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Datasheet for the decision of 18 June 2015

Case Number: T 2128/13 - 3.3.10

Application Number: 07810005.4

Publication Number: 2043704

IPC: A61L31/16

Language of the proceedings: EN

Title of invention:
METHODS OF MANUFACTURING AND MODIFYING TAXANE COATINGS FOR IMPLANTABLE MEDICAL DEVICES

Patent Proprietor:
Cook Medical Technologies LLC

Opponent:
Boston Scientific Corporation

Headword:

Relevant legal provisions:
EPC Art. 83, 56
RPBA Art. 13

Keyword:
Sufficiency of disclosure -
(no) main request and auxiliary request 5
Inventive step - (no) auxiliary requests 1 to 4
Sufficiency of disclosure - (yes) auxiliary request 6
Inventive step - (yes) auxiliary request 6

Decisions cited:
T 0409/91, T 0435/91, T 0198/88, T 0536/88

Catchword:

Europäisches Patentamt
European Patent Office
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Case Number: T 2128/13 - 3.3.10

D E C I S I O N
of Technical Board of Appeal 3.3.10
of 18 June 2015

Appellant: (Opponent)	Boston Scientific Corporation One Scimed Place MS A150 Maple Grove MN 55311 (US)
Representative:	Vossius & Partner Patentanwälte Rechtsanwälte mbB Siebertstrasse 3 81675 München (DE)
Respondent: (Patent Proprietor)	Cook Medical Technologies LLC 750 North Daniels Way Bloomington, IN 47404 (US)
Representative:	Simpson, Tobias Rutger Mathys & Squire LLP The Shard 32 London Bridge Street GB-London SE1 9SG (GB)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 31 July 2013 concerning maintenance of the European Patent No. 2043704 in amended form.**

Composition of the Board:

Chairwoman C. Komenda
Members: R. Pérez Carlón
D. Rogers

Summary of Facts and Submissions

I. The appellant (opponent) lodged an appeal against the interlocutory decision of the opposition division to maintain European patent No. 2 043 704 in the form of the then pending auxiliary request 3.

II. Notice of opposition had been filed on the grounds of insufficiency of disclosure (Article 100(b) EPC) and lack of inventive step (Article 100(a) EPC).

III. The documents forming part of the opposition proceedings included the following:

D1: US 2010/0197944
D2: WO 2004/028582
D3: WO 2005/089855
D4: US 2003/0215564
D6: US 2002/0051730
D7: US 2004/0073284

IV. The opposition division concluded that the opponent had not discharged its burden of proof in order to show that the claimed invention was not sufficiently disclosed.

It further concluded that any of documents D2, D3 or D4 could be seen as the closest prior art for the subject-matter of the then pending auxiliary request 3, that the problem underlying the claimed invention was providing a taxane coating with slower release of the taxane therapeutic agent from the coating, without compromising the desired level of durability of the coating, and that the solution to this problem, which was a method of manufacture characterised by a conditioning step at defined temperature and humidity,

for a defined period of time, was not obvious having regard to the prior art, so that the claimed subject-matter was inventive.

V. With the response to the grounds of appeal, the respondent (patent proprietor) filed a main request, identical to auxiliary request 3 pending before the opposition division, and auxiliary requests 1 to 9.

Claim 1 of the main request reads as follows:

"A method of manufacturing a coated endolumenal medical device having at least one coated surface, the method comprising the steps of:

a) *applying a taxane therapeutic agent to at least one surface of an endolumenal medical device to form a coating of the taxane therapeutic agent on at least one surface of the endolumenal medical device; and*
b) *conditioning the taxane therapeutic agent coating by maintaining the coating of the taxane therapeutic agent at a temperature of between 30 and 60°C and a relative humidity of 75 - 100% for a time period of between 12 - 24 hours to decrease the solubility of the coating of the taxane therapeutic agent in a 0.5% w/w aqueous solution of Heptakis-(2,6-di-O-methyl)-ß-cyclodextrin (HCD) elution medium at 25°C for 24 hours."*

Claim 1 of auxiliary requests 1 and 2 contains, in addition to the features of claim 1 of the main request, the following:

"wherein the taxane therapeutic agent is paclitaxel."

