking cessation. The medical indication of nicotine claimed in claim 19 concerns the treatment of psychological dependence that occurs through frequent smoking.

The "medicament" referred to in the use claims obviously concerns a transdermal patch which can be

placed in intimate contact with the skin and has specific geometrical requirements characterised by the specific surface area and thickness of the nicotine-containing medium defined in the claim.

2.3 *Inventive step*

2.3.1 It has to be stressed that the use of nicotine for treating withdrawal symptoms associated with smoking cessation and suppressing the desire to smoke was known to the skilled person at the effective date of the patent in suit. This is an undisputed fact.

2.3.2 Document (11), which discloses the transdermal administration of nicotine by means of a nicotine-containing tape agent, which can be placed in direct contact with the epidermis, represents the closest prior art (page 1, under the heading "industrial field of use").

Document (11) states that "it pertains to a nicotine-containing tape agent which transdermally administers a fixed quantity of nicotine to a smoker, without providing discomfort, to counteract the desire to smoke following a nicotine level drop within the body, for quitting smoking or reducing smoking without psychological or physiological suffering" (bridging paragraph between pages 1 and 2).

Document (11) also discloses that "nicotine has excellent transdermal absorption capability, and that nicotine is continuously transdermally absorbed and suppresses the desire to smoke for a long time" (page 3 under the heading "Means of resolving [the] problems").

The nicotine-containing medium employed in document (11) for the transdermal administration of nicotine is constituted by a "polymeric substance layer that exhibits stickiness at room temperature on a carrier" (page 3, penultimate paragraph).

Document (11) teaches that "(A)s a specific method of varying the amount of nicotine in single-dose units of the nicotine-containing tape agent, various methods can be used; for example, the concentration of nicotine in the nicotine-containing polymeric substance layer can be varied, or the thickness of the said layer can be varied, or the effective sticky surface area of the nicotine-containing tape agent can be varied" (page 7, third full paragraph).

Document (11) also discloses that "tapes are applied to the body in order from high nicotine concentration to low concentration, and the nicotine level inside the body is gradually reduced at each fixed interval, and in so doing, it is possible to quit smoking without psychological suffering" (page 7 penultimate paragraph).

Document (11) further discloses that "(T)he nicotine-containing tape agent of the present invention is something which causes transdermal absorption of nicotine, which greatly influences habitual smoking, by the smoker, and therefore there is no need to have a specialist such as a physician to administer it, handling is simple and it can be used by anyone (smokers), and moreover, since the nicotine in the said tape agent is gradually administered to the body from the skin by applying the said nicotine-containing tape

agent directly to the epidermis, blood nicotine concentration becomes nearly fixed over a long time, and as a result, there is no need to administer the aforementioned nicotine-containing tape agent" (page 7, last paragraph).

The "implementation examples" disclosed in document (11) concern the preparation and use of a copolymer of acrylate derivatives and vinyl acetate as a nicotine-containing medium. Example 1 states that "(T)he thickness after drying was 40 μ m" and the "nicotine-containing tape agent" "was cut into large shapes of 7x10cm²" (surface area). Additionally, it is also disclosed in example 1, which concerns a nicotine amount of 400 μ g/cm², that "the blood nicotine concentration reached nearly the same level as that obtained when smoking paper-rolled tobacco, and this was maintained for about 12 hours".

Example 2 in document (11) discloses the nicotine-containing medium according to example 1 with four different nicotine amounts, namely 100 μ g/cm², 200 μ g/cm², 300 μ g/cm² and 400 μ g/cm², to be applied in regressive order from the beginning of the treatment to the end (the specific study disclosed in example 2 relates to a four-week treatment).

Document (11) further teaches that with transdermal administration of nicotine "it is possible to quit smoking or reduce smoking without psychological or physiological suffering" (page 9, third paragraph from bottom).

2.3.3 In the light of this prior art, the problem to be solved lies in a further use of nicotine for the treatment of smoking cessation symptoms by providing further nicotine plasma levels.

The solution as defined in claims 18 and 19 relates to the administration of nicotine "in an amount sufficient to maintain plasma levels of nicotine substantially equivalent to trough plasma levels resulting from intermittent smoking".

The board is satisfied that the problem has been plausibly solved in the light of the description.

2.3.4 Therefore it has to be assessed whether the proposed solution is obvious in the light of the prior art.

Document (11) does not state the exact values for nicotine plasma level attained when using the patch with the higher nicotine charge in example 1 and does not disclose the actual value attained when using the patch with the lowest nicotine charge mentioned in example 2.

