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Datasheet for the decision of 27 January 2022

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Language of the proceedings: EN

Title of invention:

Hyaluronic acid composition comprising an ascorbic acid derivative

Patent Proprietor:

Q-Med AB

Opponents:

ALLERGAN, INC.
Laboratoires Vivacy

Headword:

Hyaluronic acid composition / Q-MED AB

Relevant legal provisions:
EPC Art. 87, 88, 89, 100(a), 54, 56, 123(2), 83

Keyword:
Priority - main request and auxiliary requests 1-4 (partial priority), auxiliary request 6 (yes)
Amendments allowable - auxiliary request 6 (yes)
Sufficiency of disclosure - auxiliary request 6 (yes)
Novelty - main request (yes), auxiliary request 6 (yes)
Inventive step - main request (no), auxiliary requests 1-4 (no), auxiliary request 6 (yes)

Decisions cited:
G 0001/15, G 0002/88, G 0006/88

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Case Number: T 0747/18 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 27 January 2022

Appellant: (Patent Proprietor)	Q-Med AB Seminariegatan 21 752 28 Uppsala (SE)
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Appellant: (Opponent 1)	ALLERGAN, INC. Patent Department T2 7H 2525 Dupont Drive Irvine CA 92612-1599 (US)
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Party as of right: (Opponent 2)	Laboratoires Vivacy 44 rue Paul Valéry 75116 Paris (FR)
Representative:	Tripoz, Inès Cabinet Tripoz Le Pôle Sud 22 rue Seguin 69002 Lyon (FR)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 26 February 2018 concerning maintenance of the European Patent No. 2670447 in amended form.**

Composition of the Board:

Chairman	A. Usuelli
Members:	J. Lécaillon
	A. Jimenez

Summary of Facts and Submissions

I. European patent 2 670 447 (hereinafter "the patent") was granted on the basis of 24 claims. The independent claims of the patent as granted read as follows:

"1. Use of an ascorbic acid derivative selected from the group consisting of ascorbyl phosphates, ascorbyl sulfates and ascorbyl glycosides, in an injectable hyaluronic acid composition further comprising

- a hyaluronic acid gel and
- a therapeutically relevant concentration of a local anesthetic selected from the group consisting of amide and ester type local anesthetics or a combination thereof,

for preventing or reducing the effect of the local anesthetic on the viscosity and/or elastic modulus G' of the composition due to sterilization by heat, wherein the concentration of said ascorbic acid derivative in the composition is in the range of 0.01 to 5 mg/ml."

"8. A sterilized injectable hyaluronic acid composition comprising

- a hyaluronic acid gel,
- a therapeutically relevant concentration of a local anesthetic selected from the group consisting of amide and ester type local anesthetics or a combination thereof, and
- an ascorbic acid derivative selected from the group consisting of ascorbyl phosphates, ascorbyl sulfates and ascorbyl glycosides, in an amount

which prevents or reduces the effect on the viscosity and/or elastic modulus G' of the composition caused by the local anesthetic upon sterilization by heat, wherein the concentration of said ascorbic acid derivative in the composition is in the range of 0.01 to 5 mg/ml, and the composition has been subjected to sterilization by autoclaving at a F_0-value ≥ 4."

"15. A sterilized injectable hyaluronic acid composition as defined in any one of claims 8-14 for use as a medicament."

"16. A sterilized injectable hyaluronic acid composition as defined in any one of claims 8-14 for use in a dermatological treatment selected from the group consisting of wound healing, treatment of dry skin conditions and sun-damaged skin, treatment of hyper pigmentation disorders, treatment and prevention of hair loss, and treatment of conditions that have inflammation as a component of the disease process, such as psoriasis and asteototic eczema."

"17. A sterilized injectable hyaluronic acid composition as defined in any one of claims 8-14 for use in the treatment of a joint disorder by intraarticular injection."

"18. Cosmetic, non-medical use of a sterilized injectable acid composition as defined in any one of claims 8-14 for improving the appearance of skin, preventing and/or treating hair loss, filling wrinkles or contouring the face or body of a subject."

