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**Datasheet for the decision
of 26 February 2008**

Case Number: T 1176/05 - 3.3.02

Application Number: 96910810.9

Publication Number: 0820322

IPC: A61M 15/00

Language of the proceedings: EN

Title of invention:

Metered dose inhaler for fluticasone propionate

Patentee:

SMITHKLINE BEECHAM CORPORATION

Opponent:

3M Innovative Properties Company

Headword:

Metered dose inhaler/SMITHKLINE BEECHAM CORPORATION

Relevant legal provisions:

EPC Art. 56

Relevant legal provisions (EPC 1973):

-

Keyword:

"All requests - Inventive step - No: obvious combination"

Decisions cited:

-

Catchword:

-



Case Number: T 1176/05 - 3.3.02

DECISION
of the Technical Board of Appeal 3.3.02
of 26 February 2008

Appellant: SMITHKLINE BEECHAM CORPORATION
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Decision under appeal: Decision of the Opposition Division of the
European Patent Office posted 20 July 2005
revoking European patent No. 0820322 pursuant
to Article 102(1) EPC.

Composition of the Board:

Chairman: U. Oswald
Members: J. Riolo
J. Van Moer

Summary of Facts and Submissions

- I. European patent No. 0 820 322, based on European application No. 96 910 810.9, was granted on the basis of 28 claims.

Independent claim 1 as granted read as follows:

"1. A metered dose inhaler characterised in that part or all of its internal surfaces are coated with a polymer blend comprising one or more fluorocarbon polymers in combination with one or more non-fluorocarbon polymers, for dispensing an inhalation drug formulation comprising fluticasone propionate, or a physiologically acceptable solvate thereof, and a fluorocarbon propellant, optionally in combination with one or more other pharmacologically active agents or one or more excipients."

- II. Opposition was filed against the patent under Article 100(a) EPC for lack of inventive step, Article 100(b) EPC for insufficiency of disclosure and under Article 100(c) EPC.

The following documents *inter alia* were cited during the proceedings before the Opposition Division and the Board of Appeal:

- (2) EP-A-0 642 992
- (3) Ullmann's Encyclopedia of Industrial Chemistry, VCH (1991)
- (26) Declaration by Prof. Stephen Shaw
- (30) Supplemental declaration by Prof. Stephen Shaw
- (43) Declaration by Dr. Batzar

III. By its decision pronounced on 22 June 2005, the Opposition Division revoked the patent under Article 102(1) EPC because neither the main request nor the auxiliary request fulfilled the requirements of inventive step.

Regarding the main request, the Opposition Division argued as follows:

Document (2) was regarded as the most relevant prior art document.

It disclosed a metered dose inhaler comprising an aluminium can which contains a suspension of an antiasthmatic drug, such as formoterol, preferably in 1,1,1,2-tetrafluoroethane, wherein drug deposition to the container walls is overcome by a plastic coating on the walls. In particular, PTFE or FEP are the preferred plastic coatings.

The subject-matter of independent claim 1 of the main request was accordingly distinguished from (2) by the following technical features:

- (a) the inhaler can contains fluticasone propionate as antiasthmatic agent
- (b) part or all of the internal metallic surfaces of the can are coated with a polymer blend of one or more fluorocarbon polymers in combination with one or more non-fluorocarbon polymers.

As regards feature (a), the Opposition Division considered that, since fluticasone propionate was a well known antiasthmatic drug as agreed by the patentee, the skilled person obviously would take it

into consideration to provide for an alternative inhalation medicament.

As far as feature (b) was concerned, as no test results had been presented hitherto which could support any kinds of surprising effect, the problem to be solved by the invention was the one derived from the application, namely providing an MDI comprising a coated drug-containing can wherein the coating on the can walls is more difficult to remove than a pure fluorocarbon polymer coating.

Having regard to the textbook (3) relating to fluoropolymer coatings useful in many technical fields, which taught that mixtures of PTFE (polytetrafluoroethylene) dispersions and heat-resistant hydrocarbons such as polyimide, polyether sulfone (PES) or polyphenylene sulfide improve poor adhesion of fluoropolymer to a substrate, it was clear that a fluorocarbon coating specialist in a team concerned with the problem to be solved in the contested patent would replace the pure PTFE coating in document (2) by a polymer blend of PTFE with PES as suggested in the latter document.

