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D E C I S I O N
of 16 March 2005

Case Number: T 0591/01 - 3.3.2

Application Number: 90906651.6

Publication Number: 0486499

IPC: A61K 31/34

Language of the proceedings: EN

Title of invention:
Stable ascorbic acid compositions

Patentee:
DUKE UNIVERSITY

Opponents:
Société anonyme dite: L'OREAL
BIODERM, INC.
Cellex-C Cosmaceuticals, Inc.

Headword:
Ascorbic acid/DUKE UNIVERSITY

Relevant legal provisions:
EPC Art. 52, 54, 56, 69, 83, 84, 100, 106, 107, 108, 123(2)
EPC R. 64

Keyword:
"Main request and first auxiliary request: novelty (no) the feature "topic" cannot serve to distinguish the claimed composition from identical compositions used in the state of the art for administration per os"
"Second and third auxiliary requests: inventive step (no)- inclusion of a second, commonly used pharmaceutically accepted carrier into aqueous solutions of a known medicament cannot render the use known per os of such modified solutions inventive"

Decisions cited:
T 0020/81, T 0289/84, T 0080/96

Catchword:
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Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 0591/01 - 3.3.2

D E C I S I O N
of the Technical Board of Appeal 3.3.2
of 16 March 2005

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Decision under appeal:
Interlocutory decision of the Opposition Division of the European Patent Office posted 20 March 2001 concerning maintenance of European patent No. 0486499 in amended form.

Composition of the Board:

Chairman: U. Oswald
Members: G. F. E. Rampold
P. Mühlens

Summary of Facts and Submissions

I. European patent No. 0 486 499 ("the Patent"), entitled "Stable Ascorbic Acid Compositions", was granted on 6 August 1997 with 22 claims, based on European patent application No. 90 906 651.6 (International application No. PCT/US 90/01968). The independent claims of the Patent as granted for all designated Contracting States, except ES, read as follows:

"1. A topical composition containing from at least 1% ascorbic acid (w/v) in water and a carrier suitable for topical application wherein the ratio of water to carrier is at least 1:1 and wherein the composition has a pH of no more than 3.5.

16. Use of a topical composition according to any of claims 1 to 15 for the manufacture of a medicament for retarding damage to skin by ultraviolet light.

17. Use of a topical composition according to any of claims 1 to 15 for the manufacture of a medicament for preventing or treating skin pathologies.

20. Use of a topical composition according to any of claims 1 to 15 for the manufacture of a medicament for increasing the rate of wound healing.

21. Use of a topical composition according to any of claims 1 to 15 for the manufacture of a medicament for decreasing the incidence of skin neoplasms due to ultraviolet radiation damage to the skin.

22. Use of a topical composition according to any of claims 1 to 15 for the manufacture of a medicament for treating pathologies of the eye."

II. Oppositions to the grant of the Patent were independently filed by three parties in the following sequence:

opponent I (Société L'OREAL; **party to the appeal proceedings as of right** under Article 107 EPC, second sentence) filed opposition on 29 April 1998;
opponent II (Bioderm Inc.; **appellant I**) filed opposition on 30 April 1998;
former **opponent III** (Cellex-C Cosmaceuticals, Inc.) filed opposition on 5 May 1998.

The opponents requested revocation in full of the Patent, invoking the following grounds:

(a) exclusion from patentability (Articles 100(a) and 52(2)(a) EPC),

(b) lack of novelty (Articles 100(a) and 54 EPC),

(c) lack of inventive step (Articles 100(a) and 56 EPC),

(d) insufficient disclosure (Articles 100(b) and 83 EPC), and also

(e) added subject-matter (Articles 100(c) and 123(2) EPC).

III. Of the numerous documents cited in the course of the first- instance opposition and subsequent appeal proceedings, the following are also referred to in this decision:

(1) English translation of JP-A-44-22 312;

(2) Rudelin et al, "The stability of ascorbic acid in various liquid media"; J. of Am. Pharm. Assoc. Vol. XLIV, 241-244, 1955;

(8) Derwent Abstract No. 77-42683Y [24]; abstract of NL-A-75 138 92, published on 1 June 1977;

(9) "Ascorbic Acid (Vitamin C) in Wound Healing", Annotated Bibliography, Copyright March 1941 by Merck & Co. Inc., Rahway, N. J., pages 1-15;

(13) G. Kahn et al, "Ultraviolet light protection by several new compounds"; Arch. Dermatol. Vol. 109, 510-517, 1974;

(14) The Merck Index, published by Merck & CO., Inc. Rahway, N. J., USA, 1976, pages 110-111;

(19) US-A-4 711 780

(30) Elsevier Science B.V. EMBASE No. 1977154390; abstract from J. Formosan Med. Ass. 75/4,243-250, 1976; "Topical use of ascorbic acid in the management of pressure sore; quantitative estimation with a new method".

IV. By its interlocutory decision, pronounced at the close of the oral proceedings on 14 December 2000, with written reasons notified on 20 March 2001, the opposition division maintained the Patent in amended form on the basis of the patentee's second auxiliary request comprising a set of 15 claims. The sole independent claim of this request for all designated contracting states, except ES, reads as follows:

"1. Use of a topical composition containing from at least 1% ascorbic acid (w/v) in water and a carrier suitable for topical application wherein the ratio of water to carrier is at least 1:1 and wherein the composition has a pH of no more than 3.5 for the manufacture of a medicament for increasing the rate of wound healing."

Dependent claims 2 to 15 relate to specific embodiments of the use according to claim 1.

V. In the above decision, the opposition division concluded that the various objections of the opponents under Article 83 EPC on the ground of insufficiency of disclosure and also those under Article 52(2)(a) EPC on the ground of exclusion from patentability and under Article 123(2) EPC on the ground of added subject-matter were unfounded and would thus not in themselves prejudice maintenance of the patent in the form as granted.

