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Datasheet for the decision of 29 June 2017

Case Number: T 0703/15 - 3.3.10

Application Number: 07752891.7

Publication Number: 1996246

IPC: A61L27/54, A61L29/16, A61L31/16

Language of the proceedings: EN

Title of invention:
TAXANE COATINGS FOR IMPLANTABLE MEDICAL DEVICES

Patent Proprietor:
Cook Medical Technologies LLC

Opponent:
Withers&Rogers LLP/N.Wallin/H.Wright/A.Tombling

Headword:

Relevant legal provisions:
EPC Art. 100(b)

Keyword:
Sufficiency of disclosure - (no)

Decisions cited:
T 0409/91, T 0435/91

Catchword:

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Case Number: T 0703/15 - 3.3.10

D E C I S I O N
of Technical Board of Appeal 3.3.10
of 29 June 2017

Appellant: (Opponent)	Withers&Rogers LLP/N.Wallin/H.Wright/A.Tombling 4 More London Riverside London SE1 2AU (GB)
Representative:	August & Debouzy avocats 6-8 avenue de Messine 75008 Paris (FR)
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 London SE1 9SG (GB)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 3 February 2015 concerning maintenance of the European Patent No. 1996246 in amended form.**

Composition of the Board:

Chairman	P. Gryczka
Members:	R. Pérez Carlón
	C. Schmidt

Summary of Facts and Submissions

I. The appellant (opponent) lodged an appeal against the interlocutory decision of the opposition division which maintained European patent 1 996 246 in the form of the then pending auxiliary request 2, which is the main request of the respondent (patent proprietor) in these appeal proceedings.

II. Notice of opposition had been filed *inter alia* on the ground of insufficiency of disclosure (Article 100(b) EPC).

III. The opposition division concluded that the invention was disclosed in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art, as the parametric definitions in claim 1 were redundant since they were inherent properties of dihydrate paclitaxel and amorphous paclitaxel.

IV. With the statement setting out the grounds of appeal, the respondent filed auxiliary requests 1 to 8. Auxiliary request 9 was filed during the oral proceedings before the board, which took place on 29 June 2017.

V. Claim 1 of the main request and of auxiliary request 6 reads as follows:

"A coated implantable medical device comprising an implantable medical device having at least one surface and a coating on the at least one surface, wherein the coating comprises a first layer comprising a taxane therapeutic agent in a first taxane solid form having a vibrational spectrum including at least two peaks between 1735 and 1705 cm^{-1} and having a solubility of

less than 20% wt. after 24 hours in porcine serum at 37°C, the first layer positioned between the abluminal surface of the medical device and a second layer comprising a taxane therapeutic agent in a second taxane solid form having a vibrational spectrum including only one peak between 1735 and 1705 cm^{-1} and having a solubility of greater than 50% wt. after 24 hours in porcine serum at 37°C; wherein said first taxane solid form is dihydrate paclitaxel and said second taxane solid form is paclitaxel in an amorphous solid form."

Claim 1 of auxiliary request 1 contains, in addition to the feature of claim 1 of the main request, the following:

"and wherein the coating is free of a polymer."

Claim 1 of auxiliary requests 2 and 7 contains all the features of claim 1 of the main request, adding that

"and wherein at least 20% of the first layer comprises the taxane therapeutic agent in the first taxane solid form."

Claim 1 of auxiliary requests 3 and 8 contains all the features of claim 1 of the main request adding that

"wherein more than 50% of the first layer comprises the taxane therapeutic agent in the first taxane solid form; and wherein more than 50% of the second layer comprises the taxane therapeutic agent in the second taxane solid form."

Claim 1 of auxiliary request 4 combines the features of claim 1 of auxiliary requests 1 and 2. Similarly,

claim 1 of auxiliary request 5 combines the features of claim 1 of auxiliary requests 1 and 3.

Lastly, claim 1 of auxiliary request 9 contains all the features of claim 1 of the main request and, in addition, the following:

"wherein the porcine serum has a constant flow rate of 16 mL/min; and wherein the porcine serum is a modified porcine serum prepared by adding 0.104 mL of a 6.0 g/L heparin solution to porcine serum at 37°C and adjusting the pH to 5.6 +/- 0.3 using a 20% v/v aqueous solution of acetic acid."

VI. The arguments of the appellant relevant for the present decision were the following:

The claimed invention was not sufficiently disclosed, as the patent in suit did not describe how to prepare medical devices with a coating containing a layer comprising dihydrate paclitaxel having a solubility of less than 20% wt. after 24 hours in porcine serum at 37°C. This feature did not describe the solubility of dihydrate paclitaxel, but related to the whole coating layer. In view of the discrepancy between the term "solubility" and the units in which it was expressed, the feature should be interpreted as meaning the solubility rate. The data provided in the patent in suit showed that dihydrate paclitaxel in the coating required by claim 1 did not have the required solubility and, for that reason, the claimed invention was insufficiently disclosed. The appellant also requested that auxiliary request 9 not be admitted into the proceedings.

