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Datasheet for the decision of 11 January 2013

Case Number: T 0559/08 - 3.2.02

Application Number: 01953399.1

Publication Number: 1296742

IPC: A61M 37/00

Language of the proceedings: EN

Title of invention:
Intradermal delivery of substances

Patent Proprietor:
Becton, Dickinson and Company

Opponent:
Terumo Kabushiki Kaisha

Headword:
-

Relevant legal provisions:
EPC Art. 100(c), 56, 111(1)

Keyword:
"Added subject-matter (no)"
"Remittal (no)"
"Inventive step (no)"

Decisions cited:
-

Catchword:
-

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Case Number: T 0559/08 - 3.2.02

D E C I S I O N
of the Technical Board of Appeal 3.2.02
of 11 January 2013

Appellant: (Patent Proprietor)	Becton, Dickinson and Company 1 Becton Drive Franklin Lakes, NJ 07417-1880 (US)
Representative:	Stothers, Christopher Arnold & Porter (UK) LLP Tower 42 25 Old Broad Street London EC2N 1HQ (GB)
Respondent: (Opponent)	Terumo Kabushiki Kaisha 44-1, Hatagaya 2-Chome Shibuya-ku Tokyo 151-0072 (JP)
Representative:	Oser, Andreas Prüfer & Partner GbR Patentanwälte Sohnckestrasse 12 D-81479 München (DE)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted 27 March 2008 revoking European patent No. 1296742 pursuant to Article 101(3)(b) EPC.**

Composition of the Board:

Chairman: E. Dufrasne
Members: P. L. P. Weber
M. Stern

Summary of Facts and Submissions

I. The appeal of the patent proprietor is against the decision of the Opposition Division, taken in the oral proceedings on 26 February 2008 and posted on 27 March 2008, to revoke European patent No. 1296742 because subject-matter of claim 1 according to the main request and subject-matter of claim 1 according to the auxiliary request lacked novelty over D2. In the annex to the summons to oral proceedings, the Opposition Division had also considered the subject-matter of claim 1 of the patent as granted to lack an inventive step over D2 as the closest prior art.

The notice of appeal was filed on 27 February 2008 and the appeal fee paid on the same day. The statement setting out the grounds of appeal was filed on 6 August 2008.

II. In its statement setting out the grounds of appeal the appellant requested that the decision under appeal be set aside and that the patent be maintained as granted.

III. In its reply to the statement setting out the grounds of appeal the respondent requested the dismissal of the appeal. It objected, inter alia, that claim 1 of the patent as granted included subject-matter extending beyond the content of the application as filed (Article 100(c) EPC) and that the patent did not disclose the invention according to claim 1 of the patent as granted in a manner sufficiently clear and complete to be carried out by a person skilled in the art (Article 100(b) EPC).

IV. With its reply to the summons of the Board filed on 11 December 2012, the appellant submitted first to tenth auxiliary requests in case the granted version of the patent could not be maintained.

V. Oral proceedings were held on 11 January 2013.

The final request of the appellant was that the decision under appeal be set aside and that the patent be maintained on the basis of the tenth auxiliary request or, in the alternative, of the ninth auxiliary request, both filed on 11 December 2012.
Former main request and first to eighth auxiliary requests were withdrawn during the oral proceedings.
Additionally the appellant requested remittal of the case to the first-instance department, should the Board decide that the subject-matter of any claim 1 is novel.

The final request of the respondent was that the appeal be dismissed.

VI. The following documents are cited in the decision:

D2: US-A-5848991
D3: US-A-5997501

VII. Claim 1 of the patent as granted reads as follows:

"Use of a substance selected from the group consisting of hormones, antitoxins, substances for the control of pain, substances for the control of thrombosis, substances for the control or elimination of infection and vaccines, for the manufacture of a medicament for use in the treatment or prevention of hormone

deficiency, toxicity, pain, thrombosis or infection or in the expression of protective immunity by delivery of said substance into an intradermal space within the skin of a human subject through a small gauge needle inserted into the intradermal space, the needle having an outlet having an exposed height at a depth within the intradermal space sufficient to allow the skin to seal around the needle and the rate and volume of delivery of the substance being controlled, such that leakage of the substance to the surface of skin is substantially prevented."

