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# D E C I S I O N
# of 2 December 1998

**Case Number:** T 0153/97 - 3.3.2

**Application Number:** 92900942.1

**Publication Number:** 0553298

**IPC:** A61K 9/12

**Language of the proceedings:** EN

**Title of invention:**
Aerosol Formulation comprising beclomethasone 17,21 Dipropionate

**Patentee:**
Minnesota Mining and Manufacturing Company

**Opponent:**
SkyePharma AG
Norton Healthcare Ltd.

**Headword:**
Aerosol Formulation/MINNESOTA MINING AND MANUFACTURING

**Relevant legal provisions:**
EPC Art. 54, 56, 69

**Keyword:**
"Main request - novelty - no"
"First and second auxiliary request - novelty - yes"
"Inventive step - no - obvious substitution of a component"

**Decisions cited:**
T 1000/92, T 0607/93

**Catchword:**

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Beschwerdekammern | Boards of Appeal | Chambres de recours

**Case Number:** T 0153/97 - 3.3.2

**D E C I S I O N**
**of the Technical Board of Appeal 3.3.2**
**of 2 December 1998**

**Appellant:** (Opponent)
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**Decision under appeal:** **Interlocutory decision of the Opposition Division of the European Patent Office posted 27 December 1996 concerning maintenance of European patent No. 0 553 298 in amended form.**

**Composition of the Board:**

**Chairman:** P. A. M. Lançon
**Members:** U. Oswald
R. E. Teschemacher

## Summary of Facts and Submissions

I. European patent No. 0 553 298 was granted with two sets of claims (twelve product claims and one method claim for the contracting states AT, BE, CH, DE, DK, FR, GB, IT, NL, SE; and twelve method claims for the contracting state ES) in response to European patent application No. 92 900 942.1 published with the international publication No. WO 92/06675.

Product claim 1 and method claim 13 for the designated contracting states other than ES read as follows:

"1. An aerosol formulation comprising a therapeutically effective amount of beclomethasone 17,21 dipropionate, a propellant comprising a hydrofluorocarbon selected from the group consisting of 1,1,1,2-tetrafluoroethane, 1,1,1,2,3,3,3-heptafluoropropane, and a mixture thereof, and ethanol in an amount effective to solubilize the beclomethasone 17,21 dipropionate in the propellant, the formulation being further characterized in that substantially all of the beclomethasone 17,21 dipropionate is dissolved in the formulation, and that the formulation contains no more than 0.0005% by weight of any surfactant.

13. A method of preparing a solution aerosol formulation comprising the step of combining a therapeutically effective amount of beclomethasone 17,21 dipropionate, a propellant selected from the group consisting of 1,1,1,2-tetrafluoroethane, 1,1,1,2,3,3,3-heptafluoropropane, and a mixture thereof, and an amount of ethanol effective to solubilize the beclomethasone 17,21 dipropionate in the

propellant."

II. Two oppositions were filed against the granted patent. According to the grounds of opposition, the patent was opposed under Article 100(a) EPC for lack of novelty and lack of inventive step. Of the numerous documents cited during the opposition proceedings the following remain relevant to the present decision:

(1) EP-A-0 372 777

(2) US-A-2 868 691

(5) Reprint from "Pharmaceutical Technology", March 1990, R. Dalby et al, CFC Propellant Substitution: P 134a as a Potential Replacement for P-12 in MDIs

(6) "Frankfurter Allgemeine Zeitung", 25 October 1989, No. 207, page 7.

(7) Brochure "Hoechst zum Ersatz von FCKW", September 1990

(8) "Pharmazeutische Zeitung", No. 9, March 1990, pages 30/31

(19) Minerva Pneumologica, Vol. 14, 1975, pages 34 to 45,

III. According to the interlocutory decision of the Opposition Division under Article 106(3) EPC, posted on 27 December 1996, the patent in amended form was found to meet the requirements of the EPC.

The Opposition Division took the view that the aerosol formulation of claim 1 as granted (main request) "containing no more than 0.0005% by weight of any surfactant" was novel because of the fact that it was only possible to arrive at the claimed subject-matter by a selection from features out of four lists disclosed in document (1).

