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D E C I S I O N
of 30 January 2006

Case Number: T 0043/02 - 3.3.04

Application Number: 91909364.1

Publication Number: 0528034

IPC: A61K 38/00

Language of the proceedings: EN

Title of invention:
Remedy for asthma

Patentee:
Mitsubishi Pharma Corporation

Opponents:
BRITANNIA PHARMACEUTICALS LIMITED
BOEHRINGER INGELHEIM PHARMA KG

Headword:
Remedy for asthma/MITSUBISHI PHARMA CORPORATION

Relevant legal provisions:
EPC Art. 56

Keyword:
"Main request: inventive step (no)"

Decisions cited:
T 0091/98

Catchword:
-

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Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 0043/02 - 3.3.04

D E C I S I O N
of the Technical Board of Appeal 3.3.04
of 30 January 2006

Appellant: (Opponent 01)	BRITANNIA PHARMACEUTICALS LIMITED 41-51 Brighton Road, Redhill Surrey RH1 6YS (GB)
Representative:	Blake, John Henry Francis Brookes Batchellor 102-108 Clerkenwell Road London EC1M 5SA (GB)
Respondent: (Proprietor of the patent)	Mitsubishi Pharma Corporation 6-9, Hiranomachi 2-chome Chuo-ku Osaka-shi (JP)
Representative:	TBK-Patent Bavariaring 4-6 D-80336 München (DE)
Other Party: (Opponent 02)	BOEHRINGER INGELHEIM PHARMA KG D-55216 Ingelheim/Rhein

Decision under appeal: **Interlocutory decision of the Opposition Division of the European Patent Office posted 13 November 2001 concerning maintenance of the European patent No. 0528034 in amended form.**

Composition of the Board:

Chairman: R. Gramaglia
Members: M. Wieser
R. Moufang

Summary of Facts and Submissions

I. European Patent No. 0 528 034 (application No. 91 909 364.1), having the title "Remedy for asthma" was granted on the basis of 7 claims, of which claim 1 read as follows:

"1. The use of a pulmonary surface active material in the manufacture of a medicament for the treatment of asthma in humans."

Claims 2 to 7 related to specific embodiments of the use of claim 1.

II. Notices of opposition were filed by opponents 01 and 02 requesting the revocation of the European patent on the grounds of Articles 100(a) and 100(c) EPC (Articles 54, 56 EPC and 123(2) EPC). By a decision dated 13 November 2001 the opposition division maintained the patent on the basis of the claims of the main request then on file, which differed from the granted claims by the addition of the wording "after the onset of asthmatic attacks" at the end of claim 1.

III. The opposition division considered that the claims as amended satisfied the requirements of Articles 84, 123(2), 54 and 56 EPC. The decision under appeal, however, did not deal with the question of whether or not the claims were directed to patentable subject matter avoiding the prohibition of Article 52(4) EPC, an issue raised by the then opponent 01 (see letter of 9 July 2001, page 2, fourth full paragraph).

IV. The appellant (opponent 01) filed an appeal against the decision of the opposition division, submitted a statement of grounds of appeal and paid the appeal fee.

V. The respondent (patentee) answered to the grounds of appeal.

VI. Opponent 02, which was a party as of right to the proceedings, did not file any observations.

VII. With a letter dated 25 May 2004 the parties were summoned to oral proceedings. Opponent 02 informed the board with a letter dated 20 October 2004 that it would not take part in the oral proceedings. With letter dated 22 October 2004, the respondent announced that it would not attend the oral proceedings and withdrew its request for oral proceedings.

VIII. On 12 November 2004, the board notified the parties by telefax that the oral proceedings due to take place on 23 November 2004 had been cancelled.

IX. By a telefax sent on the same day, the appellant requested oral proceedings unless the board intended to make a decision in its favour. The telefax included the copy of a letter to the board bearing the date "14 October 2004" and containing further appellant's arguments in support of its case. The appellant repeated its conditional request for oral proceedings in a further letter dated 15 November 2004.

X. With a communication pursuant to Article 12 RPBA, the board informed the parties that the appellant's letter bearing the date "14 October 2004" had never reached

the board in a form other than said telefax sent by the appellant on 12 November 2004, a date falling after the respondent has withdrawn its request for oral proceedings (22 October 2004) and after the board had announced the cancellation thereof. In view of this, the respondent was given the opportunity to comment on the issues addressed in that letter within a period of two months from the date of the communication.

