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**Datasheet for the decision
of 11 December 2008**

Case Number: T 0639/05 - 3.3.02

Application Number: 98902707.3

Publication Number: 0967975

IPC: A61K 31/08

Language of the proceedings: EN

Title of invention:

Fluoroether compositions and methods for inhibiting their degradation in the presence of a lewis acid

Patentee:

ABBOTT LABORATORIES AND CENTRAL GLASS COMPANY LIMITED

Opponent:

Baxter International Inc.

Headword:

Sevoflurane anaesthetic/ABBOTT, CENTRAL GLASS

Relevant legal provisions:

EPC Art. 123(2)(3), 54, 83, 84

Relevant legal provisions (EPC 1973):

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Keyword:

"The product claimed lacks novelty over the prior art"
"The use claimed is insufficiently disclosed"

Decisions cited:

G 0002/88, G 0005/83, G 0006/88, G 0001/93, T 0574/93,
T 0256/87

Catchword:

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Case Number: T 0639/05 - 3.3.02

D E C I S I O N
of the Technical Board of Appeal 3.3.02
of 11 December 2008

Appellant: Baxter International Inc.
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Illinois 60015-4633 (US)

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Respondent: ABBOTT LABORATORIES
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and
CENTRAL GLASS COMPANY LIMITED
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Representative: Modiano, Micaela Nadia
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Decision under appeal: Decision of the Opposition Division of the
European Patent Office posted 6 May 2005
rejecting the opposition filed against European
patent No. 0967975 pursuant to Article 102(2)
EPC, version 1973.

Composition of the Board:

Chairman: U. Oswald
Members: M. C. Ortega Plaza
P. Mühlens

Summary of Facts and Submissions

- I. European patent No. 0 967 975, which was filed as application number 98 902 707.3, based on international application WO 98/32430, was granted on the basis of five claims.

Claim 1 as granted read as follows:

"1. An anesthetic composition comprising:
a quantity of sevoflurane; and
a quantity of water providing a concentration of water in said anesthetic composition of between 0.015% w/w and a saturation level of water in said quantity of sevoflurane, wherein no soda lime is present in the composition."

Independent claim 2 as granted read as follows:

"2. A method of preventing degradation by a Lewis acid of a quantity of sevoflurane, the method comprising the steps of:
providing a quantity of sevoflurane;
providing a Lewis acid inhibitor in an amount sufficient to prevent degradation of said quantity of sevoflurane by a Lewis acid; and
combining said quantity of sevoflurane and said Lewis acid inhibitor."

- II. The following documents among the many documents and exhibits cited during the proceedings are relevant for the present decision:

(1) EP-A-0 701 985

- (2) Abbott Laboratories' disclosure statement to USPO
(29 July 1998)

- (4) EP-A-0 700 888

- (5) David P. Strum, *Anesth. Analg.* 78, pages 340-348,
1994

- (A1) Declaration of Mr Yoichi Kumagai dated 14 February
2005, filed together with Exhibits A and B

- (A2) Declaration of Ms Leticia Delgado-Herrera dated
14 February 2005

- (A3) Declaration of Mr Alberto Marinai dated
14 February 2005

- (A7) Exhibit concerning correspondence between
Ms Gorman, Pharmacist of the Queen Charlotte's and
Chelsea Hospital (26 March 1992) and Abbot
Laboratories about phase separation in a
sevoflurane bottle; analysis of purity and
statement of water content by Abbott Laboratories.

- (A14) R.F. Wallin, *Anesthesia and Analgesia* vol. 54(6),
pages 758-766, 1975

- (A15) First expert report of Prof. R.D. Chambers in the
UK High Court of Justice (dated 2 February 2006)

- (E1) Copy of Mr K. Cromack's testimony at trial in US
litigation

(E5) Copy of Abbott Laboratories' submission to the USP (US Pharmacopeia) dated 24 September 2001

(E6) Copy of an internal report prepared by Abbott Laboratories HPD research and development that was "discovered" as part of the US litigation and thus is now public

(E14) Affidavit of Dr Lessor (called "witness statement") dated 9 September 2005

(E18) Second expert opinion of Professor J, Dunbar Kilburn (complete copy distributed by the appellant at the oral proceedings before the board) in the UK High Court of Justice dated 2 March 2006

- III. Opposition was filed and revocation of the patent in its entirety was requested pursuant to Articles 100(c) (the subject-matter of the patent extends beyond the content of the application as filed), 100(b) (insufficiency of disclosure) and 100(a) EPC (lack of novelty and inventive step).
- IV. The appeal lies from a decision of the opposition division rejecting the opposition under Article 102(2) EPC, version 1973.
- V. The opposition division considered that although the disclaimer in claim 1 as granted did not fulfil the requirements set out in decisions G 1/03 and G 2/03 owing to the fact that document (5) did not prejudice novelty, the granted claim did not contravene the requirements of Article 123(2) EPC, in consideration of the principles set out in decision G 1/93.

As regards insufficiency of disclosure, the opposition division considered that the disclosure of the patent in suit was enabling, since a reasonable amount of trial and error did not represent an undue burden to the skilled person when reproducing the invention.

Moreover, in the opposition division's view some of the testing conditions contained in the contested patent had been created artificially by the researchers. However, these test conditions served as a model for degradation under extreme conditions.

Additionally, the opposition division was of the opinion that the contested patent taught that Lewis acids caused degradation on sevoflurane and proposed to combine sevoflurane with a Lewis acid inhibitor as a preventive measure.

In relation to the novelty issue, the opposition division considered that the pharmaceutical composition claimed in claim 1 was novel over the prior art. In particular, the opposition division considered that the compositions disclosed in document (1) did not relate to a "final pharmaceutical product ready to be used as an anaesthetic". The opposition division stated in its decision that the analysis made for document (1) also applied to the content of document (4). Moreover, the opposition division was of the opinion that the information disclosure statement made by Abbott Laboratories to the USPTO (numbered document (2)) merely showed that the sold manufactured products contained minimum amounts of water; the highest water

content in some individual lots was only a small amount over 100 ppm.