"21. Cosmetic, non-medical method of improving the appearance of skin, preventing and/or treating hair

loss, filling wrinkles or contouring the face or body of a subject, comprising

a) providing a sterilized injectable hyaluronic acid composition as defined in any one of claims 8-14, and
b) injecting said sterilized injectable hyaluronic acid composition into the skin of a subject."

"23. A method of manufacturing a sterilized hyaluronic acid composition comprising:

a) mixing a hyaluronic acid gel, a therapeutically relevant concentration of a local anesthetic selected from the group consisting of amide and ester type local anesthetics or a combination thereof, and an ascorbic acid derivative selected from the group consisting of ascorbyl phosphates, ascorbyl sulfates and ascorbyl glycosides, in an amount which prevents or reduces the effect on the viscosity and/or elastic modulus G' of the composition caused by the local anesthetic upon sterilization by heat, wherein the concentration of said ascorbic acid derivative in the composition is in the range of 0.01 to 5 mg/ml, and
b) subjecting the mixture to sterilization by autoclaving at a F_0-value $\geq$ 4."

II. Two oppositions were filed against the patent on the grounds that its subject-matter lacked novelty and inventive step, it was not sufficiently disclosed and it extended beyond the content of the application as originally filed.

III. The opposition division took the interlocutory decision that, on the basis of the auxiliary request 9, the

patent met the requirements of the EPC. The decision was based on the patent as granted as main request and on auxiliary requests 1-9. Auxiliary request 9 contained 15 claims. Claims 1-5 of auxiliary request 9 corresponded to granted composition claims 8-12, wherein the feature introduced by "preferably" in dependent claim 3 (corresponding to granted claim 10) was deleted. Claims 6-15 corresponded to granted claims 15-24.

IV. The decision of the opposition division, posted on 26 February 2018, cited *inter alia* the following documents:

D1: WO 2011/086458 A1
D2: WO 2012/097272 A1
D3: EP 11 153 232
D5: US 2006/122147 A1
D9: "Sodium Ascrobyl Phosphate: A Stable Vitamin C", Online Article by Sesame, 3 Nov 2010, http://www.vivawornan.net/2010/11/sodium-ascorbyl-phosphate-a-stable-vitamin-c/
D12: WO 2005/067994 A1
D14: WO 2014/032804 A1

V. The opposition division decided in particular as follows:

(a) The main request met the requirements of Article 123(2) EPC. In particular the amended features of claims 1, 8 and 23 were individually disclosed in the original application and their combinations were supported by the cross-references in the original description.

(b) The granted patent, in particular the experiments reported therein, provided sufficient disclosure of the subject-matter claimed in the main request.

(c) The subject-matter of the main request was novel.

(d) The priority claim was not valid for claims 3, 6, 7, 10, 13 and 14 and D3 (priority document) was thus relevant prior art for the assessment of novelty under Article 54(3) EPC. D3 anticipated the subject-matter of the main request as well as of auxiliary requests 1-5.

(e) Auxiliary request 6 fulfilled the requirements of Rule 80, Articles 123(2) and 123(3), 83 and 54 EPC. However the subject-matter of the use claims 1-5 of auxiliary request 6 did not involve an inventive step over D5 or D12 as closest prior art documents because the claimed effect had not been shown over the whole scope of said use claims. The same finding of lack of inventive step applied *mutatis mutandis* to auxiliary requests 7-8.

(f) Auxiliary request 9, which had been limited to composition claims, met the requirements of the EPC. In particular said auxiliary request involved an inventive step.

VI. The patent proprietor (appellant - patent proprietor) as well as opponent 1 (appellant - opponent 1) and opponent 2 lodged an appeal against the above decision of the opposition division. Opponent 2 withdrew its appeal on 11 June 2021 and is hence party to the appeal proceedings as of right (Article 107 EPC).

VII. With its statement setting out the grounds of appeal the appellant - patent proprietor defended its case on the basis of the patent as granted as the main request, and on the basis of auxiliary requests 1-9 filed during first instance proceedings and resubmitted with its reply to the opponents' statements setting out the grounds of appeal.