XI. The respondent did not file any submissions in response to the board's communication.

XII. The following documents are referred to in the present decision:

(D1) Becher G., Biom. Biochim. Acta, Vol. 44; No. 9, pages K57-K61, (1985);

(D2) Bangham A.D. et al., Colloids and Surfaces, Vol. 10, pages 337-341, (1984);

(D3) EP-A-0 119 056;

(D4) Enhörning G. in "Surfactant and Respiratory Tract", L. Ekelund, B. Jonson, L. Malm Editors, Elsevier Science Publishers (Biomedical Division), pages 273-281 (1989);

(D5) US-A-4,828,844;

(D10) Kallós P. et al., Int. Archs Allergy Appl. Immun., Vol. 73, pages 77-85 (1984);

(D11) Enhörning G. in "Progress in Respiration Research", Vol. 25, P. von Wichert and B. Müller Editors, Karger, Basel, pages 265-270 (1990).

XIII. The appellant's objections relevant to the present decision were essentially as follows:

– "Treatment after the onset of an asthma attack" as recited in claim 1 also encompassed the situation where the administration of the drug took place at any time after the onset of an asthma attack, e.g., after an attack had vanished and before the onset of the (next) asthmatic attack. Insofar as the claim covered such a situation, the closest prior art was represented by document (D1), which related to pre-treatment experiments carried out in guinea pigs. The only difference between the wording of claim 1 and the disclosure of document (D1) lay in the fact that claim 1 related to humans. However, since guinea pigs were an effective model for humans as evidenced by document (D10), it was obvious to transfer the knowledge gained from guinea pig to humans.

– Otherwise the closest prior art for the claimed invention was considered to be represented by document (D4) or (D11). In particular document (D11) posed the question "is asthma related to surfactant deficiency?" and stated that if the answer was "yes", then the way to deal with it was to administer surfactant as an aerosol spray. The answer was to be found in document (D4), i.e. the confirmation that asthma was related to surfactant

deficiency. The claimed subject-matter therefore lacked inventive step.

– Document (D4) showed that existing successful medications for asthma promoted surfactant release.

– Reliable animal models were available (documents (D1) and (D10)).

XIV. The arguments by the respondent relevant for the present decision were essentially as follows:

– The administration of a surfactant "after the onset of an asthma attack" as recited in claim 1 in no way encompassed the situation where the administration of the drug took place at any time after the onset of an asthma attack since after the onset meant that the attack must have started but not yet terminated. Accordingly, any assessment of inventive step based on document (D1) as closest prior art failed.

– Contrary to the appellant's contention, document (D11) rather related to the question "are there other diseases than respiratory distress syndrome (RDS) due to surfactant deficiency?". Document (D11) was merely speculative and hypothetical about any treatment of asthma with the application of pulmonary surfactant (PSF). Based on document (D11), the problem to be solved was not only to provide an efficient treatment against asthma by overcoming surfactant deficiency in the respiratory bronchioles of humans but also to design a potent agent therefor. The solution as

subject-matter of claim 1 was nowhere disclosed or suggested in the cited prior art. In particular, document (D4) merely expressed the idea that surfactant administration was useful for the treatment of asthma as a simple hypothesis which required further investigation based on an excellent animal model and the author believed that the only rational approach for investigation was the prevention of an attack by administering an active agent via the bronchial pathway prior to the exposure to allergens.

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

The respondent requested that the appeal be dismissed.

Reasons for the Decision

Articles 84, 123(2)(3), 54 and 52(4) EPC

1. Although the appellant has argued that claim 1 as amended did not comply with the requirements of Article 84 and 123(2) EPC, the board sees no reason to decide on these grounds in view of its decision on inventive step given below. For the same reason the board refrains from deciding whether the claims of the amended patent are directed to novel and patentable subject matter avoiding the prohibition of Article 52(4) EPC.

Inventive step

2. In the decision under appeal, the opposition division decided that subject-matter of claim 1 involved an inventive step (Article 56 EPC). The opposition based this finding on the following three step assessment:

- As a first step the opposition division defined the technical problem underlying the invention of the contested patent as the provision of a treatment of asthma in humans after the onset of asthmatic attacks and considered that the subject-matter of claim 1 solved this problem.

- As a next step the opposition division identified document (D1) to represent the closest prior art.

