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Datasheet for the decision of 5 March 2015

Case Number: T 2474/11 - 3.3.07

Application Number: 01112230.6

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Title of invention:
Stable pharmaceutical solution formulations for pressurised metered dose inhalers

Patent Proprietor:
CHIESI FARMACEUTICI S.p.A.

Opponent:
NORTON HEALTHCARE LIMITED

Relevant legal provisions:
EPC Art. 56

Keyword:
Inventive step - (no)

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Case Number: T 2474/11 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 5 March 2015

Appellant: (Opponent)	NORTON HEALTHCARE LIMITED Regent House 5-7 Broadhurst Gardens Swiss Cottage London NW6 3RZ (GB)
Representative:	Gillard, Richard Edward Elkington and Fife LLP Thavies Inn House 3-4 Holborn Circus London EC1N 2HA (GB)
Respondent: (Patent Proprietor)	CHIESI FARMACEUTICI S.p.A. Via Palermo, 26/A 43100 Parma (IT)
Representative:	Adam, Holger Kraus & Weisert Patentanwälte PartGmbB Thomas-Wimmer-Ring 15 80539 München (DE)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 27 September 2011 rejecting the opposition filed against European patent No. 1157689 pursuant to Article 101(2) EPC.**

Composition of the Board:

Chairman	A. Usuelli
Members:	R. Hauss
	P. Schmitz

Summary of Facts and Submissions

I. European patent No. 1 157 689 was granted on the basis of four claims.

Claim 1, which is the only independent claim, reads as follows:

"1. An aerosol composition which comprises as active ingredient formoterol fumarate in a solution of a liquefied HFA 134a propellant and ethanol as a co-solvent, and hydrochloric acid in an amount such that the solution has an apparent pH between 3.0 and 3.5."

II. A notice of opposition was filed in which the revocation of the patent in its entirety was requested for lack of inventive step under Article 100(a) EPC.

III. The appeal by the opponent lies from the decision of the opposition division, announced on 26 July 2011 and posted on 27 September 2011, rejecting the opposition.

IV. The documents cited in the course of the opposition and appeal proceedings included the following:

D1: WO 94/13262 A1
D2: WO 99/65460 A2
D3: Compendium Suisse des Médicaments, 499-500 (1992)
D7: The Merck Index, 11th edn. 1989, 663-664

V. In the decision under appeal, the opposition division considered that document D2, which disclosed pharmaceutical aerosol formulations of formoterol fumarate in the propellant system HFA 134a / ethanol, represented the closest prior art (D2: examples 8, 9). The technical problem to be solved was the provision of an aerosol composition comprising formoterol fumarate showing reduced chemical degradation of formoterol

fumarate. That problem was solved, as shown in the examples of the opposed patent, by adding hydrochloric acid in an amount providing an apparent pH between 3.0 and 3.5. The chemical instability of formoterol in solution aerosol formulations was part of the common general knowledge and was mentioned as a concern in document D2. Starting from the teaching of document D2, the skilled person was thus motivated to consult document D1, which provided a general teaching for reducing the chemical degradation of a number of drugs in HFA/ethanol aerosol solution formulations. The solution proposed in D1 consisted in the addition of an acid. According to the teaching of document D1, the acid was to be chosen, and its quantity to be adjusted, depending on the chemical nature of the drug. Since D1 did not provide any further guidance with regard to formoterol fumarate, the skilled person was required to perform experiments which were beyond the scope of routine work in order to determine the specific conditions for stability improvement of that drug and to arrive at the composition as defined in claim 1 of the opposed patent. As a consequence, the claimed subject-matter was not obvious.

VI. The appellant (opponent) lodged an appeal against that decision; with a letter of reply dated 6 August 2012 the respondent (patent proprietor) submitted arguments.