As regards novelty, the opposition division found, however, that compositions according to claim 1 as granted (see I above) lacked novelty over those disclosed in Tables 1 to 3 of citation (1) and in

Tables I and II of citation (2), because the feature "topic" did not serve to distinguish the claimed compositions in the Patent from the cited state of the art. It held further that the disclosure of citations (13) and (19) was likewise prejudicial to the novelty of the claimed compositions in the Patent and that citation (13), erroneously referred to as citation (3) in the decision under appeal, was also novelty-destroying prior art in respect of the subject-matter of claims 16 to 18 as granted, relating to the use of a topical composition according to claim 1 for the manufacture of a medicament for retarding damage to skin by ultraviolet light (see I above).

Thus, in the opposition division's judgment, the patentee's main request that the oppositions be rejected, failed for lack of novelty.

As to the second auxiliary request, which was maintained by the patentee as the sole additional request during the oral proceedings before the department of first instance (see IV above), the opposition division held that the state of the art cited by the opponents against this request neither disclosed nor in any way suggested the use of a topical composition of ascorbic acid, including all the technical features of claim 1, for increasing the rate of wound healing. The patent as amended in accordance with the second auxiliary request was thus found to meet the requirements of the Convention.

VI. Two parties involved in the opposition proceedings appealed against this decision in the following sequence:

- **appellant I** (**opponent II**) filed its appeal on 17 May 2001 by facsimile of the same date;

- **appellant II** (**patentee**) filed its appeal on 29 May 2001 with its letter of 28 May 2001.

Both appellants paid the appeal fees and filed their statements of grounds within the prescribed time limit.

VII. Former **opponent III** had already withdrawn its opposition in the proceedings before the department of first instance and had thus ceased to be a party to the proceedings.

VIII. In the course of the written appeal proceedings, **both appellants** and **opponent I** (party to the appeal proceedings as of right under Article 107 EPC, second sentence) defended their interests by filing on a number of occasions observations and new documents in reply to the arguments and evidence filed by the respective adverse party.

IX. **Both appellants** and **opponent I** as a party as of right were represented at the oral proceedings held on 16 March 2005 before the board of appeal.

At the beginning of the hearing, **appellant II** sought to introduce, by way of a so-called "new main request" and "new first and second auxiliary requests", three sets of claims wherein all independent claims had been further amended by specifying that the claimed compositions contain "*from at least 5% ascorbic acid (w/v)*". Following inspection of the newly filed

requests, the board expressed certain reservations as to the compliance of the amended claims with Article 123(2) EPC.

In reply to the board's reservations, **appellant II** requested a short break for deliberation which was allowed. After the break **appellant II** withdrew these newly filed requests and presented, instead, the following four requests:

X. As **main request**, it requested that the decision under appeal be set aside and that the Patent be maintained as granted (see I above).

XI. As **first auxiliary request**, **appellant II** requested that the decision under appeal be set aside and that the patent be maintained on the basis of claims 1 to 22 forming its second auxiliary request, filed with its letter of 16 February 2005, and **newly filed as its first auxiliary request** in the oral proceedings before the board. Claim 1 reads as follows, with the amendments indicated below in bold italic letters:

"1. A topical composition containing from ***at least 5% ascorbic acid (w/v)*** in water and a carrier suitable for topical application wherein the ratio of water to carrier is at least 1:1 and wherein the composition has a pH of no more than 3.5."

XII. As its **second auxiliary request**, **appellant II** requested that the decision under appeal be set aside and that the Patent be maintained on the basis of claims 1 to 21 forming its second auxiliary request, filed on 27 July 2001 with the statement of the grounds of appeal, and

newly filed as its second auxiliary request in the oral proceedings before the board. The independent claims read as follows:

"1. Use of a topical composition containing from at least 1% ascorbic acid (w/v) in water and a carrier suitable for topical application wherein the ratio of water to carrier is at least 1:1 and wherein the composition has a pH of no more than 3.5 for the manufacture of a medicament for retarding damage to the skin by ultraviolet light.

2. Use of a topical composition containing from at least 1% ascorbic acid (w/v) in water and a carrier suitable for topical application wherein the ratio of water to carrier is at least 1:1 and wherein the composition has a pH of no more than 3.5 for the manufacture of a medicament for preventing or treating skin pathologies.

5. Use of a topical composition containing from at least 1% ascorbic acid (w/v) in water and a carrier suitable for topical application wherein the ratio of water to carrier is at least 1:1 and wherein the composition has a pH of no more than 3.5 for the manufacture of a medicament for increasing the rate of wound healing.

6. Use of a topical composition containing from at least 1% ascorbic acid (w/v) in water and a carrier suitable for topical application wherein the ratio of water to carrier is at least 1:1 and wherein the composition has a pH of no more than 3.5 for the manufacture of a medicament for

decreasing the incidence of skin neoplasms due to ultraviolet radiation damage to the skin.

7. Use of a topical composition containing from at least 1% ascorbic acid (w/v) in water and a carrier suitable for topical application wherein the ratio of water to carrier is at least 1:1 and wherein the composition has a pH of no more than 3.5 for the manufacture of a medicament for treating pathologies of the eye."

XIII. As its **third auxiliary request appellant II** requested that the appeal of **appellant I** be dismissed. The claims of this request are accordingly those of the patent as maintained by the opposition division (see IV above).

XIV. After detailed discussion of the formal aspects and the substantive merits of the above-mentioned requests, **appellant II** intended to file towards the end of the hearing further amendments to the claims by way of a so-called **"new fourth auxiliary request".** However, immediately after presentation of this new request to the other parties and the members of the board, **appellant II** became aware of a drafting error in the amended claims and decided to withdraw its "new fourth auxiliary request", before the chairman had opened the discussion on the formal admissibility of this late-filed request.