Thus, the Opposition Division concluded that the subject-matter of the amended independent claim 1 of the main request did not meet the requirement of inventive step and was therefore to be rejected.

As the main request could not be allowed for this reason, other objections raised by the opponent such as lack of enablement and extension beyond the original disclosure were not to be decided.

Claim 1 of the auxiliary request read:

"A metered dose inhaler for dispensing an inhalation drug formulation wherein the inhaler:

contains the inhalation drug formulation, and comprises a can made of aluminium or an alloy thereof, characterised in that:

the inhalation drug formulation comprises a suspension of fluticasone propionate and a fluorocarbon propellant which is 1,1,1,2-tetrafluoroethane, or 1,1,1,2,3,3,3-heptafluoro-n-propane or mixtures thereof, optionally in combination with one or more other pharmaceutically active agents or one or more excipients,

and all of the internal metallic surfaces of the can are coated with a polymer blend of PTFE and PES."

Concerning this request, the Opposition Division first argued that the following amendments made to claim 1 as granted were allowable under Article 123(2) and (3) EPC:

(a) The wording "part or all of its internal surfaces are coated with a polymer blend comprising one or more fluorocarbon polymers in combination with one or more non-fluorocarbon polymers" has been replaced by the feature "all of the internal metallic surfaces of the can are coated with a polymer blend of PTFE and PES".

(b) The metered dose inhaler contains the drug formulation (added feature).

The metered dose inhaler comprises a can made of aluminium or an alloy thereof (added feature).

(d) The drug formulation comprises a suspension of fluticasone propionate and a fluorocarbon propellant which is 1,1,1,2-tetrafluoroethane, or 1,1,1,2,3,3,3-heptafluoro-n-propane or a mixture thereof (added feature).

(e) The wording "or a physiologically acceptable solvate thereof" has been deleted.

The Opposition Division considered that these amendments mentioned were indeed based on claims 2, 12, 13, 15, 16 and the description on page 8, lines 13 to 24 as originally filed, and restricted the scope of protection conferred to ensure that the amendments were allowable under Article 123(2) and (3) EPC.

Moreover, the deletion of the feature discussed under item (e) above did not violate Article 123(3) EPC since it related to an alternative embodiment which may be deleted from the claim as granted without extending the scope of protection beyond the original disclosure.

The Opposition Division argued that it could not go along with the opponent's arguments that the amended independent claim 1 should not be allowed since it resulted from a multiple selection which could not be derived from the application as published. The features introduced into claim 1 as granted were derived from multiple dependent claims which were interrelated through the fact of their dependency and could therefore be combined.

Regarding inventive step, it held that the inventive step reasoning and conclusions were also relevant for

claim 1 of this set of claims since the polymer blend PTFE/PES was equally taught by the prior art (3).

- IV. The appellant (patentee) lodged an appeal against the said decision.
- V. In a communication from the Board dated 6 February 2008, the attention of the appellant was drawn to the established case law relating to technical prejudice and comparative tests.

The communication also contained the Board's preliminary opinion that the subject-matter of the patent in suit seemed not to involve an inventive step vis-à-vis documents (2) and (3) in combination.

- VI. Oral proceedings were held before the Board on 26 February 2008.
- VII. The appellant submitted a main request and six auxiliary requests.

Claim 1 of the main request reads:

"1. "A metered dose inhaler for dispensing an inhalation drug formulation wherein the inhaler:
contains the inhalation drug formulation, and
comprises a can made of aluminium or an alloy thereof, characterised in that:
the inhalation drug formulation comprises a suspension of fluticasone propionate or a physiologically acceptable solvate thereof and a fluorocarbon propellant which is 1,1,1,2-tetrafluoroethane, or 1,1,1,2,3,3,3-heptafluoro-n-

propane or mixtures thereof, optionally in combination with one or more other pharmaceutically active agents or one or more excipients,

and all of the internal metallic surfaces of the can are coated with a polymer blend of PTFE and PES."

Compared with claim 1 of the main request, claim 1 of the first auxiliary request is merely restricted to "consists essentially" instead of "comprises".