Claim 1 of auxiliary request 3 contains all the features of claim 1 of the main request and, in addition, the following:

"wherein:

the coating includes a first weight percentage of a first solid form of the taxane therapeutic agent characterized by a vibrational spectrum having fewer than three peaks between 1735 and 1700 cm^{-1} and a solubility of greater than 50% wt. after 24 hours in porcine serum at 37°C;

the conditioning of the taxane therapeutic agent coating is effective to decrease the first weight percentage and to provide a taxane therapeutic agent in a second taxane solid form within the coating, the second taxane solid form characterized by a vibrational spectrum comprising at least three peaks between 1735 and 1700 cm^{-1} and a solubility of less than 20% wt. after 24 hours in porcine serum at 37°C; and

the taxane therapeutic agent is paclitaxel, the first solid form is amorphous paclitaxel and the second solid form is dihydrate paclitaxel."

Claim 1 of auxiliary request 4 contains all the features of claim 1 of the main request and, in addition, the following:

"wherein:

the coating includes a first weight percentage of a first solid form of the taxane therapeutic agent;

the conditioning of the taxane therapeutic agent coating is effective to decrease the first weight percentage and to provide a taxane therapeutic agent in a second taxane solid form within the coating; and

the taxane therapeutic agent is paclitaxel, the first solid form is amorphous paclitaxel and the second solid form is dihydrate paclitaxel."

Claim 1 of auxiliary request 5 contains all the features of claim 1 of the main request and, in addition, the following:

"the method further comprising a sterilization step, and wherein the conditioning step is separate from said sterilization step."

Lastly, claim 1 of auxiliary request 6 contains all the features of claim 1 of the main request and, in addition, the following:

"wherein:

the taxane therapeutic agent is paclitaxel; and

the method further comprises a sterilization step, and wherein the conditioning step is separate from said sterilization step."

VI. The arguments of the appellant relevant for the decision were as follows:

The claimed invention did not make available to the skilled reader every variant encompassed by the functional definition in claim 1 according to which the coating had to be subjected to a conditioning step in order "to decrease the solubility of the coating of the taxane therapeutic agent", as the skilled reader could only determine by trial and error whether a specific form of a specific taxane would or would not become less soluble after the required conditioning step. For this reason, the subject-matter of claim 1 of the main request and of auxiliary request 5 was not sufficiently disclosed.

This objection was not solved by limiting the required taxane to paclitaxel, since a conditioning step could not reduce the solubility rate of every paclitaxel form, the patent did not contain sufficient guidance for selecting the conditions required by said conditioning and the skilled reader could not rely on the disclosed mechanism, since a reduction of the solubility rate of paclitaxel could be also due to other reasons such as the presence of an additional polymeric coverage. Thus, the invention as claimed in auxiliary request 6 was not sufficiently disclosed.

With respect to inventive step, any of documents D2, D3 or D4, which disclosed medical devices coated with paclitaxel and subsequently sterilised with ethylene oxide was the closest prior art. The appellant argued that the problem solution approach was not adequate to the present case and that the claimed invention merely linked an effect to an already obvious process which was for this reason not inventive. This objection applied in the same manner to the subject-matter of auxiliary requests 1 to 4. Regarding auxiliary request

6, document D6 disclosed a preconditioning step separate from the sterilisation but linked to it which the skilled person would combine with the teaching of D2, D3 or D4 so that the subject-matter of claim 1 was not inventive.

Lastly, it requested reimbursement of the appeal fee if the board considered figure 12 of D1 to be of any relevance to the decision.