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

"Solubility" was a thermodynamic property and had a clear meaning, so that the description of the patent in suit did not need to be taken into consideration for interpreting it. It referred to the amount of paclitaxel dissolved in porcine serum in equilibrium with its solid form. Paclitaxel dihydrate inherently had a solubility of less than 20% wt. after 24 hours in porcine serum at 37°C, so the latter feature was in fact redundant.

Even if the required solubility were not an inherent property of paclitaxel dihydrate, the skilled person would not have any difficulty in achieving the required solubility, either by using less porcine serum, by increasing the amount of paclitaxel in the coating, or by measuring solubility under static conditions.

For these reasons, the claimed invention was sufficiently disclosed.

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

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

- The respondent requested that the appeal be dismissed, i.e. that the patent be maintained as upheld by the opposition division, or, alternatively, that the patent be maintained on the basis of one of auxiliary requests 1 to 9, filed with letter dated 24 December 2015 (auxiliary requests 1 to 8) and in the oral proceedings before

the board (auxiliary request 9).

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

Reasons for the Decision

1. The appeal is admissible.

Sufficiency of disclosure

2. According to the case law of the Boards of Appeal, the requirements of sufficiency of disclosure are met only if the claimed invention can be performed by a person skilled in the art without undue burden over the whole area claimed, 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).

3. Claim 1 is directed to a medical device having a coating with "*a first layer comprising a taxane therapeutic agent in a first taxane solid form having a vibrational spectrum including at least two peaks between 1735 and 1705 cm^{-1} and having a solubility of less than 20% wt. after 24 hours in porcine serum at 37°C*". This first taxane solid form is dihydrate paclitaxel.

4. The first issue to be examined is the meaning of the term "solubility" in claim 1. It is not disputed that the units in claim 1 do not correspond to the usual thermodynamic property solubility, which is normally defined as the amount of a compound dissolved in a solvent and is therefore expressed as a concentration. Instead, the units used for "solubility" in claim 1 are

weight percent *per amount of time*.

Thus, the skilled person, in view of the discrepancy between the normal definition of "solubility" and the units employed in claim 1, would seek guidance in the patent in suit.

4.1 With the exception of claim 1, each time the patent in suit uses the unit weight percent per amount of time, dissolution rates are concerned (figures 6, 7, 9).

In addition, in general, units define a physical quantity more accurately than names. The skilled reader will for this reason consider the feature "solubility" in claim 1 to refer to dissolution rates, as it includes time as a variable (weight percent after 24 hours).

4.2 The respondent argued that the term solubility in claim 5 had usual meaning, and that there was no need to rely on the description in order to interpret it.

However, this argument is not convincing, since the units used in claim 1 do not correspond to the normal meaning of "solubility".

4.3 The respondent further argued that paragraph [0139] of the patent in suit disclosed that the rate of elution of amorphous paclitaxel in porcine serum at 25°C was about 100 times faster than that of dihydrate paclitaxel. In contrast, the difference in "solubility" required by claim 1 was far lower. The skilled reader would thus deduce that the percentages in claim 1, which were of the same order of magnitude, could not refer to solubility rates.

However, the percentages in claim 1 (less than 20%, more than 50%) also cover the situation in which the elution rate of one form is 100 times faster than that of the other, as disclosed in paragraph [0139]. Thus, there is no reason why the passage on paragraph [0139] should lead to the conclusion put forward by the respondent.

5. The other issue to be examined in this context is whether, as the opposition division concluded and the respondent argued in these appeal proceedings, the "solubility" indicated in claim 1 is an inherent property of dihydrate paclitaxel, and thus redundant in claim 1, or whether, as argued by the appellant, said feature further restricts the claimed subject-matter.

5.1 The respondent argued that, from a purely grammatical pointview, the feature referred to the "solubility" of the taxane form, i.e. of dihydrate paclitaxel. Claim 1 contained two parametric requirements, namely a specific vibrational spectrum and a specific "solubility". It was apparent that the vibrational spectrum related to the taxane form *per se*, as a vibrational spectrum of a coating could not be measured, and there was no reason why the feature "solubility" should be any different.

5.2 It is not disputed that the patent in suit does not disclose any link between the required "solubility" threshold, which only appears in the claims of the patent specification, and either paclitaxel dihydrate or any other taxane solid form.