- Finally, the opposition division concluded that the prophylactic use of PSF taught in document (D1) and the mechanism assigned thereto in no way suggested the use of PSF for the treatment of asthma after the onset of asthmatic attacks. Similarly, none of the other cited documents either taken alone or taken in combination with the teaching of document (D1) would have prompted the skilled person in the art to use PSF for treating asthma after the onset of asthma attacks with a reasonable expectation of success.

3. In accordance with paragraph [0005] of the patent in suit and in view of the wording of claim 1 under consideration, the invention underlying the patent in suit as amended serves the purpose to provide a drug

for the treatment of asthma in humans after the onset of asthmatic attacks.

4. The appellant maintains that the wording "after the onset of an asthma attack" in claim 1 also encompasses the situation where the administration of the drug takes place at any time after the onset of an asthma attack, e.g., after an asthma attack had vanished and before the onset of the (next) asthmatic attack, while the respondent denies this proposition. However, it has not been disputed by the parties during the opposition and present appeal proceedings that the subject-matter of amended claim 1 reads, regardless of the appellant's claim interpretation, at least in part, on such a treatment in which the administration of the medicament takes place after the onset of an asthmatic attack, i.e. when the human patient suffers from acute asthmatic symptoms, in accordance with the respondent's interpretation of claim 1. The board agrees as well that the subject-matter of claim 1 relates, at least in part, to the provision of a drug for the treatment of asthma in humans in which the medicament is administered when the human patient suffers from acute asthmatic symptoms.

5. Insofar as claim 1 relates to such an acute asthmatic pathology and its treatment, the closest prior art has to be identified accordingly. In line with the established case law of the boards of appeal the closest prior art is normally a teaching in a document conceived for the same purpose or aiming at the same objective as the claimed invention and having the most relevant technical features in common, i.e. ideally

requiring the minimum of structural modifications to arrive at the claimed invention.

6. In the present case the closest prior art should hence be a document relating to the same pathology and the treatment thereof, namely acute asthmatic symptoms and their treatment.

7. The opposition division considered document (D1) to represent the closest prior art. However, the board observes that document (D1) does not deal with the treatment of acute asthmatic symptoms. Rather it investigates on the possible protective effects of lung surfactant in antigen-induced immediate bronchial response. The author of document (D1) concludes that pulmonary surface active material, such as natural surfactant, may be **protective** against receptor mediated allergic reactions in the lungs and bronchi, as is the case in allergic bronchial asthma. In conclusion, prophylaxis of asthma by coating bronchiole receptors with a surfactant is a different physiological and pathological situation from trying to alleviate an acute asthma attack. Therefore, document (D1) does not qualify as the closest prior art.

8. Rather, the board considers that the classical drugs used in the art for treating acute symptoms of asthma in humans represent prior art closer to the claimed subject-matter than document (D1). Examples of such compounds are disclosed *inter alia* in document (D11) on page 268, line 36, namely the β_2-adrenergic agents classically used in human asthma treatment to relieve patients from acute symptoms (see also document (D4) by the same author, page 279, third full paragraph).

Indeed, the board considers these compounds used in the treatment of acute asthma symptoms to have the same purpose as the invention as defined in claim 1.

9. The respondent argues that the author of document (D11) believed that the only rational approach for investigation was the prevention of an attack by administering a surfactant via the bronchial pathway **prior** to the exposure to allergens (see last sentence on page 280 of document (D4)). However, the board observes that document (D11) does relate to "alleviating the acute symptoms of asthma" (see page 268, last four lines to page 269, first two lines).

10. In the board's judgement, starting from this closest prior art teaching, the objective technical problem underlying the claimed subject-matter is hence the provision of an alternative drug for the treatment of the acute phase of asthma in humans, wherein the medicament is administered during the asthmatic attack, i.e. when acute asthmatic symptoms manifest themselves.

11. As a solution to this problem, claim 1 proposes a pulmonary surface active material (PSF). The board is satisfied, in the light of the examples disclosed in the patent in suit, that the problem has been solved by this medicament. The board notes in this context that the patent in suit does not give an indication of advantages or surprising results of the use of PSF in the treatment of asthma in humans over the use of the classical β_2-adrenergic agonists considered to represent the closest prior art.

12. The decisive question to be answered is thus whether or not the cited prior art documents contain information or pointers that will guide a skilled person embarking on solving this problem, to modify or substitute the closest prior art compounds and to arrive at the claimed subject-matter in an obvious way.