VII. The arguments of the respondent relevant for the decision were the following:

The appellant had not discharged its burden of proof that the patent was not sufficiently disclosed. There was no reason to doubt that the solubility rate of every taxane was inevitably reduced by the conditioning step so that the claimed invention should be considered sufficiently disclosed. Further, the patent provided a general principle underlying the change in solubility rate, namely that an unsolvated form was transformed into a solvate by the conditioning step, whose generalisation should be allowable. Taxanes shared a core structure and were known molecules, so that the skilled person could find every embodiment of claim 1 with a reasonable amount of trial and error. For these reasons the claimed invention was sufficiently disclosed.

With respect to the subject-matter of auxiliary requests 1 to 4 and 6, document D7 was the closest prior art. The problem underlying the claimed invention was providing a further method of manufacturing a paclitaxel coated endolumenal medical device. The solution proposed in auxiliary requests 1 to 4 was conditioning the coated endolumenal medical device, and

there was no hint in D6 to the claimed solution as it only referred to sterilisation. Even if the skilled person could have used the sterilisation conditions required by claim 1 having regard to D6, there was no reason why it would have done it, in particular since D6 was not a textbook and it did not disclose standard, generally applicable sterilisation conditions. With respect to the subject-matter of claim 1 of auxiliary request 6, since the available prior art did not disclose a conditioning step separate from a sterilisation, the subject-matter of this request was inventive.

VIII. Oral proceedings before the board of appeal took place on 18 June 2015.

IX. The final requests of the parties were the following:

- The requests of the appellant were to set aside the decision under appeal and to revoke the patent. The appellant further requested the reimbursement of its appeal fee if the board would rely on document D1 for its decision.

- The requests of the respondent were, as a main request, to dismiss the appeal, or alternatively to maintain the patent upon the basis of one of auxiliary requests 1 to 9, all filed under cover of a letter dated 27 June 2014. The respondent further requested that document D9 not be admitted into the proceedings.

X. At the end of the oral proceedings, the decision was announced.

Reasons for the Decision

1. The appeal is admissible.

Main request, sufficiency of disclosure

2. Claim 1 of the main request is directed to a method of manufacturing a coated endolumenal medical device comprising two steps. Step (a) requires applying a taxane to a surface of the device to form a coating. Step (b) requires conditioning this coating at defined temperature and humidity for a defined period of time to decrease the solubility rate of the coating, said solubility rate being determined under defined conditions.

A number of compounds embraced by the term "taxane" in the sense of the claimed invention can be found on paragraphs [86] to [95] of the description.

The claimed method, in particular the conditioning step (b) is defined by a functional feature indicating the result to be achieved, namely to decrease the solubility rate of the taxane coating under defined conditions.

3. According to the case law of the Boards of Appeal, the requirements of sufficiency of disclosure are only met if the claimed invention can be performed by a person skilled in the art in the whole area claimed without undue burden, using common general knowledge and having regard to the information in the patent in suit (T 409/91, OJ 1994, 653, Reasons 3.5; T 435/91, OJ 1995, 188, Reasons 2.2.1). The disclosure of one way of performing the invention is only sufficient if it allows the invention to be performed in the whole range claimed. A claim containing functional features defined

by means of a result to be achieved comprises an indefinite and innumerable host of possible alternatives and is sufficiently disclosed as long as all these alternatives are available to the skilled person.

In the present case, it needs to be examined whether or not the host of variants encompassed by the functional definition "to decrease the solubility of the coating..." required by step (b) of claim 1 are made available to the skilled reader, and in particular whether the skilled person is in the position to identify within the required ranges the specific temperatures, humidity levels and time periods of the conditioning step that decreased the solubility rate of every taxane therapeutic coating.

4. It has not been contested that the patent provides one way to carry out the invention, namely by coating a medical device with amorphous paclitaxel and subjecting the coated device to a specific conditioning step.

The patent further proposes a mechanism according to which the conditioning step achieves the conversion of non-hydrated into hydrated forms.