Compared with claim 1 of the main request, claim 1 of the second auxiliary request is restricted to "consists essentially" instead of "comprises" and to 1,1,1,2-tetrafluoroethane as fluorocarbon propellant.

Compared with claim 1 of the main request, claim 1 of the third auxiliary request is restricted to "consists essentially" instead of "comprises" and to fluticasone propionate as drug.

Compared to claim 1 of the main request, claim 1 of the fourth auxiliary request is restricted to "consists essentially" instead of "comprises", to fluticasone propionate as drug and to 1,1,1,2-tetrafluoroethane as fluorocarbon propellant.

Compared with claim 1 of the main request, claim 1 of the fifth auxiliary request is restricted to "consists essentially" instead of "comprises", to fluticasone propionate as drug and to salmeterol xinafoate as optionally active agent.

Compared with claim 1 of the main request, claim 1 of the sixth auxiliary request is restricted to "consists

essentially" instead of "comprises", to fluticasone propionate as drug and to 1,1,1,2-tetrafluoroethane as fluorocarbon propellant and to salmeterol xinafoate as optionally active agent.

During the oral proceedings the respondent first indicated that, in response to the Board's communication, it did not intend to argue that a technical prejudice existed against the combination of the teaching of document (3) with document (2).

In summary, it essentially held that the skilled person would not combine documents (2) and (3) for two main reasons:

1) The combination of documents (2) and (3) was not obvious because they related to different technical fields as submitted in the expert's reports (26) and (30).

2) There was no reasonable expectation of success in the light of the concern about drug deposition on the surface of the polymer blend expressed by both experts in documents (43) and (30).

VIII. During the oral proceedings, the respondent essentially supported the Opposition Division's argument that the combination of documents (2) and (3) was obvious because document (3) was representative of the general knowledge of the skilled person and because the concerns expressed by the experts were ill-founded.

It further maintained its objections with respect to Article 123(2) and lack of sufficiency on the basis of

the arguments already adduced before the Opposition Division.

- IX. The appellant requested that the decision under appeal be set aside and that the patent be maintained on the basis of the main or auxiliary requests 1 to 6 filed with its letter dated January 2008.

The respondent requested that the appeal be dismissed.

Reasons for the Decision

1. The appeal is admissible.
2. *Main request*

Claim 1 of the main request is identical to claim 1 of the auxiliary request before the Opposition Division with the addition of the wording "or a physiologically acceptable solvate thereof" after "fluticasone propionate". (This wording is based on the wording of claim 1 of the application as originally filed.)

2.1 Article 123 EPC

The Board agrees with the Opposition Division's favorable conclusions regarding Article 123 EPC with respect to the auxiliary request.

Claim 1 of the present main request is identical to claim 1 of the auxiliary request before the Opposition Division with the addition of the wording "or a

physiologically acceptable solvate thereof" after "fluticasone propionate".

This wording is based on the wording of claim 1 of the application as originally filed.

Having regard to the Board's conclusions in the assessment of inventive step (see below, point 2.3.6) and to the fact that the respondent did not put forward new arguments compared with those submitted and dealt with before the Opposition division, there would appear to be no need to devote further attention to this issue.

Accordingly, the Board concludes that the subject-matter of the main request fulfils the requirements of Article 123 EPC (see above under III, and the Opposition Division's decision, point 3.1).

2.2 Article 100b) EPC.

The Opposition Division did not deal with this objection in its decision.

In the light of the numerous working examples provided in the patent in suit, and in the absence of any concrete evidence from the respondent, the Board has no reason to doubt that the skilled person would be able to make a metered dose inhaler as claimed in claim 1 just by repeating any of these examples.

Having regard to the Board's conclusions in the assessment of inventive step (see below, point 2.3.6

there would appear to be no need to devote further attention to these issues.

2.3 Inventive step

2.3.1 The contested patent relates to a metered dose inhaler comprising an aluminium can having its internal metallic surface covered with a plastic coating of PTFE-PES on the wall, which contains a suspension of an antiasthmatic drug (fluticasone propionate) in 1,1,1,2-tetrafluoroethane (column 6, lines 24 to 39).