XV. The arguments presented by **appellant I** (**opponent II**) and the **party to the proceedings as of right (opponent I)** (both these parties are hereinafter referred to in this decision as "the parties" or "both parties") in their written submissions and at the oral

proceedings before the board, in so far as these are still relevant to the claims in the current requests, can be summarised as follows:

Re the main and the first auxiliary requests:

[01] Citation (1) disclosed in Tables I and II aqueous solutions containing 5.28% (w/v) (52.8 mg/ml) of ascorbic acid and additionally 10, 20 or 50% (w/v) of polyethylene glycol, corresponding to ratios of water to polyethylene glycol of 9:1, 8:1 and 1:1. All aqueous solutions had been adjusted after the addition of polyethylene glycol to a pH value of 3. The disclosure of (1) was accordingly prejudicial to the novelty of claim 1 of both the main request and the first auxiliary request. In view of this clearly novelty-destroying state of the art, both parties expressed astonishment on learning that appellant II (patentee) was maintaining, even at the appeal stage, its opinion that citation (l) did not anticipate the claims of the patent in suit.

[02] The parties noted that particular reliance had been placed by appellant II on decision **T 289/84** of 10 November 1986 which did not rule out the allowability of a claim to a topical formulation containing a known compound as the active ingredient although other formulations with the same active ingredient were already disclosed in the state of the art. (cf. point 3.4 of the Reasons). In the present case, the claims provided for a formulation for topical administration (ie adapted by the addition of specific compounds for that particular purpose). The parties emphasised, however, that decision **T 289/84** was not

relevant as in that case the formulations considered were different whereas, in the present case, the formulations disclosed in the prior art and those claimed in the patent were the same.

[03] Further, the parties referred to decision **T 80/96** (OJ EPO 2000, 50) which stated that in a claim directed to a preparation comprising a known structurally-defined active agent and at least one auxiliary substance (ie where something extra is added to the active agent), the addition of an unspecified auxiliary substance could not, in view of the unlimited number of substances which may be considered, be deemed a substantive and distinctive addition to the active agent, unless the substance was specified in such a way that a person skilled in the art could recognise what it was. No such disclosure was made in the Patent and therefore the compositions disclosed should be compared like for like.

[04] Although appellant II further argued that citation (1) was particularly directed to solutions to be taken internally, and that therefore the examples given in (1) could not be topical compositions, it was in the opinion of both parties clear that *any* solution that could safely be taken internally could also safely be applied to the skin.

[05] Both parties still maintained that citation (2) also anticipated claim 1. This citation disclosed a wide variety of stable ascorbic acid formulations. Table 3 disclosed solutions containing 20 mg/ml (2% w/v) ascorbic acid. For example, solution 3 comprised 4% carboxymethylcellulose (a well-known

carrier for topical application) as a solvent. Accordingly, the formulation contained over 1% ascorbic acid in water and a carrier suitable for topical application wherein the ratio of water to carrier was 96:4, it being implicit that the composition has a pH of no more than 3.5.

[06] Further, in the view of the parties, claim 1 lacked novelty over the disclosure of citation (13). This reference described the investigation of the photo-protective capabilities of some 30 compounds. It detailed the rationale or evaluation of such compounds as UV protectants. Among the compounds listed on Table 1 on page 511 was ascorbic acid. Table 3 on page 515 showed the results of topical studies of ascorbic acid on human erythema inhibition. The ascorbic acid was shown, in the methods section of the right-hand column of page 514, to be applied as a solution of 100 mg/ml (10% w/v) in 50% anhydrous alcohol. Accordingly, the cited document disclosed a topical composition containing > 5% w/v (10% ww/v) ascorbic acid in water and a carrier (alcohol) suitable for topical application wherein the ratio of water to carrier was at least 1:1 and wherein the composition had a pH of no more than 3.5. This was implicit as indicated by the reference to citation (14). Alcohol was clearly indicated within the Patent as being a possible carrier (see page 3, lines 51-55).

[07] Finally, the parties argued that claim 1 lacked novelty over citation (19). This document disclosed a medication for treating the surface epithelium. Example 6 disclosed two vaginitis douche solutions. The first solution, when made up with 100 ml of sterilised

water, contained 2.5% ascorbic acid and 1% carrier (mucopolysaccharide and polysaccharides). Hence the solution displayed a ratio of 100:1 of water to carrier. It was implicit that the pH was below 3.5.

Re the second and third auxiliary requests:

[08] In the opinion of the parties, the only features by which independent claims 1, 2, ***5***, 6 and 7 of the second auxiliary request and **claim 1** of the third auxiliary request differed from claim 1 of the Patent as granted were that the composition was useful for retarding damage to the skin by ultraviolet light, preventing or treating skin pathologies, **increasing the rate of wound healing**, decreasing the incidence of skin neoplasms due to the ultraviolet radiation damage to the skin and treating pathologies of the eye.

[09] If the description was referred to for guidance, in accordance with the protocol to Article 69 EPC, the parties found that the only wounds mentioned in the Patent were those caused by UV radiation. In particular, the examples related to the prevention and treatment of UV burns. This point was particularly relevant to **claim 5** of the second auxiliary request and **claim 1** of the third auxiliary request where the type of wound was not specified in the claim, which therefore covered any type of wound. The opposition division thus wrongly concluded that claim 1 of the current third auxiliary request (which is identical with claim 1 as maintained by the opposition division) met the requirement of Article 54 EPC. The only feature that distinguished that claim from originally-granted claim 1 was the feature that the composition was useful

for increasing the rate of wound healing. This was, however, already amply described in the state of the art.