Figure 9 discloses (line 922) that after 24 hours (1440 minutes) the percentage of a coating consisting only of dihydrate paclitaxel, which is a preferred

embodiment of claim 1, dissolved in porcine serum is already more than 20% at 25°C. At 37°C, as required by claim 1, this percentage will be even higher. Thus, the patent in suit provides evidence that not every coating containing dihydrate paclitaxel has the "solubility" required by claim 1.

For this reason alone, it is thus concluded that the feature "having a solubility of less than 20% wt. after 24 hours in porcine serum at 37°C" is not made redundant by the feature "said first taxane solid form is dihydrate paclitaxel".

6. A particularly preferred embodiment of the present invention - [0009], [0011], [0012], examples, claim 4 - relates to a medical device having a coating whose layers consist essentially of solid paclitaxel, whereby said layers comprise either only one paclitaxel form, or combinations of dihydrate and amorphous paclitaxel. According to the most preferred embodiment of the claimed invention, the coating layer does not include polymers which retard the solubility of the taxanes present (claim 4 of the main request).

6.1 In the following, it will be examined whether these most preferred embodiments are sufficiently disclosed, i.e. whether or not the patent in suit has made available to the skilled reader an implantable medical device having a first layer comprising a taxane which is dihydrate paclitaxel, having a "solubility" of less than 20% wt. after 24 hours in porcine serum at 37°C, by disclosing at least one way to carry out the invention, by providing sufficient instructions, or by relying on the skilled reader's common general knowledge.

6.2 In this context, the most favourable interpretation of the feature "solubility" for the respondent is that it refers to dihydrate paclitaxel present in the coating, and not to the solubility of the whole coating, as the solubility of a coating comprising a mixture of slower-dissolving dihydrate [0143] and faster-dissolving amorphous paclitaxel [0143] will necessarily dissolve faster than dihydrate paclitaxel alone.

6.3 It is not disputed that none of the coatings disclosed in the patent in suit has a "solubility" below the required threshold.

It is further not disputed that the patent in suit does not provide any teaching on how to change the "solubility" of dihydrate paclitaxel to bring it below the required threshold.

The respondent has relied on general technical knowledge, and argued that the skilled person would not have any difficulty in providing dihydrate paclitaxel having the required "solubility" by either

- using less porcine serum, or
- increasing the amount of dihydrate paclitaxel, or
- measuring it under static conditions.

6.4 The claimed devices are intended to release paclitaxel within a body vessel [0040]. It can thus be assumed that the "solubility" conditions required by claim 1, which the respondent acknowledges are not fully defined, should mimic the conditions in such a vessel. For this reason, the skilled person would rule out using small amounts of porcine serum or static conditions.

6.5 With respect to the argument that the skilled person could increase the amount of dihydrate paclitaxel in the coating in order to reduce the "solubility" below the threshold defined in claim 1, figure 6C of the patent in suit discloses the elution of dihydrate paclitaxel in porcine serum at 25°C. Elution profiles 732-734, which correspond to stents coated with a 7:3 mixture of amorphous and dihydrate paclitaxel, show that, as argued by the respondent, a lower elution rate of dihydrate paclitaxel can be achieved by increasing its paclitaxel content.

In contrast, elution profiles 736-738, which relate to stents coated with a 4:1 mixture of amorphous and dihydrate paclitaxel lead to the opposite result, i.e. an increase of the total amount of paclitaxel coating implied a slower elution rate.

Thus, the experimental data in the patent in suit does not support the argument of the respondent that the "solubility" could be reduced by increasing the amount of paclitaxel in the coating, as this is not always the case.

6.6 As the dissolution rate of amorphous paclitaxel is 100 times higher than that of dihydrate paclitaxel [143], any combination of dihydrate and amorphous paclitaxel will dissolve even faster (lines 904 to 920).

7. The appellant has not relied on any further evidence showing that, at the date of filing, a skilled person knew how to obtain a coating comprising dihydrate paclitaxel having the required "solubility".

As the application does not contain the required

information allowing a skilled person to obtain medical devices comprising a coating containing dihydrate paclitaxel having a "solubility" of less than 20% wt. after 24 hours in porcine serum at 37°C, the board concludes that the subject-matter of claim 1 of the main request is not disclosed in a manner sufficiently clear and complete for it to be carried out by such a person, and thus that the ground under Article 100(b) EPC precludes the maintenance of the patent as granted.

8. It is not disputed that the situation with respect to sufficiency of disclosure is the same for claim 1 of any of the auxiliary request on file, and that the arguments set out above also apply *mutatis mutandis*, with the consequence that none of the requests on file is allowable.

9. In these circumstances, it is not necessary to decide whether or not auxiliary request 9 is admitted into the proceedings.

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:

C. Rodríguez Rodríguez P. Gryczka

Decision electronically authenticated