According to the patent in suit, the coating with a fluorocarbon polymer such as PTFE significantly reduces the problem of drug deposition on the can walls (column 1, lines 50 to 55, and column 5, lines 34 to 37).

Moreover, the description indicates that the fluorocarbon polymer can be blended with a non-fluorinated polymer such as polyimide, polyethersulfone (PES) or polyphenylene sulphide in order to improve adhesion of the polymer coating to the can walls.

As agreed with both parties, the Board considers that document (2), which also deals with a metered dose inhaler for dispensing an inhalation drug formulation, represents the closest prior art.

In that respect, document (2) discloses a metered dose inhaler comprising an aluminium can which contains a suspension of an antiasthmatic drug (e.g. formoterol), preferably in 1,1,1,2-tetrafluoroethane, wherein drug deposition to the container walls is significantly

reduced by coating the walls with a fluorocarbon polymer. In particular, PTFE is preferred as the plastic coating (column 4, line 50, to column 5, line 3; column 5, lines 31 to 54).

Both parties also agreed that the skilled person in this instance is constituted by a team that would typically be found in a pharmaceutical company comprising an aerosol drug formulator, a person knowledgeable about the manufacture of respiratory devices and a specialist in the field of polymers and plastic coatings.

- 2.3.2 The Board notes that there is no evidence on file to show that the only advantage cited in the contested patent vis-à-vis document (2), namely the improved adhesion of the polymer coating to the can walls achieved by the addition of PES, is not effective.

Moreover, it can only be assumed from the disclosure as originally filed that the drug deposition in the patent in suit is similar to that occurring in the prior art document (2), since this effect is linked solely to the use of PTFE, as it is already the case in the prior art (page 2, lines 8 to 11).

In that respect too, the Board observes that the respondent did not provide any evidence to the contrary.

Thus, as the experiments submitted by the appellant in the technical reports are not intended to demonstrate anything other than what is already contained in the patent in suit (i.e. similar drug deposition and

improved adhesion), and in the absence of any evidence demonstrative to the contrary, the problem to be solved by the subject-matter of claim 1 of the main request of the patent in suit as against document (2) can only be seen in the provision of a metered dose inhaler for dispensing an inhalation antiasthmatic drug formulation with a coating having improved adhesion to the can walls.

It also follows that the technical reports submitted by the appellant are superfluous and that the question whether they constitutes a valid comparison therefore appears to be irrelevant, since they were not deemed to demonstrate any further improvements.

- 2.3.3 This problem is solved by adding PES to the prior-art PTFE coating.

In the light of the description and examples in the patent in suit, and in the absence of any specific evidence to the contrary, the Board is satisfied that the problem has been solved.

- 2.3.4 Thus the question to be answered is whether the proposed solution would have been obvious to the skilled person in the light of the prior art.

In that respect, the Board notes that, according to the textbook Ullmann's Encyclopedia (3), the fluoropolymer PTFE has poor adhesion to many substrates (page 380, right-hand column, paragraph entitled "Polytetrafluoroethylene").

In the very same paragraph, this textbook teaches that "recently, mixtures of PTFE and PES have been developed to improve their poor adhesion".

The Board has no doubt that the "skilled person" is well aware of this disclosure, since, as agreed by both parties, that person is a team including a specialist in the field of polymers and plastic coatings.

In the light of document (3), it is also clear, as stressed by the appellant during the oral proceedings, that the adhesion problem with PTFE coatings is a crucial one.

Accordingly, the Board is convinced that the skilled person (team), faced with the problem defined under 2.3.2, would have added PES to the prior-art coating as advocated by document (3).

2.3.5 The Board does not agree with the appellant's two main lines of argument.

With regard to the argument that the combination of documents (2) and (3) is not obvious because they relate to different technical fields as submitted in the expert's reports (26) (in particular, paragraph 36) and (30) (in particular, paragraph 8), the Board notes that the teaching of document (3) is not at all restricted to the field of cooking ware. It is indeed clear that the reference to frying pans in document (3) concerns a case where a ceramic-powder is used as the first coat and not a blend of PTFE and PES.

Accordingly, the teaching of document (3) appears to be a general teaching which would apply to many technical

fields. Moreover, even if the disclosure in (3) had been strictly restricted to the field of cooking ware, this would not imply that the blend can only be used in this field.