The subject-matter of claim 13 as granted, however, being not dependent on claim 1 and relating to a method of preparing a solution aerosol formulation was not limited to a concentration of 0.0005% by weight of surfactant, and therefore lacked novelty in comparison with the disclosure of Examples 10 to 12 in document (1).

In view of the fact that according to an auxiliary request claim 13 was limited to a surfactant concentration of 0.0005% by weight of the formulation, the Opposition Division concluded that this request fulfilled the requirements of Article 54 EPC.

For the assessment of inventive step, the Opposition Division regarded document (1) as the closest prior art. In the light of the said prior art, the problem to be solved was "...to provide an alternative formulation to the one as disclosed in document (1)...wherein the presence of unnecessary compounds is kept at a minimum". Since document (1) clearly taught to include as an essential component a surfactant in solution aerosol formulations and since the formulations according to this prior art contained surfactants in concentrations of well above the claimed upper limit of 0.0005% by weight, there was no reason for a person skilled in the art to assume that a stable

formulation could be obtained without a surfactant.

Although a plurality of additional prior art documents on file, eg document (19) which was considered the most relevant prior art next to document (1), showed that solution aerosols for therapeutic applications could be formulated in the absence of a surfactant, the subject-matter of the patent in suit was not rendered obvious by any combination of the teaching of the documents on file.

IV. Appellant 01, who is the proprietor of the patent in suit, Appellant 02, who is Opponent 01, and Appellant 03, who is Opponent 02, lodged appeals against the said decision.

V. Oral proceedings took place on 2 December 1998, during which Appellant 01 filed two auxiliary requests.

**Auxiliary request I** related to the patent as amended before the Opposition Division that means the set of claims as granted with method claim 13 being limited in accordance with claim 1 such that "*the formulation contains no more than 0.0005% by weight of any surfactant*".

Claim 1 of **auxiliary request II** related to the same aerosol formulation as defined in claim 1 of the auxiliary request I but with the further limitation that "*ethanol is present in an amount of about 2 to about 12 percent by weight*".

Coming to the main request with the set of claims as granted, Appellant 01 argued inter alia that in contrast to the Opposition Division's point of view, a proper interpretation of method claim 13 inevitably led to the

conclusion that only a single method step was defined in this claim and that the definition of this single step was complete in terms of the components to be combined. In accordance with Article 69 EPC there was in any case the necessity to take into account the description and the working examples of the patent in suit when reading the wording of the claims. Since the components to be combined according to the description and examples of the patent in suit were those and only those specified in claim 13, the wording of claim 13 did not permit to combine substantial amounts of other components, for example high amounts of surfactants above 0.0005 wt% known from document (1) with those components specified. Accordingly, the subject-matter of claim 13 as granted was clearly novel in comparison with the disclosure of document (1) and since claim 1 as granted includes an upper limit of the overall surfactant content of no more than 0.0005% wt% of the formulation, there was no reason for an objection to the set of claims as granted under Article 54 EPC.

Moreover, since claim 1 unambiguously defines the amount of ethanol as an effective amount to solubilize BDP, reducing the ethanol content as shown in the description - ie well below the 25wt% ethanol as required by Examples 10 to 12 of document (1) - was a further feature distinguishing the subject-matter of claim 1 from the said prior art formulation.

For the assessment of inventive step Appellant 01 emphasised that it was only technically meaningful to start from document (1) as the closest prior art. It was pointed out that document (19) referred to by Appellant 02 as the

closest prior art was filed about thirty years before the priority date of document (1). It was proven by numerous citations, eg document (5), that during this period of time the development in the field of solution aerosols suitable for pharmaceutical applications went in the direction of using a surfactant as one of the essential components for formulating the said aerosols. There was no reason why a person skilled in the art should disregard this main stream in pharmaceutical aerosol technology. For supporting this argumentation reference was made to decision T 1000/92.

In the circumstances of the present case, Appellant 02's allegation was irrelevant that document (2) showed in the form of a more generalized teaching that the aid of surfactants in solution aerosols was not necessary. The chemical structure of surfactants as excluded by the teaching of the patent in suit were not known at the publication date of document (2).