[10] The vaginitis douche composition disclosed in Example 6 of citation (19) was a topical composition as defined in Black's Medical Dictionary (see **[07]** above). The results of the application of this douche composition showed healing of ulcerations (ie use in wound healing) and prevention of them forming. This disclosure too was, in the parties' judgment, prejudicial to the novelty of the use of the claimed composition for increasing the rate of wound healing.

[11] Moreover, citation (13) also disclosed a wound healing composition which comprised at least 1% ascorbic acid (2% and 10% respectively) in water and a carrier suitable for topical application (see **[06]** above).

[12] Citation (9) is entitled "Ascorbic acid Vitamin C in wound healing: annotated bibliography". Only the title page of this reference was filed during opposition proceedings because opponent I took the view that the title page was sufficient to show that there was nothing new or inventive in the use of ascorbic acid in wound healing. However, this reference had not been properly considered by the opposition division in the interlocutory decision under appeal because only the title page was presented (see Reasons of the impugned decision, page 10, point 5.1: "However, document D9 is not relevant since it is only the title page of a book").

At the appeal stage, a full copy of citation (9) was provided and turned out to be relevant for the assessment of the inventive step of the subject-matter of the above-mentioned claims because citation (9) indicated that as long ago as 1937 the role of ascorbic acid in wound healing was well known. Citation (9) consisted of a number of summaries of scientific papers, each of which discussed or showed the role of ascorbic acid in wound and bone healing [see for example Nos. 1 to 4 on pages 3 and 4 and Nos. 1 and 2 on page 6 of (9)].

[13] Finally, citation (8) also disclosed medicaments for external use comprising mixtures of ascorbic acid with a neutral carrier. This carrier could be water and/or an ointment base. The cited document suggested the use of these medicaments for treating burns and other wounds.

[14] In conclusion, the parties submitted that, even if novelty was acknowledged, the claimed subject-matter of the above-mentioned claims in the second and third auxiliary requests did not involve an inventive step in view of the teaching of the above-cited state of the art.

XVI. The arguments of **appellant II (patentee)** presented in writing and during the oral proceedings before the board of appeal, in so far as these are still relevant to the claims in the current requests, can be summarised as follows:

Re the main and the first auxiliary requests:

[15] Appellant II disagreed with the opinion of the opposition division in the contested decision that the teaching of citation (1) was prejudicial to the novelty of the claimed composition in claim 1 of the patent as granted. This citation related to methods for suppressing anaerobic decomposition of aqueous vitamin C solutions to be taken internally (see page 1, first paragraph; page 3, penultimate paragraph). Thus, there could be no doubt that citation (1) related to compositions for internal use which were adapted for oral ingestion. There was no disclosure in (l) teaching or even suggesting that the compositions described therein were suitable for topical application.

[16] According to appellant II, it had been ruled in decision **T 289/84** (*loc. cit.*) that oral compositions were not adapted for topical administration and, particularly, that "the fact that a chemical compound and pharmaceutical formulations containing the same as active ingredient are known does not rule out a claim directed to a specific mode of formulation not disclosed by the prior art" (*loc. cit.*). The reasoning for this was that the teaching of a document such as (1) was addressed to the expert pharmacist, and no such expert, when instructed to prepare, eg an oral composition, would realistically conceive preparing a formulation adapted for topical administration (cf. points 3.2 and 3.3 of the Reasons).

[17] The expert would, rather, adapt the composition disclosed in citation (1) to the intended use by adding certain additives, such as those listed on page 3, last

paragraph, of citation (l), ie alcohol, sugars, fragrances, colouring agents, etc. In particular, an expert would consider adding fructose, sucrose and the like, as is evident from page 1, second paragraph, of citation (l). In the cited document it was moreover stated:

"Furthermore, this anaerobic decomposition phenomenon is known to be aided by the addition of fructose, sucrose, and the like, which is a crucial problem when the vitamin C is to be included in an internalizable solution". It could be inferred from this that the person skilled in the art would include small quantities of, at least, sugars in such oral compositions. Although these additives were generally used in fairly small quantities, they established a "material" difference. The adaptation of the claimed composition to topical administration resulted thus in distinguishing technical features, even if it was chosen to express these features in claim 1 in functional terms.

[18] At the hearing before the board, appellant II submitted for the first time that, for the purpose of assessing novelty, the claimed aqueous solutions of ascorbic acid in the Patent which are provided as stable topical compositions in "ready-for-use" form had to be compared with the disclosure in citation (1) relating to ampoules which were filled with aqueous solutions of ascorbic acid and permutated with nitrogen gas, and then heated to 100°C. It was demonstrated in (1) that a reduced vitamin C content had been observed for the aqueous solutions disclosed in (1).

Re the second and third auxiliary requests:

[19] In the opinion of appellant II, none of the documents cited by appellant I considered or even suggested compositions as defined in the present claims, containing ascorbic acid stabilised in a large amount of water (ratio of water to carrier greater than 1) at a pH of no more than 3.5. Similarly, none of these documents considered or even suggested the use of such formulations in the treatment of skin conditions, for example burns or sunburns, or for increasing the rate of wound healing. The prior art expressly avoided such a low pH, since it was considered that such a low pH would cause irritation or even skin peeling. For this reason alone, the present claims were based on an inventive step over the cited state of the art.

[20] In the opinion of appellant II, there could be no doubt that a series of medical benefits using vitamin C, such as an increased rate of wound healing, including healing of UV damage to skin, bone fractures, burns, ulcers, etc. had been disclosed in the cited state of the art. However, these disclosures related to oral administration of vitamin C. At the priority date of the Patent, oral administration was the only route for administering vitamin C which was generally accepted and recognised in the medical art.