5. The first issue to be examined is whether the conditioning step required by claim 1 inevitably reduces the solubility rate of every coating containing a taxane, in other words, whether the required functional definition is nothing more than the direct and inevitable consequence of the further features of claim 1.

The patent discloses in paragraph [0006] that taxane solvated forms typically dissolve more slowly than the

corresponding non-solvate. Thus, the patent does not base its teaching on the assumption than every solvated taxane inevitably dissolves more slowly than its non-solvated solid forms. For this reason alone, it is concluded that a decrease of the solubility rate is not the inevitable consequence of the conditioning step required by claim 1.

6. The next issue to be examined is whether the patent, nevertheless, contains sufficient information allowing the skilled person, without an undue burden, to turn a failure into success or whether, on the contrary, the claims extend to subject-matter which, after reading the patent specification, would still not be at the disposal of the skilled reader.

The claimed invention relies on the conversion of non-hydrated forms of taxane into hydrated forms. However, the patent does not disclose which hydrated forms further to paclitaxel dihydrate dissolve more slowly that their corresponding unsolvated forms.

The term "taxane" refers to a large number of compounds (see paragraphs [0086] to [0095] of the description) and the skilled person is aware that, among these compounds, the existence of (multiple) solid forms of each of them cannot be predicted, let alone their relative solubility rate. Therefore, the skilled person can only establish by trial and error whether or not the required conditioning step, applied to a coating containing a specific (solid) form of a specific taxane would or would not reduce the solubility rate of said coating. Thus, the functional definition of the conditioning step required by claim 1 is no more than an invitation to perform a research program in order to find forms of taxanes suitable for the claimed method,

which represents an undue burden for the skilled reader.

For this reason, it is concluded that the patent in suit does not provide sufficient guidance on how to carry out a method of manufacture of medical devices coated with any taxane in which the conditioning step required by claim 1 inevitably leads to a decrease of the solubility rate of the coating. As the patent in suit does not provide sufficient information in order to put the claimed invention into practice for every taxane required by claim 1, it does not disclose the claimed invention in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art.

7. The respondent argued that there was a general principle disclosed in the patent, namely that an unsolvated form may be transformed into a solvated form due to the required conditioning step, and a generalisation of this principle should be allowable. Taxanes shared a core structure and were not, hence, an infinite number of compounds, and their solid forms were known. For these reasons, the skilled person could find out every embodiment within claim 1 with only a reasonable amount of trial and error and thus without an undue burden.

However, the compounds defined as "taxanes" in paragraphs [0086] to [0095] are, despite sharing a core structure, a broad class of compounds, and the patent does not provide any information on any solid form further to those of paclitaxel, let alone on their solubility rates. Thus, finding taxane forms suitable for the claimed method of manufacture cannot be carried out, as alleged by the respondent, merely by a

reasonable amount of trial and error.

This argument of the respondent therefore fails to convince the board.

8. The respondent argued that claim 1 could be lacking essential features, but that was an issue under Article 84 EPC already present in the claims as granted and hence excluded from these appeal proceedings.

Notwithstanding whether claim 1 lacks essential features, the claimed invention is considered lacking sufficient disclosure for the reasons already explained.

This argument of the respondent is also unsuccessful.

9. The respondent further argued that the appellant had not discharged its burden of proof since it had not provided any evidence which could show that the claimed invention could not be carried out, and a lack of disclosure could only be established upon serious doubts, substantiated by verifiable facts.

However, the patent itself does not rely upon the assumption that every hydrated solid taxane must be less soluble than a corresponding non-hydrated form (see paragraph [0006]). The appellant, who in this case was the opponent, does not have to provide evidence on a point which is already acknowledged in the patent in suit.

This argument is therefore rejected.

10. It is thus concluded that the invention as claimed in the main request is not sufficiently disclosed for it

to be carried out by a person skilled in the art, with the consequence that the main request is not allowable.

