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Datasheet for the decision of 28 February 2008

Case Number: T 0226/06- 3.3.02

Application Number: 96911712.6

Publication Number: 0820323

IPC: A61M 15/00

Language of the proceedings: EN

Title of invention:
Metered dose inhaler for salmeterol

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:
-

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Case Number: T 0226/06 - 3.3.02

D E C I S I O N
of the Technical Board of Appeal 3.3.02
of 28 February 2008

Appellant: (Patent Proprietor)
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Decision under appeal:
Decision of the Opposition Division of the European Patent Office posted 21 December 2005 revoking European patent No. 0820323 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. 0 820 323, based on European application No. 96 911 712.6, was granted on the basis of 30 claims.

Independent claim 1 as granted read as follows:

"1. A metered dose inhaler characterised in that part or all of its internal surfaces 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 salmeterol, or a physiologically acceptable salt 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 novelty and 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) Ullmannn's Encyclopedia of Industrial Chemistry, pages 380-382, VCH (1991)
(27) Declaration by Prof. Stephen Shaw
(44) Supplemental declaration by Prof. Stephen Shaw
(45) Declaration by Dr. Batzar

III. By its decision pronounced on 30 November 2005, the Opposition Division maintained the patent in amended form under Articles 102(3) and 106(3) EPC (1973).

Concerning the main request (set of claims as granted), the Opposition Division considered that the introduction of the wording "a polymer blend comprising" before the phrase "one or more fluorocarbon polymers in combination with one or more non-fluorocarbon polymers" infringed Article 123(2) EPC, on the grounds that this addition - including polymer blends, which besides the fluorocarbon polymer and the non-fluorocarbon polymer component may contain other (undefined) materials - was not disclosed in the application as originally filed.

As to auxiliary request 1, the Opposition Division considered that its subject-matter did not contravene Article 123(2) EPC because the amendments in claim 1 were based on claims 1, 15, 18 and 19 as published and as originally filed, and dependent claims 2 to 13 were identical to claims 3 to 12 and 21 as published and as originally filed. Moreover, the amendments in claim 1 merely restricted the scope of protection conferred, so that they were allowable under Article 123(3) EPC as well.

The Opposition Division also considered that, in the absence of any concrete evidence to the contrary, the patent in suit fulfilled the requirements of Article 83 EPC because the description provided the skilled person with sufficient instructions in particular on page 9, on how to carry out the invention.

It further disregarded the clarity objection relating to the term "metallic" in claim 1, because it was clear from the wording of the claim itself that metallic did not refer to anything other than aluminium or an alloy thereof.

Concerning the novelty objection, the Opposition Division was of the opinion that the claimed subject-matter was novel because none of the available prior art, including document (2), disclosed a metered dose inhaler comprising both a polymer blend coating of PTFE and PES and salmeterol as an active agent.

With regard to inventive step in connection with this 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, 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 salmeterol as an 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 salmeterol 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, the Opposition Division was of the opinion that the test results provided by the respondent demonstrated that drug deposition is not more substantial in the case of a mixture of non-polar PTFE (polytetrafluoroethylene) with polar PES (polyether sulfone) than in the case of non-polar PTFE alone.

As this was not be foreseeable in the light of the concerns expressed by both experts, the Opposition Division concluded that the subject-matter of the amended independent claim 1 and of its dependent claims 2 to 12 in auxiliary request 1 met the requirement of inventive step.

IV. The appellant (opponent) lodged an appeal against the said decision.

V. In a communication from the Board dated 6 February 2008, the attention of the respondent was drawn to the established case law relating to technical prejudice and comparative tests.

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 was also given in the communication.

VI. Oral proceedings were held before the Board on 28 February 2008.

VII. During the oral proceedings, the appellant held essentially 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) EPC and lack of sufficiency on the basis of the same arguments provided before the Opposition Division, but did not maintain the clarity and novelty objection.

VIII. The respondent submitted 7 auxiliary requests.

Claim 1 of the main request is identical to claim 1 of auxiliary request 1 maintained by the Opposition Division, and 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 salmeterol, or a physiologically acceptable salt thereof, and a fluorocarbon propellant which is 1,1,1,2-tetrafluoroethane or 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" and the wording "one or more excipients" has been deleted.

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, and the wording "or one or more excipients" has been deleted.