VII. Oral proceedings took place on 5 March 2015.

VIII. The appellant argued as follows:

a) Document D2 represented the closest state of the art. The solution aerosol composition according to claim 1 of the patent in suit differed from the relevant example formulations described in D2 by the mandatory presence of hydrochloric acid at a

concentration providing an apparent pH between 3.0 and 3.5. The objective technical problem could be defined as the provision of HFA aerosol solution formulations of formoterol fumarate showing reduced chemical degradation of formoterol fumarate. It could furthermore be acknowledged that the claimed aerosol composition solved that technical problem.

b) In order to solve the technical problem, the skilled person starting from the teaching of document D2 would have looked to document D1, which addressed the problem of increasing the chemical stability of drugs in HFA aerosol solution formulations. If D2 provided some increase in chemical stability, that alone could not obviate the need in the art for further increases. The skilled person would not simply have assumed that further improvement in stability beyond the teaching of D2 was impossible.

c) According to the teaching of document D1, certain drugs could be stabilised by the addition of acid, formoterol being explicitly mentioned as an example of such a drug. Fumarate was listed in D1 as a suitable salt form of the drug and was also known as the anion typically used with formoterol. Aside from possible solubility limitations, the acid could in principle be any organic or mineral acid, hydrochloric acid being listed in D1 (on page 10) as the first of typically suitable mineral acids, and used in the first formulation example of D1 (table 1), which was also the sole example which described storage tests. The skilled person provided with that information would accordingly have tried using hydrochloric acid to achieve stabilisation with a reasonable expectation of success.

d) The skilled person would understand from the teaching of document D1 that all drugs listed as

suitable for use in the invention of D1, including formoterol and its salts, could be stabilised against chemical degradation by the addition of an acid. The skilled person would also understand from document D1 that the suitable acid level depended on the nature of the drug and the propellant/co-solvent system and had to be determined by carrying out some experimental work.

e) Thus the only task remaining for the skilled person, as instructed by D1, was to find the most favourable acid concentration. That task could be accomplished by routine experimentation not involving inventive skill. As a matter of course, stability tests at different concentrations of the acid would be carried out, which would enable the skilled person to find the most favourable acid level without recourse to the precise methodology described in the patent in suit. The methodology used in determining the acid level was also not relevant to the definition of the objective technical problem and the assessment of inventive step.

IX. The respondent's arguments can be summarised as follows:

a) The respondent agreed with the appellant's analysis under point VIII.a) *supra*.

b) The skilled person would not however have consulted document D1 in order to solve the technical problem: Since document D2 already taught that the addition of at least 5% by weight of a co-solvent provided chemical stability to a β-agonist drug such as formoterol in an aerosol solution formulation, the skilled person would have been satisfied that the technical problem was solved by D2 and would not have sought to obtain any further improvement in stability by consulting other

documents, such as D1. The inventive achievement consisted in the inventor realising that the problem of chemical instability was not satisfactorily solved in D2, and then providing an improvement to the formulations which was not suggested in the prior art. Document D1 was also older than document D2 and would not have been considered a potential source of information for further development.

c) If D1 were nevertheless consulted, the skilled person would not find a teaching in that document to choose, specifically, hydrochloric acid to combine with formoterol fumarate. According to D1, ascorbic acid, citric acid or an acid having the same anion as that contained in the medicament were preferred embodiments. In particular, D1 taught that the acid ideally had the same anion as the drug (thus, fumaric acid in the case of a fumarate) and that the selection of the acid and its concentration must be adapted depending on the nature of the drug component. Apart from that general teaching, D1 focused mainly on formulations containing ipratropium bromide as the drug, and did not provide any specific guidance with regard to formoterol.

d) Nor could it be inferred from the information presented in D1 that every drug listed in that document, including formoterol fumarate, was acid-sensitive in the sense that its rate of degradation could be reduced by the addition of acid. Reference example 1 of the patent in suit showed for instance that salbutamol (identical to albuterol listed on page 8 of D1) was not stabilised by the addition of citric acid or acetic acid.

e) Moreover, assuming that hydrochloric acid had been selected to be combined with formoterol fumarate, the skilled person would not have been able, without

recourse to the specific methodology developed by the inventors of the patent in suit, to determine the level of acidity which was critical in obtaining the desired stabilising effect. By merely testing a few samples with different acid concentrations, the very narrow suitable concentration range (represented by the range of apparent pH of 3.0 to 3.5) could not have been found without great difficulty, in particular as the teaching of D1, in the context of the embodiment described on pages 12 and 13, suggested a significantly higher molar ratio of active agent in relation to acid.

A test report had been submitted to the EPO in April 2004 showing that formoterol fumarate was not stabilised by a concentration of hydrochloric acid which was adapted to give the theoretical pH of an aqueous solution of 0.002% by weight citric acid, based on the embodiment shown in table 4 of D1, in which 0.002% by weight citric acid was used to stabilise the drug fenoterol in a propellant/co-solvent system. This supported the view that the skilled person would not be successful in stabilising a composition of formoterol fumarate merely by following the teaching of D1.