Moreover, it was necessary to take into account that document (1) was the first prior art disclosure of a solution aerosol for pharmaceutical use containing the P134a propellant but also containing, in conformity with the so-called main stream in the field, a surfactant. The patent in suit clearly represented a deviation from the said mainstream. As a consequence, only on the basis of an ex post facto analysis was it possible to regard obsolete document (19) as the closest prior art.

In the light of the disclosure in document (1) the problem to be solved could be seen in the provision of formulations of BDP which were easy to manufacture, but stable, having a

long shelf time and exhibiting desirable respirable fraction.

Having regard to comparative examples, there was clear evidence that a reduction in ethanol content without the omission of surfactant did not lead to an enhanced chemical stability of BDP, but rather an increase in chemical degradation of BDP. Therefore, only a combination of each of the claimed features solved the stated problem.

Since it was proven that document (1) in accordance with the so-called main stream in aerosol technology clearly taught that surfactants were an important stabilizer for solution formulations and since this prior art as well as numerous other documents mentioned ethanol merely beside other co-solvents such as dimethyl ether, the skilled person would not automatically envisage removing the surfactant component and would not simultaneously reduce the ethanol content but had also the possibility to adjust other solution parameters in order to achieve a good product stability and a desirable respiration fraction. Document (2) also contained technical information that other parameters than the ethanol content, such as the overall vapour pressure and/or the droplet size of the aerosol, could have an influence on the respirable fraction of the formulation.

Since document (19) neither contained information about the origin of the marking "Clenil Spray" nor described a method how to formulate a commercial product, nor contained information about the function of the P 113 component and particularly not how a change of the propellant system would influence the ingredients of the formulation, for a skilled

person this prior art left open more questions than providing concrete technical information in the field of aerosol technology. Accordingly, the disclosure of document (19) was more or less speculative and hence it was fully justified not only to set aside this document as a suitable starting point for the assessment of inventive step but also to exclude this prior art from a combination with the disclosure in any other of the cited documents.

The other documents on file either did not relate to specific aerosol formulations, especially not to BDP aerosols, or did not relate to propellant compositions which the skilled person would take into account for a substitution by the claimed propellants.

In the view of Appellant 01 the auxiliary requests clearly could be regarded as a fair response to Appellant 02 and 03's objections regarding the broadness of the scope of the claimed subject-matter.

VI. Appellants 02 and 03 contested these arguments and took the view that the subject-matter of the claims as granted (now main request) and that of the auxiliary requests lacked novelty in the light of the disclosure in document (1), particularly having regard to Examples 10 to 12 of that prior art.

Since the subject-matter of the claims according to each of the requests was clearly defined, there was no need to refer to Article 69 EPC in order to construe further features implicitly delimiting the claimed subject-matter. Moreover, since claim 13 of the main request related to the production

of the same formulation as defined in claim 1 but lacked one of the product parameters, such a claim would then contravene Article 84 EPC.

As regards inventive step Appellants 02 and 03 took the view that there was no basis to disregard the disclosure of document (19) as being speculative since this document was in accordance with document (2) an example of the traditional teaching in solution aerosol formulations and in particular represented an absolute standard for BDP formulations.

Document (19) in reality represented a more suitable starting point for the assessment of inventive step than document (1). Since numerous documents showed that the whole thrust in 1990 was to substitute CFC propellants by less environmentally destructive products such as P134a or P227, starting then from document (19), it was only a matter of routine work to arrive at the claimed subject-matter.

As a general rule for obviousness in the field of formulating solution aerosols, the skilled person's approach could be summarized under five points:

- First of all, for economic reasons and because of the risk of side-effects, unnecessary compounds or functions were avoided;

- Secondly, additional components, if necessary, were included only in minimum amounts;

- Thirdly, since dimethyl ether was highly inflammable,

ethanol was commonly used and was therefore the first choice of co-solvents;

- As the fourth point, it was well-known that BDP could be satisfactorily dissolved without a surfactant and hence surfactants were merely optional components;

- Finally, it was a matter of routine work to optimize aerosol formulations as to the proportionality of the amounts of components when changing the propellant system.