Additionally, the opposition division considered that the method claims met the requirements of novelty since the "prevention of degradation by Lewis acids" was a technical feature imparting novelty over the content of the prior art.

The opposition division did not define the closest prior art. It defined, however, the problem to be solved as "to provide a final pharmaceutical composition where sevoflurane is protected from degradation by Lewis acids, and a method for preventing said degradation".

The opposition division considered that the subject-matter claimed in the set of claims as granted met the requirements of Article 56 EPC.

- VI. The opponent (appellant) lodged an appeal against said decision and filed grounds thereto and additional exhibits.

- VII. The appellant claimed for the first time with its letter of 23 May 2006 a public use with respect to the subject-matter of claim 1, and submitted some documents in support thereof. Additional documents were filed with the letter of 20 December 2007.

- VIII. The respondent (patentee) filed counter-arguments in response to the grounds of appeal.

IX. In response to a communication by the board sent as an annex to the summons for oral proceedings, the respondent filed further arguments and three auxiliary requests.

Claim 1 of auxiliary request 1 differs from claim 1 as granted in that the disclaimer at the end of the claim was deleted.

There are two versions of auxiliary request 2, with and without the disclaimer in claim 1. Moreover, claim 1 of auxiliary request 2 differs from claim 1 of the main request in that the expression "An anesthetic composition" was replaced by "Composition for use in anesthesia".

As in the case of the second auxiliary request, there are two versions of auxiliary request 3, with and without the disclaimer. Claim 1 of the third auxiliary request is identical to claim 1 of the second auxiliary request. However, independent claim 2 of the third auxiliary request was reworded as follows:

"2. The use of a Lewis acid inhibitor for preventing degradation by a Lewis acid of a quantity of sevoflurane wherein the Lewis acid inhibitor is added to the quantity of sevoflurane in an amount sufficient to prevent degradation of said quantity of sevoflurane by a Lewis acid."

X. In response to said communication by the board the appellant filed further arguments and further exhibits.

XI. Oral proceedings took place on 11 December 2008.

The parties were asked about their requests at the beginning of the oral proceedings and, as a response thereto, the respondent filed a further set of claims as auxiliary request 4. This set of claims contained only use claims. Claim 1 of the fourth auxiliary request is identical to claim 2 of the third auxiliary request.

A discussion about the admissibility of the late-filed auxiliary request 4 took place. After deliberation the Chairman announced that auxiliary request 4 was admitted into the proceedings. Immediately thereafter the Chairman expressed the board's preliminary opinion in relation to the presence of the disclaimer in product claim 1, and about the novelty of the product claims. In particular, the Chairman stated that the board agreed in principle with the opposition division's conclusion about the disclaimer in claim 1 as granted and that the product claim 1 of all requests except auxiliary request 4 (only use claims) lacked novelty vis-à-vis documents (1) and (4) in view of the fact that the distillate contained water at about the saturation level.

At the oral proceedings the appellant and the respondent did not add any arguments about the presence of the disclaimer in product claim 1.

XII. The appellant's arguments, as far as relevant for the present decision, may be summarised as follows:

The appellant did not contest the admissibility of the auxiliary requests filed a month before the oral

proceedings, but it questioned the admissibility of auxiliary request 4, which was filed at the oral proceedings before the board. In particular, it submitted that to admit this new request at such a late stage of the proceedings would be unfair. Furthermore, in its view, auxiliary request 4 did not address issues raised with the opposition.

As regards the novelty issue of product claim 1 as granted, the appellant referred to its written submissions. Moreover, the appellant added that the respondent's allegation that the sevoflurane products obtained in documents (1) and (4) were not suitable as anaesthetic compositions was speculative.

Additionally, the appellant submitted that the prior art disclosed sevoflurane compositions suitable as anaesthetic, with a water content of about the saturation level, which were encompassed by claim 1. Thus, claim 1 lacked novelty.

The appellant also contested the respondent's construction of claim 1 and alleged that the words "final product" and "ready for use" could not be read into the claim as limiting features. Moreover, the appellant stated that the claim should not be read differently depending on the point of time (at the effective filing date or thereafter). The appellant further submitted that the water content was a feature of the claimed product and hence it was immaterial for the novelty assessment whether or not at the effective filing date of the patent the notional skilled person would have had a prejudice against the presence of water. Moreover, document (A14) taught about hydrolysis

in water as a solvent but did not disclose a general prejudice against the presence of water in the amounts claimed. Additionally, document (A14) did not teach about HFIP as a by-product of the hydrolysis in water. Furthermore, document (A14) taught about sevoflurane being stable without additives for at least one year.

The appellant submitted that the sevoflurane products of documents (1) and (4) contained water at saturation level; however, neither document (1) nor document (4) mentioned the presence of water as being a problem. On the contrary, document (1) clearly disclosed a distillation process for providing sevoflurane as a pharmaceutical product for use as anaesthetic. The key disclosure in document (1) was example 2 and there was no dispute that the sevoflurane product of example 2 of document (1) had a high (organic) purity and water content about saturation level. Thus, the expression "anaesthetic composition" did not limit the product claim vis-à-vis prior-art documents (1) and (4). Moreover, the expression "anaesthetic composition" did not imply specific pharmaceutical regulation standards which, anyway, varied from country to country. In this context the appellant cited decision T 226/98 (date of decision 7 February 2001, OJ EPO 2002, 498).

The appellant denied that the sevoflurane product of documents (1) or (4) would contain HF. The appellant referred to its technical expert Dr Lessor (see also statement E14) who argued that there were in principle three periods in a distillation with column: the total reflux period, the period with fore-cut, or initial distillation, and the period of the main distillate. Thus, the HF which might have formed in the column in

small amounts was either condensed on the column (which is not heated) and hence fell into the distillation pot with the charge, or it was in the vapour phase and thus was removed with the initial distillate. Dr Lessor further stated that, according to his own experience (he mentioned that he had carried out some tests), the water phase contained (after phase separation owing to the cooling of the azeotrope) as highest limit 5ppm of HF, whereas the organic phase contained highly pure sevoflurane (99.995%), much less than 2 ppm HF and water at about saturation level.