The content of the claims upon which the present decision is based can be illustrated as follows:

Claim 8 of auxiliary request 1 and claim 3 of auxiliary request 4 were identical to claim 10 of the main request.

Claims 8 and 10 of auxiliary request 2 corresponded to claims 8 and 10 of the main request wherein:
- claim 8 had been amended by (i) specifying that the hyaluronic acid gel is "aqueous" and comprises "2-50 mg/ml of a hyaluronic acid" and (ii) introducing the feature "the therapeutically relevant concentration of a local anesthetic is 0.5 to 10 mg/ml of lidocaine" after the definition of the acid ascorbic concentration range, and
- claim 10 had been limited to the preferred embodiment thereof by deleting the word "preferably".

Claims 6 and 8 of auxiliary request 3 were identical to claims 8 and 10 of auxiliary request 2.

Auxiliary request 6 differed from the main request in that:
- the feature "preferably at a concentration in the range of 1 to 5 mg/ml" of claims 3 and 10 of the main request (claims 3 and 8 of auxiliary request 6) had been deleted, and

- dependent claims 6, 7, 13 and 14 of the main request had been deleted.

VIII. The following item of evidence was filed by the appellant - patent proprietor with its reply to the statement setting out the grounds of appeal:

D16: 2010 US Pharmacopeia

IX. Oral proceedings were held before the Board on 27 January 2022. During oral proceedings, the appellant - patent proprietor withdrew auxiliary request 5.

X. The appellant - opponent 1 and the party as of right - opponent 2 requested that the decision under appeal be set aside and the patent be revoked.

XI. The appellant - patent proprietor requested that the decision under appeal be set aside and the patent be maintained as granted, or that the patent be maintained on the basis of the claims of one of auxiliary requests 1 to 4 and 6 to 10 filed during first instance proceedings (auxiliary requests 1-4 filed on 22 September 2016 and auxiliary requests 6-10 filed on 15 September 2017) and resubmitted with the reply to the statements setting out the grounds of appeal.

The appellant - patent proprietor further requested that the objection amounting to a new ground of opposition under Article 100 (c) EPC not be admitted into the appeal proceedings.

XII. The arguments of the appellant - patent proprietor, as far as relevant for the present decision, can be summarised as follows:

(a) The subject-matter of the claims of the main request was novel over D1, in particular as features were missing in the specific examples.

(b) The independent claims of the main request were fully entitled to priority and, according to G 1/15, claims 3, 6, 7, 10, 13 and 14 of the main request were entitled to partial priority.

(c) The subject-matter of claim 10 of the main request not entitled to priority differed from the closest prior art formulation (example 12 of D1), in that a lower concentration of ascorbic acid derivative was used, which resulted in an increased stability of the formulation. The objective technical problem resided consequently in the provision of a hyaluronic acid gel formulation having improved stability. D1 described ascorbic acid derivatives as stabilising agent and therefore taught away from reducing the concentration thereof to increase the stability of the formulation. Hence, claim 10 of the main request met the requirements of Article 56 EPC.

(d) Auxiliary requests 1-4 fulfilled the requirements of Article 56 EPC for the same reasons as the main request.

(e) Auxiliary request 6 met the requirements of Article 123(2) EPC. In particular each added feature was disclosed in the original application in a manner which was not restricted to any particular embodiment or combination with other features. The objection of the party as of right - opponent 2 concerning the dependent claims was not to be admitted.

(f) The achievement of the claimed effect, namely the reduction of the increase in viscosity/G' due to lidocaine upon sterilisation, was sufficiently disclosed in the patent in suit.

(g) The subject-matter of the claims of auxiliary request 6 was novel for the same reasons as the main request.

(h) The claimed subject-matter differed from the one of D12, which was more suitable as closest prior art than D5, in that an ascorbic acid derivative was added to the formulations. Starting from D12, the objective technical problem (as defined during oral proceeding) resided in the provision of a hyaluronic acid gel composition with reduced viscosity increase due to the local anesthetic upon heat treatment. None of the cited prior art documents suggested to add an ascorbic acid derivative to solve this problem.