Accordingly, in the light of these common practices, the skilled person even starting from document (1) would arrive at the subject-matter of the patent in suit without the exercise of inventive skill. It was particularly pointed out that the formulations according to Examples 10 to 12 of document (1) showed the same amount of surfactant content for different types of surfactants used and apparently these examples were not optimized as to the surfactant content. There was no prejudice to further optimize the known formulations.

In reply to Appellant 01's so-called main stream argument Appellants 02 and 03 particularly relied on conventional pharmaceutical formulation practice. Reference was made to well-known textbooks, lectures, an affidavit and numerous patent specifications. A surfactant was included in formulations as known from Examples 10 to 12 of document (1) only in case of a poorly performing metering valve of the MDI equipment requiring a surfactant for lubrication. Particularly document (2) represented the basic knowledge

about solution formulations and included technical information that the use of a surfactant in such formulations was necessary only in exceptional situations.

VII. Appellant 01 requested that the patent be maintained as granted - main request.

Alternatively, he requested that the patent be maintained in the version according to page 2 (Form 2339.4) of the decision under appeal - first auxiliary request;

or on the basis of a main claim comprising the features of the present claims 1 and 4 - second auxiliary request.

Appellants 02 and 03 requested that the decision under appeal be set aside and that the patent be revoked.

## Reasons for the Decision

1. The appeal is admissible.

2. Appellants 02 and 03 neither objected under Article 100(c) EPC in regard to the patent as granted, nor filed such objections in regard to the auxiliary requests comprising only a combination and rearrangement of claims as granted and originally filed. The Board considers that the requirements of Article 123(2) and (3) EPC are satisfied.

*Main request - Novelty*

3. Document (1) relates to medicinal aerosol formulations and

in particular to formulations suitable for pulmonary, nasal, buccal or topical administration which are at least substantially free of chlorofluorocarbons, henceforth referred to as CFCs (see page 2, lines 1 to 3). According to page 6, lines 10 to 14 and Example 10 on page 7, lines 15 to 25 and line 30 of this document, a solution is prepared as follows:

- 0.005 g beclomethasone dipropionate BDP and 0.006 g Span 85 is weighed into a small beaker.

- 1.350 g ethanol is added and the mixture homogenised using a Silverson mixer.

- This mixture is dispersed into a P.E.T. bottle and an aerosol valve crimped in place.

- 4.040 g Propellant 134a is added by pressure filling. (1,1,1,2-tetrafluoroethane is referred to as **P**ropellant 134a)

The Board agrees with Appellant 01's statement that the subject-matter of claim 13 clearly relates to a single step of combining a specific drug, two specified propellants and a specified co-solvent in a method of preparing a solution aerosol formulation. However, having regard to the wording of claim 13: "A method...***comprising*** the step of combining ...beclomethasone 17,21 dipropionate... 1,1,1,2-tetrafluoroethane...and ethanol...", it is also clear that the subject-matter for which protection is sought is not intended to be limited to a single method step but may **comprise** other technically meaningful method steps.

Since the step of combining BDP and Span 85 - a surfactant component - clearly may be a technically meaningful method step in the preparation of solution aerosol formulations, in the light of the disclosure in document (1) claim 13 of the main request lacks novelty.

Having regard to the fact that the wording of claim 13, although formulated in a broad manner, clearly and unambiguously defines the matter for which protection is sought, there is no need for a further interpretation of the said claim under Article 69(1) EPC by reference to the description or worked examples of the patent in suit. It is well established case law of the Boards of Appeal that the so-called "broadness" of a claim does not necessarily affect the clarity of the claimed subject-matter, or in other words there is no general principle that broadly formulated claims inevitably have to be interpreted restrictively in the light of the description. Claim 13 of the main request is clearly not limited to the addition of surfactants in an amount below 0.0005 wt%. There is nothing in the wording of this claim which requires explanation by the description in respect of the amount of any surfactant present in the formulation. In any case, novelty of the subject-matter of a claim cannot be established *a posteriori,* that means after being confronted with a novelty destroying prior art disclosure only by giving a "delimiting **interpretation**" of the scope of the claim depending on the content of the said prior art, even if the description of the patent in suit discloses embodiments which correspond to the delimiting interpretation (T 607/93, cited in Case Law of the Boards of Appeal, 3d ed. 1998, I.C.3.2.2). The reverse would imply that the scope of the claim depends on the cited prior art

and may vary during the proceedings.