The appellant also pointed to the sentence of document (4), end of example 4, stating that the product "is used as an inhalation anaesthetic".

The appellant stated that the arguments put forward in relation to novelty of claim 1 of the main request applied *mutatis mutandis* to each product claim of auxiliary requests 1 to 3.

Additionally, the appellant submitted that claim 1 of auxiliary request 2 had been redrafted by enlarging the scope claimed, and hence contravened Article 123(3) EPC, since the composition no longer had to be anaesthetic in itself (for instance owing to low amounts of sevoflurane). Alternatively, the appellant also submitted that the claim lacked clarity since it was unclear whether or not the composition had to be ready for use as anaesthetic. Moreover, the appellant stressed that the amendment did not overcome the lack of novelty of the product claimed.

As regards auxiliary request 4 the appellant stated that the new claim construction concerned a second non-medical use as in decision G 2/88 of the Enlarged Board of Appeal (OJ EPO, 1990, 093). However, the appellant submitted that the claim lacked clarity (Article 84 EPC) and enlarged the protection over that conferred by granted claim 2 (Article 123(3) EPC). In particular, granted claim 2 related to three steps and use claim 1 of auxiliary request 4 required only one step, namely that of "adding". Additionally, there was a difference between "adding and the previously used word "combining". In the appellant's view, the difference was to include or not the washing of the container, or pure moisturising (as for instance in the circulation of sevoflurane during the inhalation cycle). In this context it referred to paragraphs [0029] and [0030] of the contested patent.

Moreover, in the appellant's opinion, the amendments could not be considered to be caused by grounds of opposition within the meaning of Rule 80 EPC.

In relation to the clarity issue, the appellant also submitted that the claim did not always require the presence of a Lewis acid (this presupposed areas of the claim without the technical effect) and that the "limitation" concerning "preventing" the degradation appeared twice in the claim, in the form of "amount sufficient to prevent degradation". It also mentioned that the indefinite article in the expression "**a** Lewis acid" caused a lack of clarity to the claim.

Furthermore, the appellant submitted that, in contrast to the second non-medical use dealt with in G 2/88, the

use claim of auxiliary request 4 related to a "negative technical effect" that of preventing degradation, which did not always take place. The appellant also submitted that, even if under certain circumstances there may be a technical effect, the patent in suit did not teach the skilled person to do something different from what he had done in the prior art. Thus, the addition of water was not, in the appellant's view, a functional feature for the use and did not define a new technical effect.

The appellant also stated that use claim 1 did not relate to a narrow scope for achieving a certain technical effect but encompassed in its full breadth entirely known uses such as that of document (4) (in particular example 2) when adding water and sodium hydroxide to a mixture containing sevoflurane and a Lewis acid.

The appellant denied that it was an analogous situation to the case of a vaccine, as submitted by the respondent. Furthermore, great care should be given when referring to decision G 5/83 which dealt with a legal fiction for allowing further medical use claims.

Additionally, the appellant submitted that there was a lack of sufficiency of disclosure (Article 83 EPC) in respect of the subject-matter claimed in auxiliary request 4. In particular, the appellant stated that sufficiency of disclosure also means that the skilled person should know "if" and "when" he is practising the invention, which is something different from reproducing the examples in order to get at the "invention". Thus, as a matter of law, the objection of

lack of sufficiency of disclosure implies more than the mere reproduction of the examples. In this context the appellant cited decision T 616/03, dated 15 September 2004, unpublished in the OJ EPO. The appellant further argued that the matter to debate was not the lack of a detailed recipe for all possible examples. The matter was that the patent gave no teaching at all to allow the skilled person to know what to do for performing the invention and what not to do for not infringing the patent. The appellant cited decision T 256/87, dated 26 July 1987, unpublished in the OJ EPO. In particular, it cited the following passage: "All that is necessary is that the skilled person reading the specification be put in the position of being able to carry out the invention in all its essential aspects and of knowing when he is working within the forbidden area of the claims". The appellant stressed that the second condition was not fulfilled in relation to the subject-matter claimed in auxiliary request 4 and stated that in view of this deficiency even the patients during inhalation of sevoflurane will infringe the patent without knowing, in view of the humidification in the expiration.

The appellant further submitted that "prevention of degradation" is required but the contested patent did not disclose which amounts were required for achieving such an effect and the skilled person was not able to work out which level of LA (Lewis acid) inhibitor is required.

Additionally, in the appellant's view the precautionary or prophylactic protection claimed was not a direct technical effect. The skilled person was not taught

either the amount of LA (Lewis acid) that would be encountered, or the nature of the LA. The appellant further argued that the term "Lewis acid" encompassed a wide range of acid strengths and that the specification of the contested patent gave no clue about these aspects of the alleged "technical effect". Thus, the intended "preventive effect" could not serve as a valid functional feature to delimit the subject-matter claimed.

The appellant pointed to paragraph [0027] of the patent in suit, where it was taught that "For any other Lewis acid inhibitor, a molar equivalent based upon moles of water should be used" and stressed that the problem was that the patent did not teach how to get the values for water as a LA inhibitor. In particular, the appellant submitted that the skilled person is put in the position to predict the worst case scenario in order to act on it, but he is not told how. In fact, the specification of the contested patent presupposes the knowledge of LA to encounter, but the skilled person did not have this knowledge. In this context the appellant cited the exhibit E1 relating to Cromack's testimony, in particular [1346] and [1347] and the exhibit E18 relating to Dunbar's second expert opinion in the UK High Court of Justice, in particular paragraph 14 about the "worst case scenario". This second expert opinion was made in connection with the respondent's submissions of 3 August 2006, starting on page 21.