XIII. The arguments of the appellant - opponent 1 and the party as of right - opponent 2, as far as relevant for the present decision, can be summarised as follows:

(a) The general disclosure of D1 as well as the specific embodiments of examples 12 and 15, anticipated the subject-matter of claim 8 of the main request. Furthermore, the use defined in claim 1 of the main request was also disclosed in D1.

(b) The main request was not entitled to priority, because the combination of features claimed and even individual features of some dependent claims were not disclosed in the priority document D3.

(c) The subject-matter of claim 10 of the main request differed from the closest prior art formulation (example 12 of D1), in that a lower concentration of ascorbic acid derivative was used. The objective technical problem resided in the provision of an alternative hyaluronic acid composition. Modifying the concentration of the ascorbic acid derivative within the generally disclosed concentration ranges thereof was a routine measure for the skilled person.

(d) Auxiliary requests 1-4 did not fulfill the requirements of Article 56 EPC for the same reasons as the main request.

(e) Auxiliary request 6 infringed Article 123(2) EPC, mainly because the combination of features claimed in the independent claims was not disclosed in the original application as such and required selections within lists.

(f) Auxiliary request 6 did not meet the requirements of Article 83 EPC. The patent in suit did not enable the skilled person to achieve the claimed effect.

(g) During oral proceedings, the appellant - opponent 1 stated that he had no objection to the novelty of auxiliary request 6. The party as of right - opponent 2 objected to the novelty of auxiliary request for the same reasons as for the main request.

(h) Both D5 and D12 could represent the closest prior art document. Starting from D12, the distinguishing

feature was the addition of an ascorbic acid derivative. No technical advantage linked thereto and relevant for the final formulation compared to the closest example of D12 had been substantiated. The objective technical problem resided in the provision of an alternative hyaluronic acid composition. The present solution was obvious in the light of D5, which disclosed the addition of ascorbic acid to formulations containing hyaluronic acid and a local anesthetic. Starting from D5, the distinguishing features were the specific choice of the ascorbic acid derivative and the amount thereof. Such modification constituted standard design optimisation which did not involve an inventive step.

Reasons for the Decision

Main request - patent as granted

2. Novelty over D1

2.1 Independent claim 8

The appellant-opponent 1 as well as the party as of right - opponent 2 argued that the subject-matter of independent claim 8 was not novel over D1, in particular over (i) the general disclosure thereof and (ii) example 12 and/or example 15 thereof.

2.1.1 General disclosure of D1

The party as of right - opponent 2 argued in the written proceedings that the general disclosure of D1 anticipated the subject-matter of claim 8 of the main request. This argument was taken up by appellant -

opponent 1 during the oral proceedings. It is based on the combination of various not interrelated passages of the description of D1. The Board observes that, even if the various elements of the present compositions may be individually generally encompassed in said passages, the description of D1 does not provide any preferred embodiment disclosing the presently claimed combination of specific features.

Concerning the specific passages cited by the appellant - opponent 1 during oral proceedings, namely paragraphs [014], [016] and [078] to [079], the Board notes that they do not directly and unambiguously disclose the present combination of features. In this context the appellant - opponent 1 brought forward that these embodiments may be combined and that the examples of D1 would disclose such a combination. The Board cannot follow this approach. The embodiments of paragraphs [014] and [016] are not disclosed in combination with those of paragraphs [078] to [079] and there is no general embodiment pointing to their combination. Furthermore paragraphs [078] to [079] do not disclose an ascorbic acid agent in individualised form but as part of a list of several antioxidants. Moreover, the presently claimed classes of ascorbic acid derivatives are not disclosed in these paragraphs. Hence, even when combining the disclosure of these paragraphs, the skilled person would not have arrived at the specific combination of hyaluronic acid, a local anesthetic and the presently claimed ascorbic acid derivatives, let alone in the presently claimed amounts. Furthermore, as detailed below the examples 12 and 15 *per se* are not novelty destroying, as further features of the present claims are not disclosed. Moreover, these examples represent merely 2 out of more than 30 examples of different compositions. These compositions contain

variable components, in particular antioxidants are not necessarily included and, when included, may be different from an ascorbic acid derivative.