[21] Thus, for example, citation (9) related to the healing of fractures in human patients and animals suffering from lack of vitamin C. From page 1 it was quite clear that vitamin C was administered orally. Therefore, (9) was not concerned with topical application of vitamin C to wounds. This document also

failed to disclose a topical composition containing at least 1% ascorbic acid in water and a carrier suitable for topical application. Furthermore, it did not teach the importance of the pH value and the ratio of water to carrier for compositions of Vitamin C suitable for topical application.

[22] According to appellant II, the present invention taught for the first time that formulations of ascorbic acid for topical use could be successfully prepared if (1) the concentration of ascorbic acid was at least 1%, more preferably at least 5%; (2) the solvent contained at least 50% water, ie , a water to carrier ratio of at least 1:1; and (3) the pH was no more than 3.5. Such a formulation had been shown to provide extended stability of ascorbic acid, a suitably hydrating solution for use on skin, and sufficient percutaneous absorption of ascorbic acid to provide significant benefit. In this context, appellant II argued that, contrary to the teaching in the prior art, only the present inventors had found the pH described in the Patent to be unexpectedly safe and effective for topical application. In fact, the enhanced percutaneous absorption was possibly achieved because of the low pH used. As described in the specification at page 4, lines 8-13, the protonated form of ascorbic acid used in the claimed invention was important dermatocologically for several reasons. First, this form removed the ionic repulsion of the two oxygen groups, thus stabilising the molecule. Second, because the protonated form of ascorbic acid was uncharged, entry into the skin, which itself has a pH of about 3-5, should be facilitated.

[23] In contrast to the assertions of appellant I, citation (13) did not, in the opinion of appellant II, contain a clear and unmistakable disclosure for the skilled person that the solutions disclosed in (13) contained only water, ethanol and ascorbic acid.

[24] Citation (19) did not teach a stable topical composition containing ascorbic acid in free acid form having a pH value below 3.5. Indeed, no pH values were disclosed in the description of (19). This citation also failed to teach the importance of the claimed water-to-carrier ratio of at least 1:1.

[25] In view of the above observations it was clear that the subject-matter of the claims as maintained by the opposition division was not only novel but also involved an inventive step in the light of the cited state of the art in the proceedings.

XVII. **Appellant I** (**opponent II)** requested that the decision under appeal be set aside, that the Patent be revoked and that the appeal of **appellant II** (**patentee**) be dismissed.

Appellant II (**patentee**) requested that the decision under appeal be set aside and that the Patent be maintained as granted (main request), or that the Patent be maintained in amended form on the basis of the first or second auxiliary request filed in the oral proceedings, and that the appeal of **appellant I** (**opponent II**) be dismissed.

The **party as of right (opponent I)** requested that the appeal of **appellant II** (**patentee**) be dismissed.

Reasons for the Decision

1. The appeal complies with Articles 106 to 108 and Rule 64 EPC and is, therefore, admissible.

Main request of appellant II *(maintenance of the patent as granted; see I and X above): novelty*

2. Citation (1) discloses the preparation of **5.28% aqueous solutions of ascorbic acid (w/v)** containing 0.3 mol (52.8 mg/ml) of **ascorbic acid (MG 176.12)** dissolved in a mixture of water and a pharmaceutically acceptable **carrier** selected from **polyethylene glycol 200, 400, 1000, 1540 and 4000**, wherein the **ratio of water to carrier is at least 1:1 (v/w)** and wherein **the pH** of the solutions has been adjusted with sodium hydroxide after the addition of polyethylene glycol to **a value of 3.0** (see (1), especially page 2, line 9 onwards, Tables 1 to 3).

In the context of the above disclosure in citation (1) it should be noted that **polyethylene glycols** are explicitly mentioned in the present patent specification as being **particularly suitable and useful carriers for topical application** of the claimed compositions (see patent specification, page 3, line 54).

2.1 The board does not agree with the contention of appellant II during the hearing before the board that, for the purpose of assessing novelty, the claimed compositions in the Patent should be compared with the

disclosure in citation (1) relating to ampoules which were filled with the above-mentioned aqueous solutions of ascorbic acid and permutated with nitrogen gas, and then heated to 100°C (see citation (1), especially page 2, lines 12-13).

Citation (1) discloses unambiguously and unequivocally that aqueous solutions of ascorbic acid containing all the technical features mentioned in point 2 above were prepared and obtained in the cited state of the art as precisely defined, complete and isolated final products **before** these were filled into ampoules and permutated with nitrogen gas and subjected to certain heat tests.

2.2 It is thus clear that compositions containing all the technical features of claim 1 already form part of the state of the art under Article 54(2) EPC.

2.3 In support of its arguments concerning novelty of the claimed subject-matter in the Patent, appellant II relied in large measure on decision **T 289/84** of 10 November 1986. In this decision, the deciding board allowed a claim to a topical formulation, although other (different) formulations with the same active ingredient were already known. The claim allowed by that board was drafted as follows:

"*A pharmaceutical formulation, characterised in that the formulation is adapted for only topical, to the exclusion of oral and injectable administration and comprises a compound of formula (I) wherein .....*"

In decision **T 289/84** (see especially point 3.3 of the Reasons) it is however stated:

"*Finally, as a kind of safety check for novelty, the Board has also satisfied itself that none of the formulations disclosed in the citations does in fact materialize the proposed distinguishing feature - irrespective of the envisaged prior-art use of the concerned formulation. This criterion would certainly not have been met by the previous intended distinguishing feature of* ***"suitability" for topical administration*** [highlighted and emphasis added by the board]**.** *As the Appellants correctly point out (page 5, paragraph 1, of their Grounds of Appeal dated 26.11.84), the words* ***"suitable for"*** [highlighted and emphasis added by the board] *express that something can be used for a given purpose, although it is not necessarily particularly appropriate for that purpose. Thus, for instance, an aqueous injection solution as disclosed in (A) would generally be suitable for topical administration, e.g. to the human skin or eye.*"

2.4 Since carriers for topical application useful in practising the claimed invention include, *expressis verbis*, **polyethylene glycols,** there cannot be the slightest doubt that the aqueous solutions of ascorbic acid disclosed in citation (1) containing all the technical features mentioned in point 2 above **would generally be suitable for topical application**, for example to the human skin. Thus, contrary to the assertion of appellant II, decision **T 289/84** strongly supports the board's view and the submissions of both parties that the subject-matter of claim 1 lacks novelty over the state of the art of citation (1).