The appellant stated, as response to the respondent's opinion, that it was not a routine exercise to work out the worst case scenario as suggested by Dr Cromack,

without defining first the nature of the LA and its strength. Moreover, the fact that the locus (during, for example, manufacturing, filling in containers and shipping) in which the LA was to be found and the amounts thereof were also indeterminate only worsened the situation of lack of information. Thus, the problem of predicting among so many unknown factors put an undue burden on the skilled person.

In this context the appellant quoted the patentee's own document Exhibit 5, first full passage on page ABT 158318, which acknowledged the unpredictable nature of the degradation process due to a complex Lewis acid degradation reaction. Furthermore, it also quoted several passages on pages ABT 158319 and 158321 in order to show that there was no test for prediction of the degradation and that in view of the lack of an early indicator Abbott recommended a level of water of at least 300ppm. The appellant further submitted that the patent failed to indicate what to do and how to detect degradation with a LA, in order to be able to prevent it. The appellant also mentioned that Exhibit E5 demonstrated that this was not routine and stated that prediction was almost impossible. Anyhow the patent did not teach how.

The appellant argued that the same product with the same amount of LA inhibitor would infringe the patent in one container but not in another and that the skilled person would not be in a position to distinguish between both situations. Furthermore, the use claim did not suggest any minimum amount as was explicitly done in exhibit E5 (it quoted the statement in the letter to USP of exhibit E5 and the

recommendations made by the patentee vis-à-vis the FDA). Although the appellant acknowledged that the requirements for a regulatory document were not prerequisites for a patent, it also pointed out that the reasons to force a lower limit of LA inhibitor were that it was not possible to make a prediction as how to prevent degradation. Thus, the remaining question was how to identify a technical effect with the functional definition in the claim, especially since the patent in suit mentioned minimum amounts of water of 150 ppm, for which no adequate prevention was shown.

The appellant argued that, although in example 1 of the patent in suit (and Fig 1) it was suggested that an amount of 260 ppm water would prevent degradation with alumina, exhibit E6 (page 12) showed that this was not correct in the case of 50 mg of activated alumina being the LA present.

Therefore, in the appellant's view, the patent in suit did not indicate what happened in real life, and did not show how to predict it, in order to provide a product which was absolutely safe. Moreover, if the skilled person was trying to use example 1 as a model he would be wrong. Furthermore, the other examples of the patent did not give more information. Hence, the quantity of LA inhibitor to be used in order to prevent degradation remained unknown to the skilled person who would not be able to work out the claimed invention.

The appellant stressed that its argumentation in relation to insufficiency of disclosure relied on the patentee's own documents, which therefore represented

common ground, and on the necessity for an objective test which, as stated by the patentee, did not exist.

The appellant further stated that the patent required the skilled person, in order to provide prevention, to predict when and how the degradation may take place. However, the patent did not guide the skilled person how to do so and did not provide for a valid model or a worst case scenario. The skilled person faced with this lack of information would not know how to start and following the examples could be wrong in the absence of a stated quantity.

The appellant's further replied to the respondent's submissions saying that one thing was to measure what you have in front of you, for instance a specific bottle, and another thing was to be able to predict how to prevent degradation.

XIII. The respondent's arguments, as far as relevant for the present decision, may be summarised as follows:

The respondent submitted that auxiliary request 4 filed at the oral proceedings did not contain any new claims when compared to auxiliary request 3, filed one month before the oral proceedings. The amendment introduced in auxiliary request 4 merely concerned the deletion of product claim 1. Claim 1 of auxiliary request 4 (which corresponded identically to claim 2 of auxiliary request 3) had been reworded as a use claim within the meaning of the Enlarged Board of Appeal decision G 2/88, in response to the board's communication sent as an annex to the summons for oral proceedings. Hence,

auxiliary request 4 should be admitted into the proceedings.

As regards the novelty issue of the product claims, the respondent did not dispute that sevoflurane and water formed an azeotrope and that the distillate product of documents (1) and (4) contained water in amounts of about the saturation level. However, the respondent contended that claim 1 as granted related to a product "ready for use" as "anaesthetic composition", suitable to be administered to the patient without harming him.

The respondent referred to its written arguments and to declarations A1, A2 and A3 in support of the submission that the prior art compositions were not "ready for use", as required by claim 1 as granted. Basically, the respondent submitted that the skilled person would not have considered at the effective filing date of the patent in suit that compositions having a water content near to the saturation level were "ready for use" as anaesthetics, owing to safety and stability concerns. In the respondent's opinion the declarations served to demonstrate that the skilled person at the effective date of filing of the patent in suit would have considered water as an impurity and would have had serious concerns about stability owing to the water content in the bottles. The respondent also pointed to exhibit (A7) in order to show that phase separation was a problem before the effective filing date of the patent in suit. Additionally, the respondent pointed to document (A14) as further proof that the skilled person would have considered the presence of water as prejudicial to the stability of sevoflurane since it underwent hydrolysis in water. In the respondent's view

document (A14) was part of the common general knowledge of the skilled person. The respondent also stressed that some degradation product of sevoflurane (it mentioned compound A, i.e. HFIP, hexafluoro-isopropyl alcohol) which was toxic might be formed. In the respondent's view, if there was hydrolysis then HFIP and HF would be formed.

The respondent also referred to declaration (A15) (pages 23 and 24) in support of its statements about the knowledge of the skilled person at the time of the "invention".

In a second line of argumentation, the respondent contended that the distillate obtained in the prior art contained hydrofluoric acid (HF) as a toxic inorganic impurity, not detectable by gas chromatography (GC). The respondent put forward that the HF present in the distillation column would not be trapped by the disodium hydrogen phosphate solution in the distillation charge and thus HF would be present in the distillate. The respondent also stated that the threshold of HF in marketed sevoflurane was less than 2 ppm, hence, an amount of 5 ppm in the distillate was much too high and would have to be removed.

The respondent contended that there would also be phase separation in a sevoflurane product containing water at the saturation level. Thus, the skilled person would have completely removed the water from the prior art products. The respondent referred to the written submissions and stressed that the Abbott Laboratories' experts must have had a "good motivation" for spending time and money drying sevoflurane, and it cited again

document (A14) in support of its view that the skilled person would expect instability of the sevoflurane product in the presence of water.