Auxiliary request 1, inventive step

11. Claim 1 of auxiliary request 1 is directed to a method for the manufacture of an endolumenal medical device comprising the step of applying paclitaxel on said device to form a coating and conditioning said coating to decrease its solubility under defined conditions.

According to the patent, this process aims at producing a medical device, from which paclitaxel is slowly released, having sufficient durability for packaging and transport (see paragraphs [0010] to [0012]).

12. Closest prior art

The parties were divided as to whether documents D2, D3, D4 or D7 represented the closest prior art.

12.1 Documents D2 and D3

Documents D2 (example 5) and D3 (examples 2 and 3) disclose methods for manufacturing balloons coated with paclitaxel. Claim 1 of D2 aims at providing a device from which the drug is released within the shortest possible time. D3 discloses a combination of stents containing a slow-release drug and balloons containing a beneficial agent (page 18, lines 5-6) which can be paclitaxel. The drug coating of a balloon is not designed to have slow-release properties since balloons, unlike stents, are only in contact with the patient's body for a relatively short period of time.

Thus, D2 and D3 do not address the technical problem

underlying the claimed invention.

12.2 Document D7

During the oral proceedings before the board, the respondent argued that document D7 was the closest prior art.

D7 discloses stents coated with paclitaxel, which is retained without requiring any additional covering or containment layer, by providing a base material having a roughened or textured surface (see paragraph [0083]). The lack of such additional covering was part of the problem addressed by the claimed invention and that, for this reason, D7 was closer to the claimed invention than any other document on file.

However,examples 4 and 5 of document D4 (see paragraph 12.3 below) disclose crimping and expansion tests carried out without such a covering layer and D4 does not disclose that any such covering could be applied. D4 thus also discloses stents lacking a covering layer on the paclitaxel coating, but discloses a conditioning step which is lacking in D7. For these reasons, it is concluded that document D7 is not closer than D4 to the claimed invention, as alleged by the respondent.

12.3 Document D4

Document D4 (see examples) relates to the manufacture of stents coated with paclitaxel. D4 discloses that the duration of the delivery of the therapeutic substance is a variable which needs to be taken into consideration (see paragraph [0073]). Example 2 of D4 discloses the preparation of a coated stent using a mixture of paclitaxel and 95% ethanol resulting in a

coating containing paclitaxel dihydrate. Paragraph [0102] discloses that catheter stent assemblies can be sterilised, for example by exposure to ethylene oxide. Lastly, examples 4 and 5 disclose the coating's stability during crimping and expansion.

The respondent argued that paragraph [0102] referred to the embodiment represented by figures 7 and 8, which related to catheter stent assemblies and failed thus to disclose, in combination, the stent coated with paclitaxel in 95% methanol of example 2 and a sterilisation step. Furthermore, D4 disclosed that the catheter assemblies of figures 7 and 8 may be sterilised "if desired", which indicated that such a step was merely optional. Lastly, the examples related to laboratory experiments, which did not necessarily have to be sterilised. For these reasons, it concluded that D4 did not disclose a paclitaxel coated stent sterilised by exposure to ethylene oxide.

According to the case law, the teaching of a document is not confined to the detailed information given in the examples, but embraces its disclosure as a whole. However, in deciding what can be directly and unambiguously derived from a document, different passages can only be combined if the skilled reader would see a good reason for combining them (T 666/89, OJ EPO 1993, 495; T 565/90, not published in OJ).

Figures 7 and 8 of D4 disclose set-ups for coating a stent already assembled on an inserting device, which reduces manipulation and handling after the coating step. Figure 8 provides a detailed set up which allows coating a catheter-stent assembly by centrifugal forces. Putting into practice the embodiments of figures 7 and 8 requires detailed coating conditions in

terms of the nature of the drug, of the solvent used, their relative concentration, etc., and this essential information can only be found in example 2. Thus the skilled person has every reason for combining example 2 and the disclosure of figures 7 and 8, including the sterilisation step disclosed in paragraph [102].