However, as mentioned in point 2.3.2 above, the smoking cessation treatment disclosed in example 2 of document (11) involves starting with a patch containing a larger amount of nicotine, i.e. $400 \mu\text{g}/\text{cm}^2$, (distributed in a medium of 70 cm^2 surface area with a thickness of $40 \mu\text{m}$) in order to obtain "nearly the same level as that obtained when smoking paper rolled-tobacco" for about 12 hours, and progressively lowering the amount of nicotine contained in the patch down to $100 \mu\text{g}/\text{cm}^2$.

Therefore, there is a clear indication in document (11) that low nicotine plasma level should be administered transdermally in the smoking cessation therapy.

Moreover, document (11) includes in its analysis of the background art a reference to the generally known nicotine-containing chewing gums in connection with the advantages of transdermal administration of nicotine in order to overcome the drawbacks of chewing nicotine-containing chewing-gums (page 3).

Therefore, the skilled person would be aware of the content of document (8), which is an article in the British Medical Journal entitled "Plasma nicotine levels after cigarette smoking and chewing nicotine gum".

Document (8) discloses two studies: the first concerning a single subject and the second concerning a smoker's clinic sample (page 1044).

Document (8) states: "In both studies blood specimens were centrifuged within two hours and the plasma kept frozen until analysis for nicotine. Blood nicotine was measured by gas chromatography" (page 1044, left-hand column under the head "Analysis").

The mean peak plasma level of nicotine after each cigarette was 46.0 ± 2.4 ng/ml in the first study. Document (8) further states that "(T)hese levels were fairly consistent especially from the third cigarette onwards, when the average was 49.2 ± 1.5 ng/ml". (page 1044, left-hand column).

The trough nicotine plasma levels obtained just before smoking in the first study can be read in figure 1 as being approx. between 15 and 25 ng/ml.

In the second study the average peak level after smoking is 30.4 ± 10.3 ng/ml and the trough levels (just before smoking) can be read in figure 2 as being approx. between 10 and 30 ng/ml (from the second cigarette onwards).

Document (8) draws the following conclusion from the studies: "Plasma nicotine levels obtained from nicotine chewing-gum only approach the levels produced by cigarette smoking when at least 10 pieces of gum containing 4-mg nicotine are taken daily and each is well chewed for about 30 minutes. This [sic] dosage of 2-mg gum does not produce an adequate plasma nicotine level. The slower rate of absorption of nicotine from chewing-gum suggests that it would be a closer substitute for non-inhaling cigar or pipe smoking. Its clinical efficacy as an aid to cigarette withdrawal **may well depend on the extent to which the smoker smokes** to obtain rapid blood nicotine peaks or **to maintain minimum trough level**" (*emphasis added*) (page 1045, right-hand column).

In other words, the skilled person looking for nicotine plasma levels useful in smoking cessation therapy would have applied the teaching in document (8) to maintain minimum trough levels, particularly in view of the known excellent transdermal absorption capability of nicotine and the fact this absorption is continuous when applying the transdermal administration mode (document (11), page 3).

Consequently, the subject-matter claimed in the use claims lacks an inventive step.

2.3.5 The appellant-patentee's arguments in favour of inventive step do not hold for the following reasons:

The feature "once-daily percutaneous administration of nicotine" does not necessarily imply a single patch releasing a continuous 24-hours nicotine plasma profile. The patch may be one that releases nicotine for 16 hours (the remaining time corresponding to a smoking-free night rest) or even for a shorter time (for instance 12 hours) if the patch is used for smokers without a heavy smoking habit, or at the end of a smoking cessation therapy.

Therefore, the patch employed in the therapy reflected by claims 18 and 19 does not necessarily provide the nicotine plasma profile of 0-24 hours specified in claim 1 and absent from claims 18 and 19. Hence, the arguments concerning the geometry of the medium (characterised by a specific thickness and surface area) are irrelevant for the inventive step assessment of the use of nicotine claimed. It has to be stressed that neither the functional feature relating to the 24-hours plasma profile nor the chemical nature of the solid or semi-solid medium are defined in the use claims of the second auxiliary request.

Finally, contrary to the appellant-patentee's submissions the recognition that nicotine trough plasma levels were useful in smoking cessation therapy was already suggested in document (8).

2.3.6 Consequently, the set of claims of the second auxiliary request fails because the subject-matter claimed in independent claims 18 and 19 does not meet the requirements of Article 56 EPC.

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:

A. Townend

U. Oswald