13. Document (D11) was published in 1990 shortly before the priority date claimed for the present patent. On page 266, lines 22 to 32, with reference to the successful use of surfactant in the prevention and treatment of neonatal respiratory distress syndrome (RDS) - a disease known to be caused by pulmonary surfactant deficiency (see document (D3), page 1 lines 8 to 17) - the author queries whether also asthma could be a condition which is at least partly due to a surfactant deficiency and concludes that "*If, indeed, asthma affecting at least 7 million people in the United States, is a condition of surfactant deficiency that could be treated by supplying surfactant as an aerosol spray, this would be an area of research of enormous interest which could have far-reaching practical consequences.*"

Subsequently, the author formulates, based on a set of scientific considerations, the hypothesis that a relative surfactant deficiency resulting in collapse and closure of many respiratory bronchioles indeed may result in several features characterising asthma.

As part of his justification for this hypothesis, the author refers on page 266, lines 33 to 37, to the fact that some of the most important medications for asthma - meant are here the β_2-adrenergic agonists referred to

above - have the effect of stimulating the synthesis and/or release of surfactants (see page 268, lines 36 to 38 of document (D11)). In the opinion of the author, already this fact points to the possibility that asthma is a condition of surfactant deficiency and that the relief that the patient encounters when using this medication, might be partly due to this stimulatory effect on the surfactant system.

The author concludes in the full paragraph on page 269, that "*Animal experiments are clearly needed to test this hypothesis. If they offer promising results, it is obvious that an area of surfactant research that is of enormous interest to the clinician has opened up.*".

14. In the board's judgement, the skilled person - having knowledge of the fact that document (D11) makes it plausible, based on substantiated considerations, that asthma is a condition of surfactant deficiency and therefore could possibly be treated by supplying a surfactant, e.g. in the form of an aerosol spray, would find it obvious to test the potential therapeutic activity of surfactants (i.e. PSF) in the treatment of asthma during the acute phase.

15. Inventive step is not denied on the sole basis that a project (here: testing the potential therapeutic activity of a substance) is obvious to try. This is because the skilled person may easily conceive of inventions, yet realising them may cause problems in view of difficulties known in advance or experienced when practically embarking on the project, so that the skilled person has no reasonable perspectives of readily achieving the invention (see e.g. T 91/98 of

29 May 2001). It remains to be established whether these hindrances/uncertainties apply to the present situation.

16. As for the medicament, the board first observes that "PSF" referred to in claim 1 was known to the skilled person in the context of other treatments of human pulmonary diseases at the relevant date of the patent in suit (see paragraph [0007] thereof and documents (D2), (D3) and (D5)) and that in the context of pulmonary surfactants, the terms "surfactant" and "PSF" were interchangeable (see respondent's letter dated 6 August 2002, page 9, lines 1 to 4). These facts have never been disputed by the respondent. PSF was thus part of the therapeutic tool-box of the clinician in the field of human pulmonary medicine.

17. The respondent argues that a major hindrance was represented by the lack of a suitable animal model for acute asthma. However, the animal model referred to on page 2, lines 28 of the patent in suit, namely guinea pigs with antigen-induced broncho-constriction, wherein the respiratory function was measured after challenge with ovalbumin (see paragraph [00018]) is essentially the same as the animal model disclosed in documents (D1) and (D10), were it not for the reversed order of administration of the antigen and the surfactant.

18. Since such PSF was part of the therapeutic tool-box of the clinician in the field of human pulmonary medicine, and reliable animal models for bronchial asthma were available, the conclusion cannot be drawn that the skilled person embarking on the testing of the possible therapeutic effect of PSF during an asthmatic attack in

humans, as suggested by document (D11) had no reasonable perspectives of success. The skilled person would rather adopt a try-and-see attitude, in the sense that the result of the test could only be that either an effect was observed or perceived, or was neither observed nor perceived. In the former case the skilled person would arrive at the invention as described in claim 1. Thus in spite of understandable uncertainties which always affect any biological experiment, the board considers that in the present case the skilled person had no reasons to adopt a sceptical attitude.

19. In view of the above considerations, the board considers the subject-matter of claim 1 not to involve an inventive step.

Oral proceedings

20. Given the outcome of the case and in view of the fact that the respondent had expressly withdrawn its request for oral proceedings and announced its intention not to take part in the oral proceedings, the board has decided this case based on the written submissions of the parties to the appeal.

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:

P. Cremona R. Gramaglia