Document D4 thus discloses a method for the manufacture of catheter assemblies containing a stent, which includes a sterilisation step prior to use in a subject by exposure to ethylene oxide. Document D4 relates to the same technical problem as the claimed invention, namely to the manufacture of slow-release paclitaxel-coated endolumenal medical devices having sufficient durability during packaging and transport, and discloses a two-step process including applying a taxane coating, followed by a sterilisation step.

12.4 It is thus concluded that document D4 represents the closest prior art for assessing inventive step.

13. Technical problem underlying the invention

The respondent has not relied on any advantage of the claimed method vis-à-vis that of D4, either in terms of the method itself or of the product obtained as the result of this method, and no such advantage is apparent.

The technical problem underlying the claimed invention is thus seen in providing a further method of manufacturing a slow-release paclitaxel coated endolumenal medical device, such medical device being stable during handling and storage.

14. Solution

As a solution, the patent in suit proposes the method according to claim 1, which is characterised in that the coated endolumenal medical device is conditioned at a defined temperature and relative humidity, for a defined period of time.

15. Success

In the light of the data provided in table 8A, the problem mentioned under point 13. above is considered to be successfully solved by the method of claim 1 of the first auxiliary request. This was not contested.

16. Lastly, it remains to be decided whether or not the proposed solution to the objective problem underlying the patent in suit is obvious in view of the state of the art.

Document D4 does not disclose any details about the ethylene oxide sterilisation of the disclosed stent assemblies. The skilled person, trying to put D4 into practice, would look for the specific sterilisation conditions in the prior art and turn to a document such as D6, which discloses that it requires 40-80% humidity, 30-35°C and 6 to 14 hours (see paragraph [0173]). The temperature lies within that required by claim 1 (30-60°C), whereas the relative humidity and the time required by claim 1 (75-100% and 12-24 hours) overlap.

There is no evidence on file showing that the conditioning time and relative humidity required by claim 1 is critical. Choosing specific conditions in terms of relative humidity and sterilisation time among

those of D6 falls within the normal capacities of the person skilled in the art.

Since the solution to the problem underlying the claimed invention proposed by claim 1 of the first auxiliary request does not go beyond an arbitrary selection among equally suitable alternatives taught in the prior art, its subject-matter is not inventive, as required by Article 56 EPC.

17. The respondent argued that a sterilisation step was different from a step intended at changing the composition of the coating and thus reducing its solubility rate.

However, the patent acknowledges that, by carrying out an ethylene oxide sterilisation, the composition of the coating changes and the solubility of paclitaxel is reduced (see paragraph [0153]). There is thus no technical reason why sterilisation and conditioning cannot be considered as one and the same step.

This argument is for this reason not convincing.

18. The respondent further argued that there was no standard protocol for ethylene oxide sterilisation. Document D6 was not a textbook representing the common general knowledge but a patent document, from which no general teaching could be extracted. For this reason, the skilled person would not have looked at D6 in order to retrieve the information missing from D4 with respect to the sterilisation conditions.

However, although there may be further alternative conditions which may or may not fall within those required by the conditioning step of claim 1, this does

not prevent the skilled person from choosing them as an alternative. Even if there is no textbook available to the skilled person, as alleged by the respondent, the content of any disclosure related to the same problem, such as that of D6, would be taken into account.

This argument is, thus, also found unconvincing.

Auxiliary requests 2 to 4

19. The respondent acknowledged that there was no different analysis with respect to inventive step regarding the subject-matter of claim 1 of auxiliary requests 2 to 4, and it is concluded that these claims are not inventive for the same reasons as claim 1 of auxiliary request 1, with the consequence that none of the auxiliary requests 1 to 4 is allowable.

Auxiliary request 5

20. The arguments explained with respect to the main request in points 2. to 10. above apply, in the same manner, to the invention as claimed in auxiliary request 5, which is not limited to any specific taxane. For these reasons, auxiliary request 5 is not allowable.