2.5 Since citation (1) is clearly prejudicial to the novelty of at least claim 1, the board does not need to examine the allegations of the parties that the claims also lack novelty over a series of other citations presented by the parties in the course of the first-instance opposition and subsequent appeal proceedings.

2.6 Since a decision can only be taken on a request as a whole, none of the further claims of that request need to be examined. In these circumstances, the appeal in so far as it relates to the main request of appellant II must be dismissed, as claim 1 of this request does not meet the patentability requirements of Article 52(1) in conjunction with Article 54 EPC.

First auxiliary request of appellant II (see XI above): (a) compliance with Article 123(2) EPC; (b) novelty

3. Claim 1 has been further amended in the first auxiliary request so as to specify that the claimed composition contains "*from at least 5% ascorbic acid (w/v)*" (see XI above).

At the hearing, appellant II relied on the **sentence bridging pages 5 and 6** and on **Example 1** of the application as originally filed (ie international application No. PCT/US 90/01968 published under the PCT as WO 90/12572) as the basis for the proposed amendment.

3.1 The sentence bridging pages 5 and 6 of the application as filed reads as follows:

"*We have now discovered a new, more economical, stable topical composition which consists essentially of at least about 1 wt.% L-ascorbic acid, preferably from about 3 to 20 wt.% L-ascorbic acid, and more preferably about* ***5 to 10 wt.% L-ascorbic acid*** (highlighted and emphasis added by the board) *in water and a carrier for topical application.*"

Example 1 of the application as filed provides the following disclosure:

"*In Example I, four solutions of* ***1-10% L-ascorbic acid (w/v)*** (highlighted and emphasis added by the board) *in 80% H_2O (v/v):20% propylene glycol (v/v):1% hydroxypropylcellulose (w/v) were prepared and kept in the dark at room temperature and capped microfuge tubes (with an approximately 10% air headspace)*". "*At indicated times, aliquots were removed and the residual ascorbic acid determined spectrophotometrically. The results are illustrated in Figure 1*" (see application as filed, page 10, lines 2 to 10).

"*Figure 1. Stability of various concentrations of L—ascorbic acid in aqueous cosmetic vehicle. Different concentrations of L-ascorbic acid were made in a vehicle composed of 80% H_20, 20% propylene glycol and 1% hydroxypropylcellulose and stored shielded from light, at room temperature (with an approximately 10% air headspace). One day, 3 weeks and 7 weeks later, aliquots were diluted into a quartz cuvette 10 and the resulting spectrum was scanned from 200 to 400 nm, The optical density of the 260—265 nm peak was recorded for lower concentrations while the optical density at 280*

nm was recorded for changes in the higher concentrations of L—ascorbic acid.
1: 1% L-ascorbic acid 2: 3% L-ascorbic acid
3: ***5% L-ascorbic acid*** 4: ***10% L—ascorbic acid"***
(highlighted by the board) (highlighted by the board)
(see application as filed, page 18, lines 1 to 17).

3.2 From the foregoing it is clear that the disclosure in the application as filed might possibly provide a basis for an amended claim specifying the definite, small range of 5 to 10% ascorbic acid (w/v) or the single amounts of either 5% (w/v) or 10% (w/v) ascorbic acid, but fails to provide any support for the extremely broad, open-ended range: "*from at least 5% ascorbic acid (w/v)*" claimed in claim 1 as amended. Accordingly, the proposed amendment contravenes Article 123(2) EPC.

4. In addition to the contravention of Article 123(2) EPC, claim 1 of the first auxiliary request of appellant II relating to a topical composition a containing from **at least 5% ascorbic acid (w/v)** in water lacks novelty over the state of the art according to citation (1) for the same reasons as have been given in points 2 to 2.4 above in relation to claim 1 of the main request of appellant II.

The first auxiliary request must thus also fail.

Second and third auxiliary requests of appellant II (see IV, XII and XIII above)

5. As is apparent from IV, XII and XIII above, **independent claim 5** of the **second auxiliary request** and also **claim 1** of the **third auxiliary request** (ie the request

that the appeal of appellant I be dismissed) of appellant II are directed to the same subject-matter and are, moreover, **identically worded**. Both these auxiliary requests will thus be considered together.

5.1 The above-mentioned independent claims are directed to the use of a topical composition containing from at least 1% ascorbic acid (w/v) in water and a carrier suitable for topical application wherein the ratio of water to carrier is at least 1:1 and wherein the composition has a pH of no more than 3.5 for the manufacture of a medicament for increasing the rate of wound healing.

The type of wound is not specified in the claims, hence the claims cover the use of the composition in the treatment of any type of wound. The only specific reference to any type of wound in the patent specification is in Example X on page 6 and is the treatment of **a burn caused by UV irradiation.**

The state of the art relating to the use of ascorbic acid in the treatment of wounds and burns

6. The knowledge that ascorbic acid plays an important role in wound healing and that ascorbic acid is conventionally administered to patients as **an aid to wound healing** was already part of the state of the art at the priority date of the Patent, as exemplified below:

6.1 Citation (9), entitled "Ascorbic acid - Vitamin C - in wound healing: annotated bibliography", indicates that as long ago as 1937 the role of ascorbic acid or

vitamin C in wound healing was known. This citation is admittedly primarily concerned with the role of ascorbic acid in wound healing by oral application of the medicament.