Claim 1 according to the ninth auxiliary request differs from claim 1 of the patent as granted by the addition at its end of the following:

"..., wherein the outlet is at the depth of 1 mm to 2 mm when the needle is inserted, wherein the outlet has an exposed height of 0 to 300µm, wherein the rate and volume of delivery of the substance are controlled so as to prevent the formation of weals at the site of injection and to prevent ejection of the needle."

Claim 1 according to the tenth auxiliary request differs from claim 1 of the patent as granted by the addition at its end of the following:

" ..., wherein the outlet is at the depth of 1 mm to 2 mm when the needle is inserted, wherein the outlet has an exposed height of 0 to 300µm, wherein the substance is injected as a bolus."

VIII. The arguments of the appellant can be summarised as follows:

Added subject-matter

The person skilled in the art understood from the whole disclosure that in order to prevent leakage, it was the entire exposed height of the needle outlet which should be in the intradermal space. He would therefore also understand that when claim 1 required that the needle had an outlet having an exposed height at a depth within the intradermal space, this meant that the entire exposed height of the outlet had to be in the intradermal space.

Remittal

As inventive step had not been decided upon in the impugned decision and had not been discussed during the appeal proceedings until the oral proceedings, a remittal to the first-instance department was justified if the Board acknowledged novelty of the subject-matter of claim 1 according to any of the requests, on the basis of the right to have the case considered by two instances.

Claim 1 of the patent as granted

The teaching of D2 was not specifically directed to injection into the intradermal space, which was however specifically required by the wording of claim 1 of the patent in suit. D2 required an injection below the epidermis but the specific advantage of an injection into the intradermal space was not recognised. Even subcutaneous injections were envisaged.

Moreover the position of the needle outlet was not defined in D2, so that there was no unambiguous disclosure of it being in the intradermal space. The bevelled portion shown in the figures of D2 could not be considered to be the position of the outlet of the needle, because in D3 of the same applicant a similar device was shown with the same bevel at the distal end of the needle and it was specified starting at the last paragraph of column 8 that the outlet could be elsewhere along the needle.

Furthermore D2 was silent about the link between the depth of the needle and the leakage-prevention effect.

Tenth auxiliary request

The specific embodiment described in D2 starting at the second paragraph of column 7 required the needle to project outwardly from the lower surface of the injection device by a maximum of 1 mm. If it was considered that the bevel shown in the figures was the position of the outlet of the needle then this outlet could not be at 1 mm depth because of the wall thickness of the needle and of the bevel. Therefore the claimed range was not anticipated.

Further there was no teaching in D2 that the outlet should have a maximum exposed height of 300 µm.

Moreover there was no teaching in D2 that the intradermal delivery of one of the substances mentioned in the claim would be improved with the specific ranges mentioned in the claim.

Lastly, in D2 there was no teaching whatsoever to treat any of the mentioned illnesses by injection of a bolus as required by claim 1 according to the tenth auxiliary request. The teaching of D2 was limited to the infusion of substances to treat the illnesses. This could be seen in the different examples given in D2 in which the treatment time always lasted several hours whereas the bolus injection as defined in the patent in suit was meant to last less than about 5 to 10 minutes (paragraph [0012]).

Ninth auxiliary request

There was no teaching whatsoever in D2 about avoiding weals and ejection of the needle. In addition, the problem of ejection of the needle could not occur when the injection device according to D2 was used because this device was adhered to the skin to the patient as explained in column 7, lines 24 to 27.