Hence, the skilled person would not have directly and unambiguously derived form the overall disclosure of D1 that a sterilised combination of hyaluronic acid and a local anesthetic containing a particular amount of a given ascorbic acid derivative was particularly preferred.

2.1.2 Specific examples of D1 (example 12 and 15)

(a) Example 12

Regarding example 12 of D1, as argued by the appellant - patent proprietor, the concentration of ascorbic acid derivative in said example (0.6% w/w corresponding to 6 mg/ml) is outside the presently claimed range, so that it does not anticipate the subject-matter of claim 8 of the main request.

(b) Example 15

In so far as example 15 of D1 is concerned, the Board is of the opinion that there is no direct and unambiguous disclosure of a heat sterilization step in example 15 . As explained in paragraph [0007] of the patent the heat sterilization imparts to the composition particular properties which distinguish it from a non sterilised composition.

The argument provided by the appellant-opponent 1 and the party as of right - opponent 2 based on the fact that, D1 generally relates to heat sterilization by autoclaving under conditions

falling under the present claims and that such conditions have been used in other examples, is not convincing. Example 15 provides neither an explicit disclosure of a heat sterilization step nor an indication to combine this example with any other example or other part of D1. The further arguments of the party as of right - opponent 2 relating to Figure 7 cannot be followed either. The fact that the composition of example 15 contains as hyaluronic acid gel a commercial sterilised gel (Juvederm® Ultra, see Figure 7) does indeed not imply that the final composition of example 15 is also sterilised. While the slight initial difference in rheological properties in Figure 7 could indicate that a sterilization may have been performed there is no evidence that this was indeed the case. Such a conclusion remains speculative.

Furthermore the appellant - opponent 1 brought forward during oral proceedings that the treatment with H_2O_2 performed in example 15 would result in a sterilised product since H_2O_2 is a known sterilisation agent. According to the appellant - opponent 1, there would be no difference between a heat sterilised composition and a composition sterilised with H_2O_2, so that the composition of example 15 of D1 anticipated the subject-matter of present product-be-process claim 8. The Board cannot share this view. Example 15 merely mentions the testing of the resistance of the composition to oxidative degradation by the addition of 1/7 ratio of H_2O_2 30% on its surface and does not refer to sterilisation. The appellant - opponent 1 did not provide any evidence in support of the assertion that this treatment would amount to a sterilisation of the composition thanks to permeation of H_2O_2

through the gel. Moreover, there is also no evidence that, in the present case, a H_2O_2 treatment and a heat sterilisation would lead to products having the same properties. It cannot therefore be concluded that the composition treated with H_2O_2 in example 15 has the same properties than a heat sterilised composition according to claim 8.

2.2 Independent claim 1

2.2.1 During oral proceedings the appellant - opponent 1 stated that he had no objection regarding the novelty of claim 1 of the main request over D1.

2.2.2 During the written proceedings the party as of right - opponent 2 also objected to the novelty of claim 1 because the claimed use was allegedly disclosed in claim 1 and in paragraphs [009], [0010], [0014], [0125]-[0128] and [0157] of D1. These passages are concerned with the influence of ascorbic acid on the stability of sterilized hyaluronic gels. The party as of right - opponent 2 has not established that it can be directly and unambiguously derived from said passages that ascorbic acid derivatives reduce the effect of the local anesthetic on viscosity/G' value due to sterilization by heat. In line with the general principles established in G 2/88 and G 6/88, the presently claimed second non-medical use cannot thus be considered as anticipated by D1.

2.3 Accordingly the subject-matter of the main request is novel over D1 (Article 100(a) EPC in combination with Article 54 EPC).