Accordingly the main request, as already done by the Opposition Division, has to be rejected under Article 54(1) EPC.

*First and second Auxiliary Request - Novelty*

4. Having regard to the objections of Appellants 02 and 03, the novelty of claims 1 and 13 of the first and second auxiliary requests *vis-à-vis* document (1) must be considered.

The teaching of document (1) is not restricted to solution aerosol formulations as mentioned under point 3 above but relates more generally to both solution and suspension formulations. In fact document (1) discloses in addition to the solution aerosol formulation according to Example 10 with 0.005 g corresponding to 0.093 wt% of BDP and 0.006 g corresponding to 0.11 wt% of Span 85 surfactant, on page 4, line 45 up to page 5, line 40, long lists of other suitable surface active agents and classes of medicaments as well as drug components. It is stated on page 5, lines 51/52 following the list of drugs that "the concentration of medicament depends upon the desired dosage but is generally in the range 0.01 to 5% by weight". According to page 5, lines 8 to 11, following the list of surfactants, "the surface active agents are generally present in amounts not exceeding 5 percent by weight of the total formulation" with the further explanation that "they will usually be present in the weight ratio 1:100 to 10:1 surface active agent : drug(s), but the surface active agent may exceed this weight ratio in cases where the drug concentration in the

formulation is very low".

Neither the worked examples nor the rest of document (1) comprise technical information as to which of the weight ratios of the broad range of 1 : 100 to 10 : 1 surface active agent : drug is applicable to the numerous possible surfactant drug combinations in either solution or suspension formulations and as a consequence it is **not clearly and unambiguously derivable** from document (1) if for example 0.01 wt% BDP can be combined with 0.0001 wt% of one of the numerous surfactant components referred to as being suitable for the preparation of solution or suspension formulations. Accordingly, novelty of the subject-matter of claim 1 and claim 13 of the first auxiliary request restricted specifically to BDP containing solution formulations and a method of preparing such formulations containing no more than 0.0005 % by weight of any surfactant can be acknowledged in comparison with the disclosure in document (1).

Claim 1 and claim 13 of the second auxiliary request are further restricted to a formulation containing ethanol in an amount of 2 to 12 percent by weight and accordingly are also novel in comparison with document (1).

Since furthermore none of the other documents cited in the course of either the examination or opposition procedure discloses the combination of the features of independent claims 1 and 13, the Board is satisfied that the first and second auxiliary requests meet the requirements of Article 54 EPC.

*First and second auxiliary request - Inventive step*

5. The Board regards document (19) to be the closest state of the art in the sense of the proper starting point for examining inventive step in this case. For the purpose of this discussion, reference is made to the undisputed English translation of (19) which was supplied by Appellant 03 on 6 November 1996.

5.1 Document (19) is concerned with investigations relating to the effects of beclomethasone dipropionate on respiratory and adrenal function by using a so-called "Clenil Spray" in the form of a metered aerosol. It is subsequently indicated that every canister of said aerosol contains 15 g of liquid having the following composition:

| | |
|---|---|
| beclomethasone-17,21-dipropionate | 0.010 g |
| absolute ethyl alcohol | 1.191 g |
| Freon 113 | 2.361 g |
| Freon 12/114 (40:60) | 11.438 g |

(see translation page 2, third and fourth paragraph).

Tests were performed on a total of 20 patients (see translation page 3, first paragraph) and as a result it is observed that Clenil Spray has an improving effect on existing bronchial/bronchiolar spasm (see translation page 4, penultimate paragraph).

5.2 It was undisputed by the parties that before the priority date of the patent in suit it was well known in the art that chlorofluorocarbon so-called CFC compounds react with the

ozone layer around the earth and contribute towards its depletion, and that there was considerable pressure by various governments around the world to reduce substantially or even avoid the use of CFCs.