IX. The arguments of the respondent can be summarised as follows:

Added subject-matter

All the passages cited by the appellant linked the position of the exposed height of the needle outlet in the skin and the prevention of leakage. Therefore it was clear that the outlet could also be deeper than the intradermal space. Hence, there was no basis in the originally filed application for the interpretation of the appellant. What was required by the wording of the claim was only that a part of the exposed height was within the intradermal space.

Remittal

D2 was the only important document for inventive step and this document had been discussed at length in relation to the novelty objections. Moreover there was a general interest in a definitive decision on the question of patentability, given the date of filing of the patent.

Claim 1 of the patent as granted

D2 mentioned intradermal injection as one of the desirable ways of injecting substances. This was already mentioned in the title of the patent, but also at several places in the document such as column 3, lines 42 and 43, where it was mentioned that the drug was delivered directly to a capillary-containing tissue, which was nothing else than the intradermal space.

For the person skilled in the art the bevel shown in the figures of D2 was the place of the outlet of the needle. This was the most reasonable way to interpret such a drawing.

The avoidance of leakage was mentioned in column 3, lines 17 to 22. The person skilled in the art would also understand that the precisely controllable slow rates of delivery of the drug mentioned in D2 (column 4, lines 29 to 35) specifically allowed the delivery of the drug without leakage.

Tenth auxiliary request

If the person skilled in the art wished to improve the delivery into the intradermal space, his knowledge of anatomy and particularly of the skin would bring him to the claimed range of values. The outlet exposed height was merely a consequence of the bevel shown in the figures.

The injection of a bolus was within the scope of the teaching of D2, which was not limited to infusions. It was not because the examples given lasted longer that shorter injection durations were not envisaged in D2. In any case the injection of a bolus was a simple alternative to infusions.

Ninth auxiliary request

D2 explicitly mentioned the delivery of the substances at precisely controlled slow rates. The person skilled in the art knew that this was also to avoid weals and ejection of the needle.

Reasons for the Decision

1. The appeal is admissible.

2. Added subject-matter

The respondent submitted that claim 1 of the patent as granted contained subject-matter extending beyond the application as filed because the wording shown in bold in the feature of claim 1 below was not directly and

unambiguously derivable from the originally filed application documents.

"... a small gauge needle inserted into the intradermal space, the needle having **an outlet having an exposed height at a depth within the intradermal space** sufficient to allow the skin to seal around the needle and the rate and volume of delivery of the substance being controlled, such that leakage of substance to the surface of skin is substantially prevented."

More specifically there was no disclosure of the fact that "the exposed height" (in its entirety, as submitted by the patent proprietor) has to be within the intradermal space.

The appellant considered that this passage of the claim should be interpreted or read as meaning that "the entirety of the exposed height" should be within the intradermal space.

In the opinion of the Board the teaching of the patent is about delivering the substances into the intradermal space in order to have a better absorption of the substances and less pain for the patient, the exposed height of the outlet and depth of the needle in the skin being so as to prevent leakage. This can in particular be understood from paragraph [0003]:

"*The intradermal space is close to the capillary bed to allow for absorption and systemic distribution of the substance but is above the peripheral nerve net which may reduce or eliminate injection pain.*"

The same is made clear in [0006]: "(...) *methods that employ small gauge needles, especially microneedles, placed in the intradermal space to deliver the substance to the intradermal space as a bolus or by infusion.*"

Further in [0006]: "*It has been discovered that the placement of the needle outlet within the skin is critical for efficacious delivery of active substances via small gauge needles to prevent leakage of the substance out of the skin and to improve absorption within the intradermal space.*"

No explicit or otherwise clear statement that the entirety of the exposed height of the outlet should be within the intradermal space can be found in the patent specification.

Therefore, according to the Board's understanding, the above wording in bold only states that the outlet must have an exposed height at a depth within the intradermal space and not that the whole of the exposed height must be within said intradermal space.