3. Inventive step

3.1 Priority right (Articles 87, 88 and 89 EPC) and relevance of D1 for the assessment of inventive step

3.1.1 As detailed by the appellant - patent proprietor, the priority document (published as D3) discloses the subject-matter of the present independent claims in a similar manner as the present original application, namely in three independent claims (claims 1, 15 and 16 of D3) and in individualised separated embodiments of the description corresponding to the following features of claims 1 and 8:

(i) the ascorbic acid derivatives is "selected from the group consisting of ascorbyl phosphates, ascorbyl sulfates and ascorbyl glycosides" (see page 10 lines 1 to 4 of D3),

(ii) Hyaluronic acid is in the form of a "gel" (see page 5 lines 7 to 8 of D3),

(iii) the anesthetic is present in "a therapeutically relevant concentration" (see page 10 lines 33 to 35 of D3),

(iv) "the concentration of said ascorbic acid derivative in the composition is in the range of 0.01 to 5 mg/ml" (see page 11 lines 6 to 24 of D3), and

(v) the composition is "sterilized" and "has been subjected to sterilization by autoclaving at a F_0-value ≥ 4" (see items 24, 33 as well as page 11 lines 25 to 34 and page 14 lines 26 to 28 of D3).

Additionally the specification of the amount of ascorbic acid derivative being "an amount which prevents or reduces the effect on the viscosity and/or elastic modulus G' of the composition cause by the local anesthetic upon sterilization by heat"

in present claims 8 and 23 is derivable from the passage on page 2 lines 21-26 together with claim 16 of D3.

The Board observes that, in said passages, these features were generally described as individual embodiments of each element of the composition/use, *i.e.* these features do not appear to be inextricably linked to any other feature. Furthermore, as argued by the appellant - patent proprietor, D3 includes numerous examples disclosing combinations of these features, thus providing a pointer towards the claimed combination of features. The combination of these features is therefore directly and unambiguously derivable from the priority application. It follows, that, contrary to the view of the appellant - opponent 1 and the party as of right - opponent 2, these features and their combination in the present claims do not constitute selections within one (or more) list(s).

Accordingly, the subject-matter of the independent claims of the main request are directly and unambiguously disclosed in the priority document D3.

3.1.2 However, the features of dependent claims 6, 7, 13 and 14 as well as the features of claims 3 and 10 introduced by "preferably" are, as stated by the party as of right - opponent 2, not disclosed in D3. The Board is nevertheless of the opinion that, applying the mental fiction of partial priority according to G 1/15, the parts of claims 3, 6, 7, 10, 13 and 14 corresponding to the specific examples of D3 are individually entitled to priority because:
- they are encompassed by said claims, and
- they constitute alternative subject-matter by virtue of a generic "OR" claim.

The Board cannot therefore follow the approach of the opposition division which stated that the compositions of the examples of D3 are more specific than the claimed range so that an intermediate generalisation of said examples would be needed to acknowledge partial priority. Following G 1/15, partial priority is acknowledged only for the very specific exemplified compositions which fall under the scope of the present claims. The fact that other features, such as specific F_0-values, pH and gel concentrations, are not identified in the claims does not prevent from mentally identifying such compositions within the scope of the claims of the main request. The mental fiction of partial priority according to G 1/15 applies only to said very specific embodiments but it cannot be denied.

Therefore for any part of claims 3, 6, 7, 10, 13 and 14 disclosed in D3, the priority is valid. The remaining parts of claims 3, 6, 7, 10, 13 and 14 not disclosed in D3 are not entitled to priority.

3.1.3 The appellant - opponent 1 raised an objection of lack of inventive step based on D1 as closest prior art. This document was published during the present priority year and forms part of the prior art according to Article 54(2) EPC for the parts of the claims not entitled to priority, *i.e.* parts of claims 3, 6, 7, 10, 13 and 14.

3.2 Inventive step of claim 10 starting from D1 as closest prior art

3.2.1 The patent in suit relates to injectable hyaluronic acid compositions comprising lidocaine, wherein the effect of lidocaine on the rheology of the composition

(viscosity/G' value) upon heat sterilization is prevented or reduced through the presence of an ascorbic acid derivative.

3.2.2 In agreement with both appellants, the Board considers D1 to represent the closest prior art.

D1 concerns the stability of compositions comprising hyaluronic acid gel upon heat treatment and suggests the addition of ascorbic acid derivatives for this purpose. Furthermore compositions comprising hyaluronic acid and a local anesthetic are also generally described and examples of compositions with hyaluronic acid, lidocaine and ascorbic acid glucoside are disclosed. Although D1 does not mention the effect of lidocaine on the rheology of the composition, it underlines the importance of viscosity on injection though thin needles.