5.3 Starting from document (19) and taking into account legal requirements relating to and increasing public interest in environmental protection, the problem underlying the patent in suit may thus be seen in providing a beclomethasone-17,21-dipropionate containing aerosol formulation having acceptable therapeutical effectiveness but being less destructive to ozone.

5.4 The claimed solution of the problem is a beclomethasone-17,21-dipropionate containing aerosol formulation comprising 1,1,1,2-tetrafluoroethane (abbreviation 134a) or 1,1,1,2,3,3,3-heptafluoropropane (abbreviation 227), or a mixture thereof as the propellant. Having regard to the worked examples of the patent in suit and the statement on page 2, lines 14 to 17 of the description of the patent in suit, it appears credible that the problem has indeed been solved.

Appellants 02 and 03 did not contest the statements as to the properties of propellants 134a and 227 set out in the patent in suit.

6. It therefore remains for the Board to decide whether or not the said solution would, in view of the citations, have been obvious to a person skilled in the art faced with the problem defined above.

6.1 The Board agrees with Appellant 01's point of view that there is no hint in document (19) itself which might have given an incentive to the skilled person to investigate the propellant system of the so-called Clenil Spray. It would appear that, except perhaps for research purposes, no reason for it would have been apparent at the time of this publication.

6.2 However, if confronted with the problem as stated above, the skilled person would address every technical field where the same problem arises. Even the general public was already well aware of the ozone layer depletion around the earth, owing to widespread debate thereon and to the resulting public recommendations. Of course, the skilled person would first turn to other prior art relating to propellant systems and first of all, if available, to such systems suitable for use in pharmaceutical aerosol compositions. In this respect, document (5) directly addresses propellant substitution options available to MDI (metered dose inhaler) formulators. It is stated that "*the Montreal Protocol on Substances That Deplete the Ozone Layer*" calls for step-by-step reduction of the use and production of chlorofluorocarbon (CFC) propellants in North America and Europe and that secondary economic effects of the protocol are now being felt in the pharmaceutical industry. As a result of the scarcity of materials and in response to heavy taxation, costs are escalating rapidly for propellants - namely, P-11, P-12, and P114 - conventionally used in the formulation of metered dose inhalers (MDIs)" (see first page, left column). Although the Appellant is right when arguing that document (5) does not describe a complete substitution of CFC propellant systems by P-134a because of a lack of

stability, density and solvent strength for surfactants of P 134a in comparison with P 12, the whole thrust of this prior art can be summarized by the statement on the second page, last paragraph that "*it currently seems to the authors that non-ozone depleting P-134a is a suitable replacement for P-12*".

6.3 Document (8) having the same publication date as document (5) fully confirms this statement and additionally indicates on page 30, right column, last paragraph/page 31 left column, first paragraph, that one of the proposed substitutes for CFCs, the so-called H-CFC 22 (Hydro-chlorofluorocarbon), could only be regarded as an intermediate solution since this product, apart from other disadvantages, appears not to be suitable for pharmaceutical applications. It is then subsequently stated that the search is concentrated on chlorine free products, for example on HFC 134a used in the field of refrigeration technology and insulating foams and that this product does not destroy the ozone layer. Furthermore, it is indicated on page 31, left column, second paragraph, that studies on short time toxicology are available which did not show negative results. Accordingly, in the light of the disclosure in document (8) the skilled person faced with the problem defined above and forced to complete technical information about potential CFC substitutes, would not restrict the search exclusively to propellant systems already proposed for MDI's but would also turn to literature relating to the replacement of CFCs envisaged in other technical fields. In this respect the skilled person would come across document (7) published very close to the priority date of the patent in suit and putting beside other replacement

candidates, particular emphasis on the two HFC propellants 134a and 227. Both propellants are shown to have no influence on the stratospheric ozone layer accompanied by decreased "hot house effect". HFC 134a is indicated to replace the CFC P 12 whereas HFC 227 is indicated to replace CFCs P 11, 12 and 114 for special applications in refrigeration, air conditioning and aerosol technology.