6.2 Citation (13) discloses in the methods section of the right- hand column of page 514 the application of ascorbic acid as a solution of 100 mg/ml (10% w/v) in 50% anhydrous alcohol to the forearms of volunteers to achieve erythema "sunburn" inhibition. This clearly demonstrates that (13) discloses the use of a topical composition containing 10% w/v of ascorbic acid and a carrier (alcohol) suitable for topical application, wherein the ratio of water to carrier is at least 1:1, for the treatment or prevention of burns (wounds). The pH value of the composition is not explicitly disclosed in (13). It is, however, derivable as being no more than 3.5 from a cross-reference to the second document (14).

6.3 Citation (19) discloses in Example 6 an aqueous vaginitis douche solution. This solution, when made up by dissolving the vaginitis douche powder of Example 6 with 100 ml of sterilised water (see column 6, lines 26-33), contains 2.5% (w/v) of ascorbic acid and 1% carrier (mucopolysaccharides and polysaccharides). Hence, the solution plays a ratio of water to carrier of 100:1. The pH is again derivable as being no more than 3.5 from a cross-reference to the second document (14). The results of the application of this douche solution shows healing of ulcerations (ie use in wound healing) and prevention of them forming (see column 6, lines 48-68).

6.4 Citation (30) discloses the topical use of a 10% aqueous solution of ascorbic acid (w/v) on pressure sores for facilitating the growth of granulation tissue. Granulation tissue growth plays an integral part in wound healing.

The closest state of the art

7. In spite of the highly relevant state of the art mentioned above, the disclosure of citation (8) forms, in the board's judgment, the **closest state of the art** to the subject-matter of the independent claims mentioned in point 5 above.

7.1 The cited document (8) already discloses **medicaments for external use,** comprising a mixture of >=3 pts. wt. (preferably 5-20 pts. wt.) of **ascorbic acid** with 100 pts. wt. of a neutral carrier. The carrier can be **H_2O** and/or an ointment base.

The **external medicaments** disclosed in (8) accordingly include aqueous solutions of ascorbic acid containing at least

- 30 g/1000 g, ie 30 mg/ml or 3%(w/v), and preferably
- 50 g/1000 g, ie 50 mg/ml or 5%(w/v), to 200 g/1000 g, ie 200 mg/ml or 20%(w/v),

of ascorbic acid in water. Such medicaments are said in (8) to be particularly useful, *inter alia*, for the external (topical) **treatment of burns and other wounds.**

Document (14) which represents textbook knowledge indicates that aqueous solutions containing **5 mg/ml** of ascorbic acid have a **pH of 3**. Aqueous solutions

containing **50 mg/m**l of ascorbic acid have a **pH of 2** (see page 111, left hand column, lines 49-50). The external medicaments disclosed in (8) accordingly exhibit a pH of no more than 3.5.

7.2 As to the repeated submissions presented by appellant II in writing and orally that the term "ascorbic acid" used in the cited documents should also be given the meaning "sodium ascorbate" or "a mixture of ascorbic acid and sodium ascorbate", the board takes the following position. According to the standard interpretation in EPO practice, a disclosure or teaching in the state of the art is to be interpreted in good faith **in accordance with the ordinary meaning given to technical terms** in their context and in the light of its object and purpose. It follows that the term *"ascorbic acid"* used in (8) and any of the other cited documents has to be given its ordinary meaning in the art, ie L-xylo-ascorbic acid or L-threo-hex-2-enonic acid γ-lactone. The term *"ascorbic acid"* used in the Patent and equally in citation (8) accordingly defines the same chemical substance which is used as the active ingredient of both the medicaments disclosed in (8) and those described in the Patent as well.

It also follows that, in the absence of any indication of an **unambiguous reference point** or disclosure in the entire patent specification explaining the exact meaning of the relative terminology *"for **increasing the rate** of wound healing"* used in the Patent, this particular intended use of the medicaments indicated in the above-mentioned claims of the second and third auxiliary requests is synonymous with the use of the external medicaments disclosed in (8), namely *"for*

treating burns and wounds"). Or ,expressed differently, both the disclosure in the state of the art and in the Patent refer to the use of medicaments containing ascorbic acid for the treatment of burns and wounds and the effects thereby achieved in comparison with no treatment at all.

7.3 From the foregoing it is clear that the state of the art according to (8) already discloses the use of external (topical) medicaments containing from at least 1% ascorbic acid (w/v) in water [which, as such, is incidentally a carrier perfectly suitable and useful for topical application] for the treatment of burns and wounds. From (14) it is known that such aqueous solutions have a pH of no more than 3.5.

7.4 It is thus clear that the medicament used in (8) does not differ from the medicament used in independent claim 5 of the second auxiliary request and in claim 1 of the third auxiliary request with regard to the nature of the active ingredient (ascorbic acid) and its concentration in the aqueous solution and the range of pH values of the aqueous solution. There is also agreement in respect of the particular intended use of both medicaments. The sole difference between the two medicaments consists in the use in the Patent of a further carrier suitable for topical application in addition to water to obtain a solution of ascorbic acid in a water/carrier system. The ratio of water to carrier in this water/carrier system is at least 1:1.