The respondent also added that the washing step with sodium hydroxide disclosed in document (4) concerned the removal of remaining sulphuric acid (which was used in excess in the preparation process).

The respondent stated that the same arguments applied *mutatis mutandis* to the product claim of auxiliary requests 1 to 3.

As regards claim 1 of auxiliary requests 2 and 3, the respondent submitted that the product claim was now drafted as "a composition for use in anaesthesia" in accordance with the description which repeatedly stated that the pharmaceutical composition was to be used in anaesthesia. The respondent was of the opinion that the claim's wording was clear and supported by the description. In this context it cited decision T 574/93 dated 19 February 1998, unpublished in the OJ EPO which, in its view, concerned an analogous situation. Moreover, the claim was narrower than granted claim 1. Thus, the amended wording clearly delimited the claimed product *vis-à-vis* the prior art.

As regards auxiliary request 4, the respondent explained that in the context of the claim's wording the expression "adding" could be considered as synonymous with "combining", since the word "combining" did not necessarily imply "mixing". The respondent cited in favour of its argument paragraphs [0031] and [0030] of the patent in suit. In the second non-medical

use claim it was not necessary to recite the "other steps" which were anyhow implied by the rest of the claim's wording.

In relation to the further comments of lack of clarity made by the appellant, the respondent counter-argued that the claim had to be read by the skilled person and in a technically meaningful way. Additionally, a method for preventing degradation was not a method of manufacture and hence there was no contravention of the requirements of Article 123(3) EPC in the rewording of granted claim 2 into a use claim. The respondent cited in this context Enlarged Board of Appeal decision G 5/83, OJ EPO 1985, 64, and submitted that there was an analogy between a prophylactic treatment (it cited the case of vaccines) and a treatment preventing degradation, which hindered something from happening. Thus, claim 1 of auxiliary request 4 related to a technical effect.

The respondent further stated that degradation of sevoflurane happens and that was a serious problem in the pharmaceutical sector. Furthermore, in relation to the frequency of the degradation the respondent submitted that more than two lots had to be recalled.

Additionally, the respondent submitted that document (4) disclosed the use of sodium hydroxide in water to remove the acid from the mixture (i.e. concerned a purification step) and was not used to reduce degradation of sevoflurane by a Lewis acid. According to the use claim of auxiliary request 4, the Lewis acid inhibitor was added purposively to achieve a technical effect which had not previously been made available.

The respondent put forward that the fact that the problem sometimes did not occur was irrelevant; prevention was in case it did happen.

The respondent stated that it did not deny that there was no way of predicting Lewis acid's presence and that there were no predicting tests or general model. However, the respondent alleged that there were ways to predict in specific cases what amounts of LA one would encounter and by means of statistics to provide for a worst case scenario, which was different from providing for a predictive test.

The respondent also mentioned that there was no way to know in advance how much LA would be contained in the bottle or the container but one would carry out tests. In this context the respondent cited Exhibit E18, point 14 which mentioned known methods for determining the presence of metal ions, as for example Inductively Coupled Plasma, which in combination with atomic emission spectroscopy, atomic adsorption or mass spectroscopy could be used to detect the presence of trace metals. Testing the samples in this way the skilled person would be able to determine the amount of LA present.

Additionally, the respondent alleged that example 1 gave a model based on extreme conditions. The matrix showed the results of simply testing what worked. If one could not see inhibition then one had to increase the amount of LA inhibitor. This was also true for the other examples which related with accelerated and stress conditions.

The respondent also added that the skilled person only had to test the bottles in hand. The examples in the contested patent employed glass treated with HF; the skilled person would look at the amount of HF and the amount of water in order to deal with the degraded glass.

The gist of the invention was not to show an amount which always worked but to find which amount would work under specific conditions.

XIV. The appellant (opponent) requested that the decision under appeal be set aside and that the patent be revoked.

The respondent (patentee) requested that the appeal be dismissed or, alternatively, that the patent be maintained in amended form on the basis of one of the auxiliary requests 1 to 3, filed with the letter of 11 November 2008, or on the basis of the auxiliary request 4 filed at the oral proceedings.

Reasons for the Decision

1. *Admissibility*

1.1 The appeal is admissible.

1.2 The sets of claims of the auxiliary requests filed a month before the oral proceedings are admissible since they are a fair attempt to overcome the objections raised in the board's communication sent as an annex to

the summons for the oral proceedings. Moreover, the appellant has not disputed their admissibility.

As regards the set of claims of auxiliary request 4, it merely differs from the set of claims of auxiliary request 3 in that the product claim was deleted. Use claims 1 to 4 were present in auxiliary request 3 as independent use claim 2 and dependent claims 3 to 5. Therefore, the filing of auxiliary request 4 at the beginning of the oral proceedings represents an allowable defensive measure which does not broaden the discussion in respect of auxiliary request 3 in an unexpected way. Additionally, claim 1 (which corresponds identically to independent claim 2 of auxiliary request 3) originates from claim 2 as granted which was redrafted as a direct response to the board's communication sent as an annex to the summons for oral proceedings. Hence, auxiliary request 4 is admissible.

2. During the examination proceedings the disclaimer "wherein no soda lime is present in the composition" was introduced into the product claim following a telephone conversation with the first examiner, who wrongly pointed to document (5) (numbered document (1) in the examination proceedings) as an accidental novelty-destroying anticipation of the product claim.

Since the disclaimer was unnecessarily introduced and clearly relates to superfluous matter not linked to the "invention", the board can only come to the conclusion, in consideration of the principles set out in decision G 1/93, that granted claim 1 does not extend beyond the content of the application as filed. Hence, claim 1 of

the main request is allowable within the meaning of Article 123(2) EPC.

This analysis also applies to each of those product claims of auxiliary requests 2 and 3 which contain the disclaimer.