6.4 As argued by Appellant 01, the Board agrees that the skilled person would not ignore the other propellants mentioned in document (7). However, already one year before publication of document (7) and about one year before the priority date of the patent in suit, even the public's attention had been drawn by a press report to the use of HFC 134a in the field of pharmaceutical aerosols in order to replace the ozone depleting propellants P 11 and P 12 (see document (6) under the heading "Stoffliche Alternativen sind bekannt", second paragraph). Moreover, subsequently it is indicated that according to a further project HFC 227 appears to be the most promising long-term candidate not only in the field of aerosols but also in refrigeration and air conditioning technology (see document (6) under the heading "Stoffliche Alternativen sind bekannt", third paragraph).

6.5 In the light of these facts the Board can only conclude that the skilled person faced with the problem defined above would try to replace the propellant system of the so-called Clenil Spray according to document (19) by at least one of the promising replacement candidates HFC 134a or HFC 227 having zero ozone depletion potential in order to produce an environmentally acceptable product marketable for the future.

Having regard to the degree of pressure put on industry by legislation and by the public interest, for the incentive to try the said replacement, in the Board's view, it is a minor matter whether or not there was a particularly high degree of expected success before starting experimental work. The skilled person would in any case first of all start experimental work by testing a replacement with propellants having zero ozone depleting potential and allowing a long term solution to the problem before making a compromise with less environmentally beneficial candidates or with mixtures of CFCs and HFCs. In this respect it is to be noted that P 113 used in the formulation of document (19) shows, as argued by Appellant 01, indeed excellent solubility properties and could indeed be regarded in addition to ethanol as a co-solvent, but in view of the extremely high ozone depleting potential of this component as proven by document (7) the skilled person clearly would try to avoid this component.

6.6 In such circumstances, the Board does not misjudge the real situation in relation to toxicity and/or solubility problems caused by HFC 134a or HFC 227 replacements which are indeed postulated in the literature and which form the basis for Appellant 01's arguments for unobviousness of the invention. However, the facts presented in the present case do not allow the conclusion that a skilled person carrying out the experimental work necessary to reformulate the Clenil Spray according to document (19) in order to overcome the problems caused by the P 12/113/114 components was confronted with deterring difficulties.

6.7 The Board notes furthermore that Appellant 01 did not file

any counter evidence that the so-called Clenil Spray disclosed in document (19) must be regarded as an instable product not suitable as an aerosol formulation. Taking furthermore into account that the Clenil Spray does not contain a surfactant and contains amounts of ethanol and beclomethasone-17,21-dipropionate within the preferred ranges of the patent in suit, the Board can only conclude that this product contains ethanol in an amount effective to solubilize the beclomethasone-17,21-dipropionate in the HFC 134a or HFC 227 propellants, the use of which has been shown to be obvious. Accordingly, the question whether or not the skilled person would include a surfactant into a beclomethasone-17,21-dipropionate (BDP) solution aerosol formulation and the whole discussion relating to the prior art disclosure of the use of surfactants in aerosol solution formulations in general, particularly regarding that in documents (1), can be set aside. In any case, regarding solution formulations, document (1) merely discloses on page 3, lines 16/17 that the presence of large amounts of solubilized surfactant may also assist in obtaining stable solution formulations of certain drugs. In the light of this disclosure it is clear that even according to the teaching of document (1) a surfactant does not represent an obligatory adjuvant to solution aerosol formulations and that Examples 10 to 12 of document (1) relating to BDP and ethanol containing solution formulations with the same amount of surfactant content for the inclusion of different types of surfactants cannot be regarded as being optimized with respect to their surfactant content. Moreover, the Board is convinced that Appellant 03's so-called five point argumentation regarding the behaviour of a skilled person, who inter alia for economic reasons and because of the risk

of side-effects would avoid unnecessary compounds or functions, reflects in reality the common practice in industry when trying to modify existing pharmaceutical formulations.

6.8 In the Board's view, the mere fact that a modification of a product in order to maintain the product marketable in the future involves complex research and is extremely time consuming does not automatically confer inventiveness on the product.