For the reasons presented in points c) to e), the selection of hydrochloric acid and the determination of the critical level of acidity as defined in claim 1 were measures going beyond the teaching of D1 and which required an inventive step.

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

XI. The respondent requested that the appeal be dismissed and that the patent be maintained as granted.

Reasons for the Decision

Inventive step (Articles 100 a), 52(1) and 56 EPC)

1. Patent in suit

1.1 The patent in suit seeks to provide stable pharmaceutical solution formulations of formoterol fumarate for pressurised metered dose inhalers.

1.2 The formulations defined in claim 1, which contain the propellant HFA 134a and ethanol as a co-solvent, have an apparent pH of between 3.0 and 3.5, due to the presence of a corresponding amount of hydrochloric acid.

2. Closest prior art

2.1 Document D2 has been regarded as the closest prior art both in the decision under appeal and in the parties' submissions. The board does not see any reason to select a different starting point.

2.2 Document D2 discloses formulations for pressurised metered dose inhalers comprising a β-agonist drug, a fluoroalkane (HFA) propellant and more than 5% by weight of a solvent that is capable of solubilising or dissolving said drug (claim 1). The invention of D2 is described with reference to the β-agonist drug formoterol, wherein the term "formoterol" is understood to mean the base form as well as the weak acid form of formoterol, such as exemplified by formoterol fumarate (D2: page 4, lines 16 to 20). In particular, D2 describes several compositions comprising formoterol fumarate, HFA 134a and ethanol as the co-solvent (examples 4 to 9). According to the teaching of document D2 (page 2: lines 2 to 10), it was known

that formoterol and its derivatives were difficult to formulate in conventional aerosols. Such formulations had short shelf-lives and they required refrigeration. Thus there remained a need for aerosol formulations of such drugs that remained chemically and physically stable during storage at ambient conditions of temperature and humidity. D2 teaches that stability can be improved by the presence of more than 5% by weight of a solvent capable of solubilising or dissolving the drug, the most preferred solvent being ethanol. The formulations of examples 4 to 9 are characterised in D2 as showing no signs of chemical deterioration.

3. Technical problem and solution

3.1 The composition defined in claim 1 as granted differs from the compositions disclosed in examples 4 to 9 of document D2 in the mandatory presence of "hydrochloric acid in an amount such that the solution has an apparent pH in the range of 3.0 to 3.5".

3.2 The alleged technical effect provided by the claimed composition containing hydrochloric acid and having the specified apparent pH is an improvement in the chemical stability, or a reduction of the chemical degradation, of formoterol fumarate.

3.3 It was not contested among the parties that the alleged technical effect was indeed obtained by the claimed composition. On that basis, the objective technical problem was defined as the provision of HFA solution aerosol formulations of formoterol fumarate showing reduced chemical degradation of formoterol fumarate.

4. Obviousness of the solution

The only point of dispute between the parties is whether the claimed composition can be rendered obvious

by the available prior art, in particular by consultation of document D1. In that context the respondent argued that the skilled person would not have consulted D1, that D1 in any case did not teach a combination of hydrochloric acid with formoterol fumarate, and that the skilled person would not have been able to determine the required acid concentration by mere routine testing.

4.1 Consultation of document D1

4.1.1 The chemical instability of formoterol in solution aerosol formulations was common knowledge at the priority date of the patent in suit, as mentioned on page 2 of the application as filed (corresponding to paragraphs [0008] to [0011] of the patent specification), and is explicitly considered to be an issue in document D2 (see page 2, lines 3 to 10). This was not contested by the respondent. D2 defines its objective as providing a stable formulation of a β-agonist drug that is suitable for use as an aerosol which does not require the use of refrigeration (see page 2, lines 17 to 19). A reader skilled in the art would be aware that the need for refrigeration is linked to the concern about chemical instability.

4.1.2 Document D2 concerns both solution aerosol formulations and suspension aerosol formulations of β-agonist drugs, in particular of formoterol fumarate. According to the technical teaching of D2, suspension formulations may be stabilised by the addition of a surfactant, and solution formulations may be stabilised by the addition of more than 5% by weight of a co-solvent (such as ethanol). In the context of examples 4 to 9 relating to solution aerosol formulations of formoterol fumarate, HFA 134a and ethanol, D2 reports losses of drug, but puts those losses down to adsorption onto the valve

gasket material. D2 goes on to state that the solutions "showed no signs of chemical deterioration", without however reporting concrete experimental data in proof of the alleged chemical stability.