The following statements, for instance in paragraph [0010]: "*In contrast, microneedles useful in the invention have a length sufficient to penetrate the intradermal space (the "penetration depth") and an outlet at a depth within the intradermal space (the "outlet depth") which allows the skin to seal around the needle against the backpressure which tends to force the delivered substance toward the skin surface.*"

and in the same paragraph:

"*The exposed height of the needle outlet and the depth of the outlet within the intradermal space influence the extent of sealing by the skin around the needle.*"

are already enough to provide support for the challenged passage of claim 1, so that the objection under Article 100(c) EPC does not hold.

3. Novelty

Novelty of the subject-matter of claim 1 according to the tenth and ninth auxiliary requests was not disputed.

4. Remittal

According to Article 111(1) EPC, the Board may either exercise any power within the competence of the department which was responsible for the decision appealed or remit the case to that department for further prosecution.

In the present case the Board considers it expedient to examine inventive step over D2 in the appeal proceedings although no decision on this ground of opposition was formally taken during the opposition proceedings. In the annex to the summons to oral proceedings the Opposition Division already expressed its preliminary opinion that the subject-matter of claim 1 (of the then valid request) was not inventive over D2, which was considered to represent the closest prior art. Furthermore, D2 was discussed in depth in the appeal proceedings in relation to the novelty

objections raised against the main and auxiliary requests now withdrawn. For these reasons the Board considers that the appellant has had no difficulty to take a position on a lack of inventive step argument based on D2, and that it would unduly lengthen the proceedings to remit the case to the Opposition Division for further processing on this aspect.

Therefore, the request for remittal is rejected.

5. Inventive step

It is undisputed that the closest prior art for both the subject-matter of claim 1 according to the tenth and ninth auxiliary requests is D2. Both claim 1 according to the ninth and according to the tenth auxiliary requests are a combination of all the features of claim 1 of the patent as granted with some additional features (point VII), so that the Board will start with the analysis of claim 1 of the patent as granted, the anticipation of the features of this claim by D2 also having been questioned by the appellant.

5.1 Disclosure of the features of claim 1 of the patent as granted.

Document D2 discloses a device for intradermal drug delivery. This device is basically composed of a housing (2) having a lower surface (4) to be applied to the skin of the patient, at least one drug reservoir (10) within the housing, a single hollow needle (14) extending from the lower surface of the housing and extending outwards sufficiently to penetrate into the dermis when the housing is pressed against the skin of

the patient, and means (12, 16, 18, 20) for discharging the drug from the reservoir the subject's skin via the needle (column 1, line 66 to column 2, line 16).

Since the intradermal drug delivery device according to D2 is meant to deliver the drug below the epidermis, in particular to the interface between the epidermis and the dermis or to the interior of the dermis (column 3, lines 38 to 42), the length of the needle projection is correspondingly adapted. According to column 4, lines 10 to 13, the needle projects outwards of the housing by approximately 0.3-3.0 mm, most preferably 0.3-1.0 mm.

The typical drugs to be delivered to the patient with the device according to D2 are listed from column 6, line 42 to column 7, line 21 and include some of those mentioned in claim 1 of the patent as granted, e.g. hormones such as insulin, analgesia and sedatives.

The appellant submitted that there was no unambiguous disclosure of the needle outlet being meant to be in the intradermal space because the dimensions given for the length of the needle could be too shallow beneath the skin (0.3 mm) or in the subcutaneous region (3 mm).

The Board does not share this opinion. Claim 1 of the patent as granted does not include more information than that the drug is delivered to the intradermal space ("*... by delivery of said substance into an intradermal space within the skin of a human subject...*"). In D2, as cited above, the interface between the epidermis and the dermis, and the interior of the dermis are explicitly mentioned as places where

the drug has to be delivered. Moreover, although claim 1 of the granted patent does not include any indication of the dimensions necessary to achieve such intradermal delivery, the patent refers to a penetration into the skin of about 0.5 to 3 mm (column 4, lines 11-12) and to a needle about 300 µm to 2 mm long (claim 14), which are anticipated by the lengths of 0.3 to 3 mm and 0.3 to 1.0 mm cited in D2.