6.9 It was undisputed by the parties that the so-called Clenil Spray contains an amount of ethanol of about 7.9 percent by weight. Since claim 1 of the second auxiliary request is restricted to an amount of ethanol of about 2 to about 12 percent by weight, for the assessment of inventive step, the above argumentation also applies to this request.

6.10 Accordingly, the Board can only conclude that the skilled person would arrive at the subject-matter of claims 1 of the first and second auxiliary requests without the exercise of inventive skill.

7. Since Appellant 01 with reference to decision T 1000/92 (cited in Case Law, supra, I.D.3.3) contested the relevance of document (19) as not relating to the ozone depleting problem and because of its publication date decades before the patent in suit, as the closest prior art, it may be useful to discuss this matter in detail.

7.1 Document (19) was indeed published 30 years before the priority date of the patent in suit and, as it is undisputed

by the parties, does not relate to the ozone depleting problem whereas document (1) proposed by Appellant 01 as the closest prior art already provides an alternative solution to the said problem.

7.2 First of all it is to be noted that correspondence of the problem to be solved is not the only criterion when analysing the disclosure in the prior art in order to find a suitable starting point for the assessment of inventive step. The case law of the Boards of Appeal shows a great variety of criteria related to the particular cases such as the structural aspects or also the desired properties. It should not be forgotten that, in the present case, the patent in suit deals with a medicinal aerosol formulation. Both documents (1) and (19) describe such formulations. The fact that the ban for the use of CFCs did not exist at the time of document (19) does not disqualify it as closest state of the art.

7.4 In the absence of any proof that the so-called Clenil Spray is based on a speculative and technically meaningless disclosure, there is no plausible reason why the skilled person should disregard document (19) only because the publication date lies so far in the past. The only plausible explanation appears to be that the inventors of the patent in suit were not aware of the disclosure in document (19). In this respect the situation in decision T 1000/92 was quite different, since well-known disadvantages of the prior art would have deterred the skilled person from keeping this starting point. In contrast, the age of the document is not a valid argument against its relevance in the present case because interest in this document did not arise until the

ozone depleting problem forced industry to search for new propellant systems.

8. Anyhow, it is pointed out that the Board would likewise have reached a conclusion of lack of inventive step in respect of the first and second auxiliary requests had it been decided to choose document (1) as a starting point.

As already set out under point 6.7 above, Examples 10 to 12 of document (1) can be regarded as the relevant passage relating to BDP solution formulations. The BDP formulations according to these examples are indeed not free of surfactants.

The problem of simplification defined by Appellant 01 can be considered as solved in so far as the now claimed composition and process exclude substantially the use of a surfactant.

However, in addition to the specific disclosure of the Clenil Spray from document (19) without a surfactant and the more general teaching from document (2) saying in column 2, lines 41 to 46 "The medicament.....may be brought into stable solution...if necessary, with the aid of a co-solvent *and/or* stabilizing substance.", there are several other documents on file showing the possibility of formulating solution aerosols without the necessity of a surfactant. In the Board's view there is no one-way street situation for use of a surfactant in BDP solution formulations. Even on the basis of the disclosure in document (1) alone which states on page 3, lines 16/17, that "The presence of large amounts of solubilized surfactant may also assist in

obtaining stable solution formulations of certain drugs", there is at least an incentive to try to optimize the formulations of Examples 10 to 12 and again, in accordance with Appellant 03's five point argumentation, the Board is convinced that if the skilled person in the light of the prior art sees any hope that an adjuvant of a medical formulation which could cause side effects could be avoided, he would try to do so.

Having regard to the circumstances of the present case, it is clear that inventive step of the claimed subject-matter cannot be supported by reference to a prejudice against the prior art disclosure only on the basis of what is said by the inventors in the description of the patent in suit.

9. The reasoning set out above also applies to the set of claims 1 to 12 for the contracting state ES relating exclusively to a process for preparing an aerosol formulation but including the same essential features of the formulation as discussed above. Moreover, since Appellant 01 did not present a request exclusively relating to the contracting state ES, these claims in any case must fall.

## 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. Martorana P. A. M. Lançon