The appellant has not disputed these findings.

As regards the alternative options, i.e. auxiliary request 1, as well as auxiliary requests 2 and 3 without disclaimer, they were filed by the respondent just in case the board found the presence of the disclaimer to be contrary to the requirements of Article 123(2) EPC. Since this is not the case, these alternative sets of claims are not justified and have to be rejected. The reasons are, in particular, that the scope of protection has been enlarged (Article 123(3) EPC). The respondent did not comment on this matter and the board sees no reason for further argumentation.

3. *Claim 1 of the main request (claim 1 as granted)*

3.1 *Novelty*

- 3.1.1 The composition claimed in claim 1 as granted is characterised by the fact that it is suitable as anaesthetic, and that it contains (a) fluoromethyl-1,1,1,3,3,3-hexafluoroisopropyl ether (sevoflurane) and (b) water in an amount between 0.015% w/w (i.e. 150 ppm) and a saturation level of water in sevoflurane (ca. 1400 ppm).

Document (1) discloses a method of purifying sevoflurane, which is widely used as a pharmaceutical and particularly as an inhalation anaesthetic. The method relates to a method of suppressing decomposition of sevoflurane at the time of the distillation and thus obtaining sevoflurane of high purity (page 2, first paragraph).

Document (1) clearly states that sevoflurane "has been widely used as a **safe inhalation anaesthetic**" (page 2, line 12) (*emphasis added*).

The sevoflurane to be purified is an already pre-treated crude which is yielded from the sevoflurane synthesis consisting of reacting together 1,1,1,3,3,3-hexafluoroisopropyl alcohol (HFIP), formaldehyde and hydrogen fluoride. The crude thus obtained contains various by-products. "A means is selected to remove these by-products by passing the reaction product through **usual** treatment steps, that is, steps such as washing with acid, washing with alkali, washing with water, distillation,..." (page 2, lines 15-17) (*emphasis added*).

Document (1) teaches that the crude sevoflurane "decomposes or disproportionates" owing to "defluorohydrogenation" (i.e. elimination of HF) and that fluoromethyl-1,1,3,3,3-pentafluoroisopropenyl ether is gradually formed (page 2, lines 18-22). Therefore, in view of this contamination which is defined as "extremely unfavourable in use as an inhalation anesthetic", an "immediate solution" was desired (page 2, lines 25-26).

As an answer thereto, i.e. in order to provide a highly pure sevoflurane **for use as an inhalation anaesthetic**, document (1) discloses a method for its purification.

Document (1) teaches that the decomposition of sevoflurane can be suppressed in order to obtain a sevoflurane of high purity "by adding a compound selected from hydroxides of, hydrogenphosphates of, phosphates of, hydrogencarbonates of, borates of or sulfites of alkali metals, or alkali metal salts of acetic acid or of phthalic acid, or boric acid, in the form of solid as it is or of aqueous solution, to fluoromethyl-1,1,1,3,3,3-hexafluoroisopropyl ether (sevoflurane), and then by conducting distillation" (page 2, lines 34-38).

Document (1) further teaches that "it may become necessary to add a large amount of aqueous solution for obtaining a sufficient decomposition suppressive advantage" (page 3, lines 26-27); and that "as distillation of sevoflurane proceeds, water in the system is also distilled out" (page 3, lines 28-29).

In fact, sevoflurane forms an azeotrope with water (this fact is undisputed by the parties) and the distillate after cooling separates into two phases: inorganic (water) and organic (sevoflurane with a water content at the saturation level). This is not disputed by the patentee.

Document (1) exemplifies purified sevoflurane having a high purity in the main distillate of 99.995 (example 1 No 1). Although this purity index merely reflects the organic purity, the document permits no doubt about the

suitability of the sevoflurane product obtained as an inhalation anaesthetic (page 6, lines 9-10, under the heading "Industrial Applicability").

Therefore, the sevoflurane product obtained in document (1) fulfils all the prerequisites appearing in claim 1 of the main request, i.e. it is suitable as an anaesthetic composition and contains sevoflurane, and water at the saturation level.

3.1.2 Consequently, claim 1 of the main request lacks novelty vis-à-vis document (1) (Articles 52 and 54 EPC).

3.1.3 There was considerable dispute between the parties, in writing and during the oral proceedings, in relation to the presence or absence of HF in the main distillate according to document (1).

However, the allegation that the final product prepared in document (1) contains HF (or that document (1) does not disclose a final product suitable for anaesthetic use) would amount to an objection of non-enabling disclosure concerning document (1). The reasons are that the use as an **inhalation anaesthetic** of the sevoflurane product obtained is explicitly disclosed in document (1). This use presupposes the absence of HF (which is a toxic substance) or its presence in amounts lower than 2ppm.

In order to provide a complete disclosure, a patent application does not have to give every single experimental detail and to repeat what was commonly known to the skilled person at the filing date. It has not been disputed that, at the filing date of

document (1), safe sevoflurane, i.e. sevoflurane without toxic HF, (see page 2 of document (1), comments to background art) was commonly known and had already been commercialised. This implies that it was commonly known to the skilled person in the field how to eliminate HF (normally washing with alkali and then with water), if necessary.

Furthermore, a claim of non-enabling disclosure of a prior art document requires, in order to be successful, a serious amount of experimental evidence and technical support which has to be submitted by the party advancing the objection. Only in this way could it have been shown that the HF, allegedly present in a "contaminated" main distillate, could not have been eliminated by using the common means known to the skilled person at the filing date of document (1). In the absence of such evidence, the board is convinced that the disclosure of a sevoflurane product suitable as inhalation anaesthetic is complete in document (1).

A further line of argumentation provided by the respondent was that the skilled person would not have considered, at the effective filing date of the application in suit, a product containing water to be suitable as "final product" (or as a product "ready-for-use") for anaesthetic use.