The appellant further submitted that, independently of the length of the needle, the position of the needle outlet was not defined in D2, and when interpreted in the light of D3 (last paragraph of column 8) showing a similar device of the same applicant as that of D2, the outlet could be placed elsewhere than at the position of the bevel shown in the figures of D2.

When in D2 it is mentioned that the drug is delivered to the interior of the dermis as explained above, it is self-evident for the person skilled in the art that the needle must have its outlet positioned correspondingly, to allow the drug to be delivered to the desired place. Already for this reason, there is an implicit disclosure of the position of the outlet of the needle in D2. Moreover all the figures of D2, which depict the device used for the injection, show a needle having a bevel at its distal end. In the absence of any indication to the contrary, the person skilled in the art will understand that this bevelled part corresponds to the position of the outlet of the needle. This is namely the most common position for the outlet of a needle meant for injections into the body of a patient. Since there is no reference to D3 at all in D2, the

person skilled in the art has no reason to interpret D2 in the light of D3.

Additionally the appellant considered that the feature of the needle outlet having an exposed height at a depth within the intradermal space sufficient to allow the skin to seal around the needle such that leakage of substance to the surface of skin was substantially prevented was not disclosed in D2.

First of all, it is pointed out that in the Board's opinion (point 2) the wording of the claim does not require that the entirety of the exposed height should be within the intradermal space. Moreover, it is explicitly mentioned in column 3, lines 17 to 22 in D2 that leakage is diminished to a very large extent, if not totally. One reason mentioned in D2 for that reduction is that the drug is delivered below the epidermis. In the opinion of the Board this is nothing else but an indication of a precise depth sufficient to substantially prevent leakage. This depth disclosed in D2 anticipates the broader concept of a depth sufficient to substantially prevent leakage, as required by the wording of claim 1. Moreover, in the opinion of the Board, there is no reason why the position of the outlet according to the patent in suit would substantially prevent leakage and the same position of the outlet in the state of the art according to D2 would not. In the absence of any reason for doing otherwise the same standard of evidence must be applied to the patent in suit and the state of the art.

Therefore D2 discloses all the features of claim 1 of the patent as granted.

5.2 Tenth auxiliary request

Over claim 1 of the patent as granted, the subject-matter of claim 1 according to the tenth auxiliary request additionally includes the following features:

i) the outlet is at the depth of 1 mm to 2 mm when the needle is inserted,
ii) the outlet has an exposed height of 0 to 300 µm,
iii) the substance is injected as a bolus.

In D2 one specific embodiment is described, starting at column 7, line 22. In this embodiment the needle is said to project outwardly by 0.3 to 1 mm of the bottom surface of the device to be adhered to the skin of the patient receiving the drug. figure 3, which depicts the device according to this embodiment, shows a bevel at the distal end of the needle, which is nothing else than the place of the needle outlet. This means that when the needle projects from the bottom surface by 1 mm the needle outlet is slightly less deep given the bevel and thickness of the needle wall. The Board considers that the placement of the outlet at a depth of at least 1 mm is a simple alternative to what is proposed in this specific embodiment, this alternative being obvious when starting from the teaching of D2. It is specifically mentioned in column 3 of D2 that the drug is delivered below the epidermis, i.e. to the interface between the epidermis and the dermis or to the interior of the dermis, so that the person skilled in the art has no reason to limit the teaching of the

specific embodiment. On the contrary, he is even encouraged by D2 itself to try greater depth than the 1 mm limitation of the specific embodiment. And by doing so he will necessarily come to the claimed feature i).