The problem underlying claim 5 of the second auxiliary request and claim 1 of the third auxiliary request and its solution

8. The patent specification refers at page 3, lines 1-11, to certain causes a), b) and c) which may be responsible for the instability of ascorbic acid solutions and states at page 3, lines 12-16, that "*for theses reasons, among others, scientists working in the field have had difficulty in formulating stable solutions of ascorbic acid which would be useful for cosmetic, dermatologic, or ophthalmic needs. Nevertheless, because of the many beneficial effects attributed to ascorbic acid, numerous attempts have been made to overcome these difficulties.*"

8.1 However, appellant II has failed to persuade the board with its assertion that the problem to be solved was to provide more economical topical compositions of ascorbic acid having improved storage stability. The perceived solution of this problem is set out on page 3, lines 37-46, of the patent specification which proposes an aqueous solution of at least of about 1 weight% L-ascorbic acid and a carrier for topical application. The ratio of water to carrier is at least 1:1. A wide range of possible carriers is disclosed in the following paragraph and this list is followed by a general statement to the effect that any carriers known to those skilled in the art which are compatible with water and are biologically acceptable may be used.

8.2 However, contrary to the submission of appellant II, Example II and Figure 2 in the Patent demonstrate that neither the presence as such nor the concentration of the carrier, in this case propylene glycol, has an

effect on the stability of ascorbic acid in aqueous solution. In fact, Figure 2 shows that a solution of ascorbic acid (2% w/v) in water **having no carrier at all** is as stable as those containing the carrier in varying concentrations (10% or 20% or 40% or 60% propylene glycol).

8.3 Consequently, the conclusion must be drawn either that the problem set out in the Patent has not been solved or that the additional advantages referred to by appellant II have not been properly demonstrated. Such alleged but unsupported advantages cannot be taken into consideration in respect of the determination of the problem underlying the application and hence in the assessment of inventive step (see, for example, **T 20/81**, OJ EPO 1982, 217).

8.4 For this reason, the problem underlying the second and third auxiliary requests in respect of the closest state of the art according to (8) may only be seen in providing further topical medicaments comprising at least 1% ascorbic acid (w/v) in water and having a pH of no more than 3.5 suitable for use in the treatment of burns and wounds.

8.5 The solution to this problem lay in the provision of the compositions defined more precisely in claim 5 of the second auxiliary request and claim 1 of the third auxiliary request for the particular intended use indicated above. As explained in more detail in 7.4 above, the claimed compositions differ from those disclosed in (8) only in that a second carrier suitable for topical application has been added to the aqueous

solutions of ascorbic acid at a ratio of water to the second carrier of at least 1:1.

From the description and examples disclosed in the Patent, the board is satisfied that the problem defined in 8.4 above is plausibly solved. Since this has not been contested, it is unnecessary to make any more detailed statements in this connection.

Novelty and inventive step

9. The board considers that the **use** of a composition containing all the features of claim 5 of the second auxiliary request or claim 1 of the third auxiliary request in the treatment of burns or wounds is not directly and unambiguously derivable either from citation (8) or from any other **single** prior art document cited in the proceedings. The novelty of these claims which are drafted correctly in the "second or further medical use" format is therefore acknowledged.

10. The allowability of the above-mentioned claims depends, therefore, on the answer to the question whether or not an inventive step was necessary to arrive at the subject-matter of these claims when starting from a composition and its use, both known from the nearest prior art according to (8).

10.1 The range of possible carriers disclosed in the Patent includes, for example, alkylene glycols, or alkylene glycols in combination with one or more derivatives of hydroxyalkylcellulose, or alcohols such as ethanol and propanol, or glycols such as butylene or hexylene glycol, or polyols such as sorbitol, polyethylene or

polypropylene glycols, mineral oil, glycerol, or biologically acceptable hydroxyalkylcelluloses. The patent specification also contains a statement to the effect that "without limitation, other carriers known to those skilled in the art which are compatible with water and are biologically acceptable are expected to provide equivalent compositions within the scope of this invention".

10.2 A skilled person, faced with the stated problem (see 8.4 above) and seeking a solution to this problem, would have learned, for example, from citation (13) that a particularly suitable water/carrier system for topical application of ascorbic acid to burns and wounds can be obtained by mixing water with alcohol as the second carrier at a ratio of water to alcohol of at least 1:1. Alcohol is also clearly indicated within the Patent as being a carrier suitable for topical application (see page 3, lines 51-55)

10.3 Alternatively, this person would also have learned from citation (19) that a suitable water/carrier system for external application of ascorbic acid to wounds can be created by the addition of a mucopolysaccharides or polysaccharides as the second carrier suitable for topical application to an aqueous solution of ascorbic acid, the ratio of water to carrier being 100:1.

10.4 Moreover, those skilled in the art would immediately have realised from the disclosure of (1) that mixtures of water and a second carrier selected from polyethylene glycol 200, 400, 1000, 1540 and 4000, wherein the ratio of water to carrier lies in the preferred range mentioned in the Patent of 9:1 or 8:1

or 1:1, could also advantageously be used as water/carrier systems for topical application of ascorbic acid.

10.5 Finally, as admitted by appellant II itself in the Patent, any carrier known to those skilled in the art which is compatible with water and is biologically acceptable would be expected to provide equivalent compositions in accordance with the claimed invention.

10.6 As shown above, the solution to the problem underlying claim 5 of the second auxiliary request and claim 1 of the third auxiliary request is obvious from a combination of the teaching of citation (8) with the teachings of one of the citations (13), (19), or (1), or even with general specialist knowledge. Thus, neither of the above-mentioned claims involves an inventive step. Since a decision can only be taken on a request as a whole, none of the further claims of either the second or the third auxiliary request need to be examined.

11. To sum up, neither the main request of appellant II nor any of its auxiliary requests relates to a patentable invention. Thus, the appeal of **appellant II** must be dismissed, whereas the appeal of **appellant I** is clearly allowable.

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:

U. Bultmann U. Oswald