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 salmeterol xinafoate as drug, and the wording "or one or more excipients" has been deleted.

Compared with claim 1 of the main request, claim 1 of the fourth auxiliary request is restricted to "consists essentially" instead of "comprises", to salmeterol xinafoate as drug, to 1,1,1,2-tetrafluoroethane as fluorocarbon propellant and the wording " or one or more excipients " has been deleted.

Compared with claim 1 of the main request, claim 1 of the fifth auxiliary request is restricted to "consists essentially" instead of "comprises", to salmeterol xinafoate as drug, to fluticasone propionate or a physiologically acceptable solvate thereof as pharmacologically active agents, and the wording "or one or more excipients" has been deleted.

Compared with claim 1 of the main request, claim 1 of the sixth auxiliary request is restricted to "consists essentially" instead of "comprises", to salmeterol xinafoate as drug, and to fluticasone propionate as pharmacologically active agent, and the wording "or one or more excipients" has been deleted.

Compared with claim 1 of the main request, claim 1 of the seventh auxiliary request is restricted to "consists essentially" instead of "comprises", to salmeterol xinafoate as drug, to fluticasone propionate as pharmacologically active agent, and to 1,1,1,2-tetrafluoroethane as fluorocarbon propellant, and the wording "or one or more excipients" has been deleted.

During the oral proceedings the respondent first indicated that, in response to the Board's communication, it did not its 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 (27) and (44).

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 (45) and (44).

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

The respondent requested that the appeal be dismissed or, in the alternative, that the patent be maintained on the basis of the auxiliary requests filed on 5 September 2006.

Reasons for the decision

1. The appeal is admissible.

2. Main request

Claim 1 of the main request is identical to claim 1 of auxiliary request 1 maintained by the Opposition Division.

The appellant did not maintain the clarity and novelty objection raised during the opposition procedure with respect to this subject-matter and the Board sees no reason to disagree with the favourable conclusions of the Opposition Division in that respect (see above under III, and the Opposition Division's decision, points 3.3 and 3.4).

2.1 Article 123 EPC

The Board agrees with the Opposition Division's favorable conclusions regarding Article 123 EPC with respect to this subject-matter.

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 appellant 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 these issues.

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 Board agrees with the Opposition Division's favourable conclusions as to Article 100b) EPC.

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 appellant 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 these issues.

Accordingly, the Board concludes that the subject-matter of the main request fulfils the requirements of Article 100 b) EPC(see above under III, and the Opposition Division’s decision, point 3.2).

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 (salmeterol) in 1,1,1,2-tetrafluoroethane (column 6, lines 20 to 44).

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 33 to 42).

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 in the prior art (page 2, lines 8 to 11).

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

Thus, as the experiments submitted by the respondent 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 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 respondent are superfluous and that the question whether they constitute 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 constituted by 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 respondent 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 respondent's two main lines of argument.

With regard to the argument that the combination of documents (2) and (3) was not obvious because they relate to different technical fields as submitted in the expert's reports (27) (in particular, paragraph 36) and (44) (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. Moreover, the mere fact that a blend of PTFE and PES would also be useful in the field of cooking ware does not imply that it can only be used in this field.

In addition, the Board notes that a coating used in the field of cooking, like a coating used in the pharmaceutical field must not be harmful to the health. Accordingly, even if the disclosure in (3) would had strictly 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 - particularity since document (2), which relates to pharmaceuticals, uses PTFE, which is one of the subjects 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 respondent 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 a 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 (45) (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 respondent's

working examples and test reports, which all involve routine experimental processes. The Board therefore remains 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 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 respondent'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 salmeterol, a potent long-acting agent, might cause a breakthrough attack, 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. 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 respondent's argument that, unlike PTFE, PES is only available in a solvent other than water, the Board notes that the appellant contested the introduction of this argument because it was put forward for the first time during the oral proceedings, so that this information could not be verified.

In conclusion, the Opposition Division was wrong in deciding that the mere fact of the experts' concerns being ill-founded was sufficient to establish inventive step. As appears from the above, the skilled person would inevitably realise that just by applying the teaching of document (3) in practice, which he would do in any case because of the crucial need to solve the adhesion problem with PTFE.

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 7

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 conclusion 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:

1. The decision under appeal is set aside.

2. The patent is revoked.

The Registrar The Chairman

N. Maslin U. Oswald