Concerning feature ii) the Board considers that the mere putting into practice of the embodiment shown in figure 3 of D2 will bring about this feature. As a matter of fact, the dimensions indicated in column 4 or in column 7 for the needle outer and inner diameters, combined with the bevel shown in figure 3, will lead to an outlet height falling in the range of feature ii). No inventive step can be recognised in the putting into practice of the embodiment according to figure 3 by following the indications and prescriptions already present in D2.

The appellant submitted that there is no teaching in D2 that the intradermal delivery of one of the substances mentioned in the claim would be improved with the specific ranges mentioned in the claim. From the above it follows, however, that the conditions of delivery of the substance (depth of the needle and exposed height of the outlet) according to the specific embodiment described in D2 are almost identical to those mentioned in the claim, so that the Board does not see any reason why the delivery of the substance would be any different either.

Concerning feature iii) the Board considers that the injection of a bolus within the meaning of paragraph [0012] of the patent in suit: "*A bolus dose is a single dose delivered in a single volume unit over a*

relatively brief time period, typically less than about 5-10 min." is contemplated by the teaching of D2. While there is no specific embodiment described in D2 with a delivery time below 10 minutes, the teaching of this document is however not limited to delivery times of several hours. Claim 30 of D2 as well as column 6, line 20 onwards describe the intradermal delivery of a biologically effective amount of a liquid drug, e.g. including the delivery of a bolus. In column 4, lines 50 to 54, it is further described that "*For instance, the microprocessor can be programmed to deliver the liquid drug in a continuous infusion, in a pulsatile manner or in intermittent doses as well as in response to input from the subject, such as patient controlled analgesia.*" Typical for the delivery of analgesia on request by the patient is precisely the injection of a bolus when the patient needs it. Therefore the Board cannot see any inventive step in using the device according to D2 in order to deliver a bolus as claimed in feature iii).

For the reasons above, the subject-matter of claim 1 according to the tenth auxiliary request does not involve any inventive step pursuant to Article 56 EPC.

5.3 Ninth auxiliary request

Over claim 1 of the patent as granted, the subject-matter of claim 1 according to the ninth auxiliary request additionally includes the following features:

i) the outlet is at the depth of 1 mm to 2 mm when the needle is inserted,
ii) the outlet has an exposed height of 0 to 300 µm,

iii) the rate and volume of delivery of the substance are controlled so as to prevent the formation of weals at the site of injection and to prevent ejection of the needle.

The first two features are the same as in claim 1 according to the tenth auxiliary request, so that the Board considers these two features as non-inventive for the same reasons as mentioned in relation with the tenth auxiliary request.

Feature iii) in fact does not say more than that the delivery rate and volume of the drug are chosen so as to avoid the formation of weals and the ejection of the needle. It seems to the Board that these are straight-forward and common desires to be fulfilled for any injection. In modern medical care it is clearly not acceptable that a patient complains about weals after an injection, or that part of the drug is lost because the needle is ejected from the skin of the patient during injection. The latter is particularly true for intradermal injections, given the very short needles used. Moreover, the patent proprietor himself concedes in paragraph [0011] of the patent that "*The appropriate delivery rates and volumes to obtain these effects for a selected substance may be determined experimentally using only ordinary skill*". No inventive step can therefore be recognised in adjusting the delivery rate and volume of the drug in order to fulfil such basic requirements.

The patent proprietor considered that the prevention of the ejection of the needle from the patient's skin was not a problem when using the device according to D2

because in that device the lower surface was covered with an adhesive in order to adhere the device to the skin of the patient during injection.

The Board is not convinced by this argument because, the skin being a very flexible membrane and the needle extending into the skin by only 1 to 2 mm, even though the device may be adhered to the skin of the patient the skin surrounding the needle penetration point may give way under pressure and free the outlet of the needle.

For the reasons above, the subject-matter of claim 1 according to the ninth auxiliary request does not involve an inventive step pursuant to Article 56 EPC.

6. Given the Board's finding of lack of inventive step, there is no need to consider the ground for opposition under Article 100(b) EPC in the present decision.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

D. Hampe E. Dufrasne