First of all it has to be stressed that claim 1 of the main request does not specify that the claimed product is a product ready-for-use as inhalation anaesthetic. The expression "an anaesthetic composition", employed in the claim, is vague in this respect and merely implies that the composition is suitable as an

anaesthetic, i.e. it does not contain toxic components, and sevoflurane (active anaesthetic component) is present. Additionally, given that water is a non-toxic component (present in the respiration cycle), the presence of water in an anaesthetic composition for inhalation is allowed. In fact, water is a mandatory component of the claimed product. Hence, any composition not containing toxic components and containing sevoflurane and water (within the range defined in claim 1 of the main request) is contrary to the novelty of the subject-matter claimed. This is the case of the sevoflurane compositions and sevoflurane products disclosed in document (1).

Additionally, the respondent seeks to make use of an alleged "general prejudice" as an argument in favour of novelty by disregarding known sevoflurane compositions containing water disclosed in the prior art (in particular document (1)). In this respect it has to be said that the allegation of "general prejudice" against the presence of water has nothing to do with the suitability of the composition as an "anaesthetic composition", since it is the presence of sevoflurane (active anaesthetic drug) and the absence of toxic materials which confer such a quality on the composition.

Furthermore, a clear distinction has to be made between a physical instability which implies phase separation and a chemical instability which implies degradation.

Document (A14) is a 1975 publication in Anesthesia and Analgesia entitled "Sevoflurane: A New Inhalation Anesthetic Agent". Document (A14) states: "Hydrolytic

stability was examined by stirring **0.5 ml** sample of sevoflurane with **500 ml** of distilled water for 48 hours at 18 to 23°C" (page 759, left-hand column, second paragraph under the heading "Methods") (*emphasis added*).

The study of document (A14) states as a result: "Like most other inhalational anesthetic agents, sevoflurane has a degree of chemical and metabolic instability. In water, the compound undergoes a slight but measurable degree of hydrolysis. Sevoflurane is stable without additives for over 1 year at 45°C in amber glass bottles with polyethylene-lined caps" (page 764, right-hand column, penultimate paragraph).

Therefore, early document (A14) teaches that a slight amount of hydrolysis takes place in the presence of a high excess of water. It cannot be seen how this piece of information should disqualify the sevoflurane product disclosed in document (1) as novelty-destroying. Furthermore, if sevoflurane with an amount of water close to saturation level undergoes degradation owing to hydrolysis, then this is also the case for the sevoflurane compositions claimed in claim 1 of the main request since no technical measure has been undertaken to avoid it. Whether or not the skilled person infers that high proportions of water are to be avoided in the light of document (A14) does not help to overcome a lack of novelty over the sevoflurane product specifically disclosed in document (1).

As regards the argument of an undesirable phase separation when water is present in amounts close to the saturation level, it can only be said that this also applies to the product claimed in claim 1 of the

main request since the contested patent does not provide for any technical measure for avoiding physical phase separation.

As regards the respondent's argument that the patentee(s) (one of the patentees is the applicant of document (1)) included at the effective filing date of the patent in suit a drying step before filling the sevoflurane in containers, the following has to be said. Even if considering that a drying step was a routine step performed by the skilled person before filling sevoflurane into the containers to be commercialised, this fact does not disqualify as novelty-destroying the sevoflurane compositions containing water at the saturation level disclosed in document (1). In other words, claim 1 of the main request encompasses the sevoflurane products disclosed in document (1) since it is not restricted to a sevoflurane product filled in a container ready for inhalation. One thing is the sevoflurane compositions disclosed in document (1) and another the products actually sold by Abbott Laboratories to hospitals, for which a water content analysis is shown in document (2).

Moreover, since sevoflurane is a hygroscopic product, even if drying a sevoflurane composition which is initially saturated with water (1400 ppm), anhydrous conditions are to be provided and kept during the whole life of the product in order to maintain the product water-free. Such measures are not a mere handling routine. Hence, in the absence of any explicit mention in document (1) to a drying step or to an anhydrous final product, it can only be concluded that the sevoflurane compositions suitable for anaesthetic use

disclosed in document (1) contain water in amounts which fall within the range of claim 1 of the main request.

4. *Claim 1 of auxiliary requests 2 and 3 (with disclaimer)*

4.1 Claim 1 of auxiliary request 2 merely differs from claim 1 of the main request in that the expression "an anesthetic composition" has been replaced by the expression "Composition for use in anesthesia". Claim 1 of auxiliary request 3 is identical to claim 1 of auxiliary request 2.

4.1.1 Assuming, in favour of the respondent, that the findings in decision T 574/93 in relation to the requirements of Article 123(2) and (3) EPC and Article 84 EPC for claim 1 of auxiliary request 2 are applicable by analogy to the present case (i.e. to claim 1 of auxiliary requests 2 and 3) means that claim 1 is considered to have the structure of a first medical use claim, wherein the stated use is "anaesthesia".

The product for which said medical use is claimed remains, however, the same as that in claim 1 of the main request. Thus, the analysis made above about the lack of novelty of the constitution of the product in claim 1 of the main request directly applies to the amended claim of auxiliary requests 2 and 3.

Therefore, it has to be investigated whether the use mentioned in the amended claim is novel vis-à-vis the use disclosed in document (1) for the sevoflurane product.

It is evident that the use disclosed in document (1) for the sevoflurane product is as an "**inhalation** anaesthetic" (page 6, line 10), which is a more specific use than "anaesthesia". Hence, document (1) destroys the novelty of claim 1 of auxiliary request 2 (Articles 52 and 54 EPC).

4.2 In view of the fact that auxiliary requests 2 and 3 fail owing to the lack of novelty of claim 1, the board sees no reason to further discuss the formal aspects of claim 1, which had been objected to by the appellant.

4.3 As regards the respondent's arguments that claim 1 of auxiliary requests 2 and 3 clearly relates to a final anaesthetic product, it has to be stressed that this is also the case for the product disclosed in document (1) (see again the paragraph on page 6 under the heading "industrial applicability").