3.2.3 It was undisputed that the claimed compositions differ from example 12 of D1, considered by both appellants as the closest embodiment of D1, in the concentration of ascorbic acid derivative.

3.2.4 During oral proceedings the appellant - patent proprietor argued that, as evidenced by example 22 of the patent in suit, the technical effect linked to the claimed concentration range of ascorbic acid derivative would be an increased stability. The Board observes that example 22 provides a comparison between three specific formulations:
- one not containing any ascorbic acid derivative (formulation 22a, not according to the claims),
- one containing 0.17 mg/ml ascorbyl glucoside (formulation 22b, according to the claims), and

- one containing 8.0 mg/ml ascorbyl glucoside (formulation 22c, not according to the claims). According to the conclusion drawn in paragraph [0176] based on the results of Figure 22, formulation 22b has indeed an improved stability compared to formulation 22c. However this does not constitute a comparison with the closest prior art embodiment of D1, which discloses a formulation containing 6 mg/ml of ascorbyl glucoside (see example 12 of D1). While the results of example 22 of the patent in suit may, as argued by the appellant - patent proprietor, provide some trend regarding the effect of the ascorbyl glucoside concentration on the stability of the formulation, they do not allow to conclude that the presently claimed range of 0.01 to 5 mg/ml provides any particular effect compared to a formulation containing 6 mg/ml of ascorbic acid derivative, such as example 12 of D1. The concentration of the comparative formulation 22c (8 mg/ml) is indeed very remote from the the upper-end point of the claimed range (5 mg/ml) as well as from the concentration of the closest prior art formulation (6 mg/ml). Finally, the Board observes that D1 discloses ascorbic acid derivatives as stabilising agents. In the absence of experimental data substantiating the choice of the claimed upper-end point, an improved stability cannot be acknowledged for the claimed range over the closest prior art.

3.2.5 The objective technical problem can thus only be formulated as the provision of an alternative sterilized injectable hyaluronic acid formulation containing a local anesthetic and an ascorbic acid derivative.

3.2.6 Starting from example 12 of D1, modifying the concentration of ascorbyl glucoside forms part of the

routine work for a skilled person willing to solve the problem posed. Furthermore, as wide ranges for the amount of antioxidant agent are disclosed in paragraph [0079] and a lower concentration of ascorbyl derivative was used in D1 (see example 15), modifying the example 12 by using such a lower concentration would have appeared an obvious option to the skilled person. Accordingly, in the absence of any particular effect linked to the claimed ascorbic acid derivative concentration, no inventive step can be acknowledged for the subject-matter of present claim 10 not entitled to priority.

3.2.7 Consequently, granted claim 10 does not comply with the requirements of Article 56 EPC and the ground of opposition under Article 100(a) EPC prejudices the maintenance of the granted patent.

Auxiliary requests 1-4

4. Inventive step

4.1 The Board observes that claim 8 of auxiliary request 1 and claim 3 of auxiliary request 4 are identical to claim 10 of the main request, whereby the independent claim to which these dependent claims refer remains unchanged compared to the main request.

Furthermore, claim 10 of auxiliary request 2 and claim 8 of auxiliary request 3 are limited to the preferred embodiment of claim 10 of the main request (*i.e.* the subject-matter not entitled to priority), whereby the further features introduced in the independent claim to which these dependent claims refer are already disclosed in D1, as follows:

- "aqueous" hyaluronic acid gel, see *e.g.* claim 1 of D1, and
- "2-50 mg/ml of a hyaluronic acid", see *e.g.* paragraph [017] of D1.

No particular effect linked to these features was furthermore identified. These features cannot therefore contribute to the provision of an inventive step.

4.2 The appellant - patent proprietor did furthermore not provide any specific argument why auxiliary requests 1 to 4 would overcome the lack of inventive step finding for the main request.

4.3 Accordingly, the reasoning developed for claim 10 of the main request under point 3. applies *mutatis mutandis* to the corresponding claims of auxiliary requests 1 to 4. Hence, auxiliary requests 1 to 4 do not meet the requirements of Article 56 EPC.