In addition, the Board notes that a coating used in the field of cooking ware, like a coating used in the pharmaceutical field must not be harmful to the health. Accordingly, even if the disclosure in (3) had been restricted to the culinary/alimentary field, which is not the case, it is considered that the culinary/alimentary field, although different, is not such that it would *prima facie* not be considered by the skilled person - particularly, since document (2), which relates to pharmaceuticals, uses PTFE, the subject of document (3).

Further, assuming again that the disclosure in (3) had been restricted to the culinary/alimentary field, it is correct, as submitted by the expert, that the temperature, solvent and pressure conditions to which the coating is exposed in a frying pan and in a metered dose inhaler are very different. However, the Board would still remain convinced that the skilled person would have tried the polymer blend for at least four reasons:

- the blend is a commercially available product, i.e. readily available
- the preparation and testing of coatings does not involve an undue burden, as shown by the routine experimental processes used in the numerous working examples and the technical reports

- plastic coatings are already known from document (2) to be suitable in the field of pharmaceuticals
- the adhesion problem is crucial problem and has to be solved, as emphasised by the appellant himself during the oral proceedings.

Moreover, the Board does not agree that in the present case the skilled person would not try the blend because of his conservative nature, taking no risks and avoiding new technical fields.

In fact, having regard to document (2), the contested patent cannot be regarded as moving into new technical field since the coating of a metered dose inhaler with a plastic coating is already known, so that the present subject-matter merely concerns improvements in an already known field.

In addition, the Board is convinced that the skilled person faced with a crucial technical problem is well able to take a risk when there is a clear teaching on how to solve the problem and putting the necessary technical measures into practice does not involve major difficulties but simple routine experiments, as in the present instance (see above).

Regarding the main concern expressed by the expert in document (43) (in particular, paragraphs 15 and 31), namely that the addition of PES to the PTEF might give rise to drug deposition problems because of the presence of the higher-surface-energy (adhesion-promoting) non-fluorinated polymer (ie PES) and also to delamination problems, making it impossible to know whether the claimed coating blend would be suitable for

the pharmaceutical application owing to possible drug deposition problems, the Board does not contest that this concern might be real.

However, the key point in the present case is that the skilled person must solve the adhesion problem posed by PTFE coating and knows from document (3) that the addition of PES solves precisely this problem.

Accordingly, the testing of the coating blend to see whether or not the expert's concern was ill-founded is not a big issue, as appears from the appellant's working examples and test reports, which all involve routine experimental processes. The Board remains therefore convinced that the skilled person would rather have tried the coating blend to seek a compromise between the required adhesion improvement and, possibly, a drug deposition level acceptable for the intended use, than renounce a promising teaching.

He would then inevitably find that the possible deposition problem did not exist or at least that it was compatible with the intended use.

Finally, the Board does not follow the appellant's argument that the skilled person would not dare to try the coating blend because, having regard to the fact that the inhalation of an insufficient amount of drug might be life-threatening, the expert's concerns as to drug deposition would have deterred him from trying.

Indeed, as the skilled person does not need to carry out experiments with patients to determine whether or not drug deposition problems exist (i.e. a simply

washing the coating with a solvent followed by HPLC analyses, as illustrated in the test reports), the above considerations are not relevant.

As to the appellant's argument that, unlike PTFE, PES is only available in solvent other than water, the Board notes that the respondent contested the introduction of this argument because it was introduced for the first time during the oral proceedings, so that this information could not be verified.

- 2.3.6 In the light of these facts, the Board can only conclude that the subject-matter of claim 1 of the main request does not involve an inventive step as required by Article 56 EPC.

Under these circumstances, there is no need to consider the remaining claims.

3. *Auxiliary requests 1 to 6*

During the oral proceedings, both parties agreed that the auxiliary requests did not add anything new in relation to the assessment of inventive step and therefore merely cited again their submissions with respect to the main request.

Thus, as there are no additional distinguishing feature in these requests which appear to be non-obvious vis-à-vis the combination of documents (2) and (3), the conclusions as to lack of inventive step for the subject-matter of claim 1 of the main request applies equally to all the auxiliary requests.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar

The Chairman

A. Townend

U.Oswald