Auxiliary request 6

Amendments

21. There was no objection under Article 123 EPC.

Claim 1 of auxiliary request 6 finds a basis in the combination of claims 1 and 14 as originally filed and paragraph [0056] of the originally filed description.

Claims 2 to 8 find a basis, respectively, in claims 2 to 9 as originally filed.

The amendments restrict the scope of the subject-matter claimed by requiring paclitaxel as taxane and a conditioning step separate from the sterilisation step.

For these reasons, it is concluded that the requirements of Article 123 EPC are fulfilled.

Sufficiency of disclosure

22. Claim 1 of auxiliary request 6 is directed to a method of manufacturing a coated endolumenal medical device comprising applying paclitaxel to a surface of the device to form a coating and conditioning this coating at defined temperature and humidity for a defined period of time to decrease the solubility rate of the coating, said conditioning being separate from a sterilisation step.

23. It has not been disputed that the patent discloses one way for carrying out the invention, namely by applying amorphous paclitaxel to a medical device, which is converted to paclitaxel dihydrate by a conditioning step.

The patent further provides information on solid forms of paclitaxel in paragraphs [0006] and [0007] and proposes a mechanism which explains that the change in solubility rate of the drug after the conditioning step is due to its solvation (hydration).

Although it could be envisaged, for example, that a fully hydrated paclitaxel polymorph would not change

its solubility rate after the conditioning step, the skilled person finds in the patent sufficient information in order to transform a possible failure into success by selecting suitable candidates among paclitaxel solid forms guided by the information on solid forms provided in the patent and the proposed mechanism underlying the decrease in solubility rate.

24. The appellant argued that it was not credible that the conditions set in claim 1 were effective for reducing the solubility rate of every paclitaxel form and, for that reason, that the claimed invention was not sufficiently disclosed.

However, the solid forms of paclitaxel are only a reduced group of compounds and the skilled person finds sufficient information on how to reduce their solubility rate in paragraphs [0006] and [0007] of the patent in suit for the reasons explained in paragraph 24. above.

25. The appellant further questioned whether the patent provided sufficient evidence on the mechanism underlying the change of solubility rate induced by the conditioning. The patent only disclosed the optical inspection of the coated medical device after the conditioning step (table 8a) from which it could not be concluded that any change of solid form had indeed taken place. For this reason, the skilled person could not rely on the disclosed mechanism in order to find working embodiments further to that of conditioning amorphous paclitaxel and the claimed invention was for that reason not sufficiently disclosed.

However, the patent proposes a mechanism underlying the change in solubility rate (i.e. that a paclitaxel form

is hydrated under the conditioning conditions, which imply a high humidity) which is technically plausible and cannot be called into question by mere allegations not supported by any relevant evidence or facts. For this reason, it is considered that the appellant has not discharged its burden of proof in this respect.

26. The appellant argued that claim 1 did not exclude coatings which further contained a polymer coverage. For this reason, the change in solubility rate required by claim 1 could be due to changes in said coverage induced by the conditioning step, but the patent did not include any guidance on which polymer coverages could be suitable for this embodiment. For this reason, the claimed subject-matter included embodiments which were not at the disposition of the skilled reader.

However, step (a) of claim 1 requires "forming a coating *of the taxane* therapeutic agent" and step (b) requires "decrease the solubility of *the* coating of *the* taxane therapeutic agent". Claim 1 requires thus a decrease in the solubility of the taxane therapeutic agent and the description of the patent does not provide any basis for a different interpretation.

27. The appellant further argued that the patent did not provide sufficient guidance for selecting specific conditioning conditions within the ranges of temperature, time and relative humidity required by claim 1, in particular having regard to paragraphs [0106] and [0107] of the description.

Example 5B discloses conditions suitable for conditioning paclitaxel (100% relative humidity, 52°C, 12 hours). Which other conditions would also be effective can be determined without undue burden, since

this merely implies screening the variables involved (temperature, relative humidity, time).