4.1.3 Even if satisfactory chemical stability was attributed to the aerosol solution formulations of document D2, the person skilled in the art starting from the above-mentioned common knowledge (see point 4.1.1) and the information provided in D2 had nevertheless no reason to refrain from routinely seeking further improvement in chemical stability, which is always a concern for the formulator of pharmaceutical preparations.

Also, since document D2 does not give any detailed information on stability testing, the skilled person would perceive a need for further investigation, in particular with regard to the long-term stability required for a commercially viable product.

4.1.4 Moreover, the problem of chemical degradation of various drugs, such as formoterol, in HFA/ethanol propellant systems was already known from prior-art document D1 (page 3: paragraph 2); thus the respondent was not first to realise that concern. It is mentioned in D1 (see page 1: lines 12 to 16; page 3: paragraph 2) that certain drugs may decompose by a mechanism of interaction with the co-solvent or with water, which suggests that the co-solvent might actually be a destabilising factor.

4.1.5 In view of the above, the board considers that seeking to reduce the chemical degradation of formoterol fumarate in HFA/ethanol aerosol solution formulations, the person skilled in the art would logically have consulted documents concerning formulation stability, such as in particular document D1.

4.1.6 The mere fact that document D1 was published five years before D2 and six years before the priority date of the patent in suit does not as such constitute a plausible reason for disregarding it when assessing inventive step. Nor has the board any reason to believe that the disclosure of D1 represented outdated technology.

4.2 Combination of formoterol fumarate and hydrochloric acid

4.2.1 Document D1 relates to stabilised medicinal HFA-based solution aerosol formulations containing a co-solvent such as ethanol, with HFA 134a (1,1,1,2-tetrafluoro-ethane, designated as "HFC 134(a)" in D1) being a particularly preferred propellant (see D1: page 5, lines 8 to 9). According to D1, drugs which decompose by a mechanism of interaction with the co-solvent or water are less susceptible to chemical degradation in such solutions when an organic or mineral acid is added (see page 1: lines 1 to 15).

4.2.2 β-adrenergic agonists including formoterol are explicitly named in D1 as drugs which may be stabilised in that manner (page 8, lines 14 to 17). The drugs may be employed in salt form, fumarate being included in a list of possible salts (page 9, line 1). The fumarate is the commonly used salt form of formoterol which was also known to be used in the commercially available solution formulation Foradil® mentioned in the patent in suit (paragraph [0011]; see also D3, D7). The skilled person would thus have inferred that formoterol fumarate was covered by the teaching of document D1.

4.2.3 D1 teaches that the addition of an acid to the formulation provides chemical stability to the drug component. The acid may be any inorganic or mineral acid, such as hydrochloric, sulfuric, nitric or phosphoric acid, or it may be selected from organic

acids (see page 10: bottom paragraph; page 11: lines 1 to 3). D1 states that the selection of the acid depends on the medicament used and on the acid concentration needed to effect an acceptable rate of degradation of the medicament. Ideally, the preferred acid will have the same anion as that contained in the medicament, if any.

The skilled person would understand from this that all acids are in principle equally suitable, but that in an individual case certain acids might prove upon testing to be more or less favourable depending on the nature of the drug, the acid concentration required for stability and possible solubility limitations. When trying to adapt the invention of D1 to any specific drug, the skilled person would thus be motivated to carry out tests with one or more typical acids in varying concentrations to find a suitable combination. In the absence of concrete information suggesting that a particular acid is unsuitable, all acids are equivalent candidates and the arbitrary selection of one of them (e.g. hydrochloric acid) could not provide any contribution to inventiveness.

The preference expressed in D1, were the salt form of a drug to be used, for an acid having the same anion, is due to the desire to avoid adding a new chemical species to the formulation which might give rise to unexpected interactions. However, such a preference does not exclude other acids from consideration or raise concrete doubt about their individual compatibility. The board is not aware of any reason to regard hydrochloric acid as a cause for particular concern in that respect.