5. *Claim 1 of auxiliary request 4*

5.1 *Formal aspects*

5.1.1 Claim 1 of auxiliary request 4 originates from claim 2 as granted which was redrafted in the form of a second non-medical use claim, since it relates to the use of a known compound (LA inhibitor) for a particular purpose (preventing degradation by LA of a quantity of sevoflurane). To that extent, the use claim meets the requirements of Article 84 EPC.

Claim 1 further establishes the following: "wherein the Lewis acid inhibitor is added to the quantity of

sevoflurane in an amount sufficient to prevent degradation of said quantity of sevoflurane by a Lewis acid". However, the feature "in an amount sufficient to prevent degradation of said quantity of sevoflurane by a Lewis acid" appeared already in claim 2 as granted. Hence, said feature cannot be objected under Article 84 EPC in opposition-appeal proceedings.

5.1.2 Moreover, the method claim 2 as granted was reworded as a direct response to the board's communication sent as an annex to the summons for oral proceedings. The board is convinced that the claim was redrafted in an attempt to overcome the objections of lack of novelty raised against the granted claim. Hence, the appellant's argumentation within the meaning of Rule 80 EPC does not hold.

5.1.3 As regards the objections raised by the appellant under the meaning of Article 123(2) and (3) EPC, the following has been considered.

The use claimed in auxiliary request 4 is encompassed by the method of preventing degradation defined in claim 2 as granted, since the natural reading of the granted claim is that a quantity of Lewis acid inhibitor is added to a quantity of sevoflurane for preventing degradation by LA. This implies that "a quantity" of sevoflurane and of a LA inhibitor have to be first provided and then combined by adding the one to the other, these features being inherent to the use claimed in claim 1 of auxiliary request 4.

Moreover, this reading of the claim's wording is confirmed by the description (page 3, second paragraph

under the heading "Summary of the Invention" of the application as filed) and paragraph [0009] of the patent in suit.

Therefore, the scope of protection has not been enlarged in relation to granted claim 2 (Article 123(3) EPC) and secondly, the amendment is supported by the description as originally filed (Article 123(2) EPC).

5.1.4 Most of the appellant's formal objections about the claim being too broad and insufficiently supported by the description are falling under the meaning of Article 83 EPC and hence, will be answered under that heading.

5.2 *Sufficiency of disclosure*

5.2.1 It has to be borne in mind that dealing with subject-matter concerning a non-medical use requires investigating whether the particular purpose defined in the claim is based on **a technical effect which is described in the patent**. Only if this is the case does the technical effect amount to a technical feature on which novelty can be based (see G 2/88 and G 6/88).

Therefore, during the assessment within the meaning of Article 83 EPC for the subject-matter claimed in claim 1 of auxiliary request 4, it is relevant to investigate whether the technical effect underlying the use claim is sufficiently disclosed.

The use claimed addresses the purpose of prevention of degradation by a Lewis acid of "a quantity of sevoflurane". The means of achieving that purpose are

to add the Lewis acid inhibitor "in an amount to prevent degradation".

Therefore, the protection sought by the claim encompasses prevention against all thinkable Lewis acids, independently of the amounts and the acid strength. Moreover, the Lewis acid inhibitor is also undetermined and the required amounts are defined as result-to-be-achieved. It has also to be stressed that the claim is not restricted to the preventive use for avoiding degradation of a quantity of sevoflurane in a specific container in which it is sold. As a matter of fact the container is also undefined and may be glass, plastic, metal and possess different closing means such as a valve, etc. Moreover, the Lewis acid may be ubiquitous during the whole life of the sevoflurane, which encompasses *inter alia* manufacture, bulk manufacture, filling in shipping containers, further manipulation of the lots, refilling in other containers, storage, and utilisation in the inhalation system in hospitals. Hence, the problem of prevention is not delimited to the degradation which may happen in a particular glass bottle, as the respondent alleged at the oral proceedings, but is not delimited at all (either in relation to the *locus* or in relation to the time or form of the contact with the LA).

Hence, the use claimed addresses a general principle, that of prevention in respect to any LA against degradation occurring at any possible moment, for which the specification of the patent does not provide sufficient disclosure. Moreover, the skilled person does not possess information about this kind of degradation in the background art and, hence, his

common general knowledge cannot serve to complete the information lacking in the patent in suit.

In fact, prediction of the degradation by a Lewis acid is not possible, since there is no theoretical or experimental model which applies to all situations encompassed by the claim.

The respondent indeed acknowledged that there was no way of predicting Lewis acid's presence and that there were no predicting tests available.

It can be accepted that, although not disclosed or mentioned in the description of the contested patent, there are analytical techniques for determining the presence of metal ions, but to carry out the invention claimed (i.e. to provide an adequate prevention of degradation by choosing specific amounts of a specific LA inhibitor) puts an undue burden on the skilled person. The reasons are that the skilled person has to contemplate and investigate first every single material or device which may be in contact with sevoflurane during its whole life, before being able to think about the choice of the LA inhibitor and the amounts required.

Accordingly, the brief information in the general description of the contested patent is insufficient. Moreover, the examples, which only address the particular effect of water under specific conditions, in relation to a specific LA (aluminium oxide) and to a specific glass container, cannot be generalised or extrapolated without making use of inventive skills.

Hence, the teaching disclosed in the patent in suit does not allow the skilled person to achieve the technical effect claimed.

Furthermore, the sentence "For any other Lewis acid inhibitor, a molar equivalent based upon moles of water should be used" which appears in paragraph [0027] ignores the fact that the patent does not contain valid and generally applicable instructions in respect of the amounts of water.

Consequently, the subject-matter claimed in claim 1 of auxiliary request 4 is not sufficiently disclosed in the patent in suit.

5.2.2 As regards the respondent's allegation that the only thing required of the skilled person is to take some specific samples and make a matrix of values showing what works and what does not work, the following has to be said: following this recommendation would amount, in the light of the breadth of the claim, to an invitation to perform a research programme to find out the conditions essential for every particular case thinkable.

5.2.3 Thus, auxiliary request 4 fails because it does not comply with the requirements of Article 83 EPC.

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