28. The appellant also argued that the patent failed to provide a detailed description on how to determine whether the solubility rate had decreased and that the claimed invention was also for that reason not sufficiently disclosed.

For determining whether a decrease in solubility rate has been achieved, the solubility "in a 0.5% w/w aqueous solution of HCD elution medium at 25°C for 24 hours" before and after the required conditioning step needs to be compared. Since the decrease in solubility rate does not need to be defined in absolute values but only in relative terms, a detailed description of the test protocol is thus not necessary.

Therefore, the arguments of the appellant set up above are unconvincing.

For the reasons set out above, it is concluded that auxiliary request 6 complies with the requirements of Article 83 EPC.

Inventive step

29. Claim 1 of auxiliary request 6 is directed to a method of manufacturing a coated endolumenal medical device by

- applying a paclitaxel coating,
- conditioning the device at a defined relative humidity and temperature for a defined period of time to decrease the solubility of the coating under defined conditions, and
- sterilising,

wherein the conditioning step is separate from the sterilisation.

30. Closest prior art

The reasons explained under point 12. above also apply with respect to the method of claim 1 of auxiliary request 6 and D4 remains the closest prior art.

31. Technical problem underlying the invention

The technical problem underlying the claimed invention is seen in providing a further method of manufacturing a slow-release paclitaxel-coated endolumenal medical device stable during handing and storage.

32. Solution

As a solution, the method according to claim 1 of auxiliary request 6 is proposed, which is characterised in that it comprises a conditioning step, at a defined temperature and relative humidity and for a defined period of time, said conditioning being separate from the sterilisation of the medical device.

33. Success

The problem as defined in paragraph 31., above, is successfully solved by the method of claim 1 of the sixth auxiliary request having regard to the examples of the patent in suit. This has not been contested.

34. Lastly, it remains to be decided whether or not the proposed solution to the objective problem underlying the patent in suit is obvious in view of the state of the art

Document D4 discloses a method of manufacturing stents and catheter stent assemblies comprising ethylene oxide sterilisation but does not disclose any separate conditioning step.

Document D6 discloses conditions for sterilisation, but is silent on any conditioning step separate from the sterilisation which could decrease the solubility rate of the coating. None of the other documents on file hints towards such a possibility.

The skilled person, trying to obtain a further method of manufacturing a medical device, would thus not consider subjecting it to a conditioning step separate from the sterilisation, as required by claim 1 of auxiliary request 6, since the available prior art does not contain any indication towards the claimed solution.

The appellant has argued that the preconditioning step disclosed in paragraph [0176] of document D6 in fact amounted to the conditioning step required by claim 1. The patent, at the most, taught that the preconditioning of D6 could change the composition of the coating, but this did not amount to a technical contribution due to an inventive activity.

However, although the most preferred temperature conditions of said preconditioning given in [0176] of D6, namely 27-32°C, overlap with the range required by claim 1, the other two variables, 50-70% relative humidity and 5-7 hours, fall outside the claimed range, so that, even if, *arguendo*, the skilled person would carry out this preconditioning step having regard to D6, he would not have used the conditions required by

claim 1 and thus would not have arrived to the claimed invention.

For this reason, it is concluded that the method of claim 1 of auxiliary request 6 and hence those of the dependent claims 2-8 fulfil the requirements of Article 56 EPC.

Procedural issues

35. The respondent requested that document D9, which is an experimental report filed by the appellant during the opposition proceedings, not be admitted. Since D9 is not relevant for the present decision, it is not necessary to decide on this point.

Since the board did not rely on document D1, the condition for the appellant's request for reimbursement of the appeal fee does not apply. Therefore, the appeal fee is not reimbursed.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the department of first instance with the order to maintain the patent with the following claims and a description to be adapted:

Claims 1 - 8 of Auxiliary Request 6 filed under cover of a letter dated 27 June 2014.

The Registrar: The Chairwoman:

C. Rodríguez Rodríguez C. Komenda

Decision electronically authenticated