D1 also states that the acid may be any inorganic or mineral acid or that it may be selected from organic acids. "Representatives of this group *[i.e., organic*

acids - clarification added by the board] and preferred in this invention are ascorbic acid and citric acid, although other organic acids may also be suitable. However, according to this invention, citric acid is the most preferred acid because of MDI component compatibility." The board understands this to mean that ascorbic and citric acid are preferred within the group of organic acids, rather than that they are preferred over mineral acids, as suggested by the respondent. Even so, such a preference would not exclude mineral acids from consideration, and no reasons are given in D1 against employing them. As a matter of fact, the above-cited statement is followed by the general recommendation that acids "from either of the above groups" may be selected (page 11: lines 1 to 3), said groups being mineral acids and organic acids. The only reason mentioned in document D1 for preferring citric acid is metered dose inhaler (MDI) component compatibility (see page 10: bottom paragraph). Yet such compatibility is in any case a precondition for employing an acid in the manner suggested in D1, and containers protected against corrosion are known.

In conclusion, since no particular prejudice or disincentive against hydrochloric acid was known, the skilled person would have expected, based on the information provided in D1, that hydrochloric acid, like any other acid, was a suitable candidate for providing the desired stabilising effect on formoterol fumarate. It was therefore an obvious choice within the teaching of document D1.

4.2.4 Document D1 sets out that the drugs suitable to be used in the invention of D1 must characteristically exhibit significant degradation or decomposition in the propellant/co-solvent system and that said degradation or decomposition must be acid-sensitive in that its

rate can be effectively reduced by the addition of acid. The skilled person reading D1 would therefore infer that all drugs which are listed as suitable in that document, including formoterol and its salts, have that property. There is nothing in D1 that would make the skilled person think its teaching was not applicable to formoterol and its salts.

The test results of reference example 1 referred to by the respondent (see point IX.d) above) are not persuasive in raising doubt about the general applicability of the teaching of D1 in that respect. Reference example 1 of the patent in suit relates to a different, albeit structurally related drug (salbutamol) and describes limited storage tests with formulations comprising certain organic acids, in which stabilisation was not achieved. Only one or two concentrations of the acids were tested. Due to the limited coverage of the tests, they do not show conclusively that stabilisation by acids is never achievable in the case of salbutamol. Moreover, reference example 1 does not contain any data on formoterol fumarate. Not only were the reported test results not public knowledge before the priority date of the patent in suit, they also provide no concrete reason to doubt that stabilisation of formoterol fumarate could be achieved with hydrochloric acid.

4.3 Determination of the required acid concentration

4.3.1 Document D1 states that the range of acid concentration required to effect an acceptable rate of decomposition for medicaments in primarily non-aqueous solution aerosol formulations will depend primarily on the chemical composition of the formulation, such as choice of co-solvent(s) and the chemical nature of the medicament(s) present. This range is expected to be

0.10 to 0.0000001 N for inorganic acids (see page 15: paragraph 2). Hence it is clear that according to D1, some experimentation is required to find the most appropriate acid concentration.

4.3.2 In order to determine the acid concentration needed to effect an acceptable rate of degradation, the usual approach of the person skilled in the art would be to carry out storage tests involving a number of sample formulations. In such experiments the concentration of co-solvent and the concentration of acid would be varied to find the conditions, for a particular combination of drug and acid, which are most favourable to maintaining chemical stability.

4.3.3 The respondent argued that the inventors of the patent in suit had found that the relevant acid concentration (expressed as apparent pH) corresponded to the point of equivalence reached when titrating a composition containing the drug, a model propellant and the co-solvent with the acid.

According to the respondent the prior art, in particular D1, did not teach that, but indicated broad concentration ranges for both the drug and the acid, and in the only concrete example of D1, suggested the use of a high molar ratio of drug to acid. Thus D1 taught away from the claimed compositions. Moreover, repetition of the example presented in table 4 of D1 did not provide the desired stabilisation of formoterol fumarate.

Since the suitable concentration range corresponding to an apparent pH of 3.0 to 3.5 was quite narrow, the skilled person would not have been able to find it without use of the specialised methodology presented in the patent in suit which used a titration to identify the appropriate acid concentration.

4.3.4 In the board's opinion, the respondent's arguments under point 4.3.3 are not convincing, for the following reasons:

(a) In the embodiments described in document D1, the amount of acid required for stabilisation of ipratropium bromide in the propellant system is estimated on the basis of the pH value of an aqueous solution at which a minimum of degradation of that drug was observed (see D1: pages 11 to 12). Since said minimum of the degradation rate occurs at a pH of 3.5, a concentration of acid is proposed which would correspond in aqueous solution to a pH between 2.0 and 4.7. In the embodiment shown in Figure 1, a molar excess of ipratropium bromide versus hydrochloric acid was used (more than six times the amount), as pointed out by the respondent.

On the other hand, D1 does not contain a general teaching that the molar ratio of drug to acid should be high, nor does it present test results comparing the stability of compositions containing differing ratios. According to table 1 of D1, a large variation of the drug concentration, viz. 0.001 to 2.5% by weight of the formulation, combined with 0.01 to 0.00002 N hydrochloric acid, may actually be considered. Thus there is, in the board's opinion, no conclusive teaching in D1 that the molar amount of the drug must be higher than that of the acid, even in the case of ipratropium bromide, but still less so in the case of formoterol fumarate.

(b) The composition shown in table 4 of document D1 contains fenoterol hydrobromide as the drug, and citric acid as the acid. The test described in the report of 2004 cited by the respondent (see point IX.e above) replaced fenoterol hydrobromide by formoterol fumarate

and citric acid by hydrochloric acid. The concentrations were also modified.

As the example formulation of D1, table 4, contained a different drug and different acid, it is not plausible that the skilled person would have tried to derive any teaching relevant to formoterol fumarate from that formulation, since D1 teaches (see page 15, bottom paragraph) that the suitable acid concentration depends on the nature of the components, in particular the drug and cosolvent. What was effectively achieved in the test of 2004 was the preparation of an arbitrary formulation of formoterol fumarate and hydrochloric acid which happened to lack stability. This is however in conformity with the teaching of D1, according to which not all concentrations of acid are suitable for stabilisation of the drug (see point 4.3.1 above).

(c) According to the patent in suit, the required acid concentration was estimated based on tests carried out in a model hydrofluorocarbon fluid (HFA 43-10MEE). Stability tests with different acid concentrations (obtained by adding aliquots of 1.0 M hydrochloric acid) were carried out. A value of apparent pH was also measured in each of those formulations using a glass electrode (see example 4 of the patent in suit). Based on the results, further stability experiments comparing different acid concentrations in a system of HFA 134a/ ethanol were carried out (see example 5 of the patent in suit).

The respondent argued that the use of the method described in the patent in suit was indispensable for identifying the suitable acid concentration of the claimed formulation, since that concentration was situated in the region of a point of equivalence as shown in the titration curve of Figure 2 of the patent in suit (determined according to example 3 in a system

of HFA 43-10MEE/12% ethanol containing formoterol fumarate), where small increments of acid would cause abrupt changes in apparent pH. The inventors had also established that the quantity of acid required to get to the point of equivalence could vary depending on the content of co-solvent (see example 3 of the patent in suit).

However, the specific methodology used by the respondent to estimate the required concentration is not reflected in the technical features of claim 1; rather, any method could be used to identify stabilising concentrations of acid. The skilled person knew from D1 that the suitable concentration range of the acid could vary depending on the nature of the components of the system, especially the drug and the co-solvent, and that experimentation was required to determine suitable acid concentrations. Independently of the possibility of making a prior estimate based on some kind of model, samples having different concentrations of acid would, in the typical conventional approach, be subjected to routine stability testing, as explained in point 4.3.2 above. There is no general teaching in D1 which would restrict the experiments to certain ratios of drug to acid; in particular, the skilled person would have no reason to limit the experiments to the use of a molar excess of drug in relation to acid, as D1 specifies a broad range of acid concentrations, and the concentration of the drug would also depend on the required dosage. Since additional solvent (such as water) may affect the solvent system and may interact with the drug, the skilled person would employ the acid in a relatively concentrated form, so that only small increments would have to be added to vary the acid concentration. When a sample having a suitable acid concentration is found,

the generally suitable concentration range around it can be identified by testing samples differing from the first sample by small increments of acid concentration.

Thus the board is convinced that the skilled person would not be prevented from identifying, by mere routine experimentation, the acid concentration range which provides the required stability to the formulations.

4.4 As a consequence of the above, the composition defined in claim 1 as granted does not involve an inventive step within the meaning of Article 56 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:

S. Fabiani A. Usuelli

Decision electronically authenticated