Auxiliary request 6

5. Amendments - Article 123(2) EPC

5.1 Claim 1 of auxiliary request 6 corresponds to original claim 39 wherein the following features were added:

(i) the ascorbic acid derivatives is "selected from the group consisting of ascorbyl phosphates, ascorbyl sulfates and ascorbyl glycosides",
(ii) Hyaluronic acid is in the form of a "gel",
(iii) the anesthetic is present in "a therapeutically relevant concentration", and
(iv) "the concentration of said ascorbic acid derivative in the composition is in the range of 0.01 to 5 mg/ml".

Claim 6 of auxiliary request 6 corresponds to original claim 1 wherein the above features (i)-(iv) were added as well as the following feature:

(v) the composition is "sterilized" and "has been subjected to sterilization by autoclaving at a F_0-value ≥ 4".

Claim 19 of auxiliary request 6 corresponds to original claim 36 and has been amended in the same manner as claim 6.

5.2 These amended features (i)-(v) are disclosed in the original application inter alia as follows:

(i) original page 12 lines 14-16,
(ii) original page 5 lines 1-2,
(iii) original page 8 lines 24-26,
(iv) original page 13 lines 19-26,
(v) original page 15 lines 11-13 or original page18 lines 24-25 or original claims 26 and 38.

The triple combination of agents was already disclosed in the original claims together with the heat sterilisation aspect. In the above mentioned passages of the original description, the features are furthermore generally described as individual embodiments of each element of the composition/use, *i.e.* these features do not appear to be inextricably linked to any other feature. Furthermore, as argued by the appellant - patent proprietor, the original application includes numerous examples disclosing combinations of these features, thus providing a pointer towards the claimed combination of features. Any combination of these features is therefore directly and unambiguously derivable from the original application. It follows, that, contrary to the view of

the appellant - opponent 1 and the party as of right - opponent 2, the amended features do not appear to constitute selections within one (or more) list(s).

5.3 During the writing proceedings, the party as of right - opponent 2 additionally argued that the concentration of the ascorbic acid derivative may vary depending on the type of derivative and that the skilled person would have understood that ascorbyl phosphates were to be used in a different concentration range than the one presently claimed. The claimed range would thus not have been originally disclosed for all the claimed ascorbic acid derivatives.

The Board notes that the presently claimed broader range for the concentration of ascorbic acid derivative as well as ascorbyl phosphates as one preferred class of ascorbic acid derivatives are generally described in the original application. The fact that another narrower preferred sub-range for ascorbyl phosphates is further described does not change the fact that the broader range is disclosed in general for ascorbic acid derivatives and thus also for ascorbyl phosphates. Moreover the achievement of any effect is not an issue of compliance with the requirements of Article 123(2) EPC.

5.4 During the written proceedings, the party as of right - opponent 2 also objected that the dependent claims would introduce further arbitrary choices and thus also infringe Article 123(2) EPC. The appellant - patent proprietor argued that, as the dependent claims were not objected to under Article 100(c) EPC in opposition, the present objection of the party as of right - opponent 2 amounted to the introduction of a new ground

for opposition and should not be admitted into the appeal proceedings.

The Board observes that, in its notice of opposition, the appellant - opponent 1 explicitly stated that the dependent claims of the main request did not meet the requirements of Article 123(2) EPC. It follows that the ground for opposition under Article 100(c) EPC was actually raised in first instance for the present dependent claims. The Board considers nevertheless that a similar reasoning as the one made for the independent claims applies to the subject-matter of the dependent claims, which is thus considered to be directly and unambiguously derivable from the original application

5.5 As a result, auxiliary request 6 complies with the requirements of Article 123(2) EPC.

6. Sufficiency of disclosure

6.1 During oral proceedings, the appellant - opponent 1 took up the objection raised during the written proceedings by the party as of right - opponent 2. These two parties contested that the patent taught how to achieve the effect claimed in the independent claims. According to the submissions of appellant - opponent 1, the viscosity and/or elastic modulus G' increase which occurs upon heat treatment of a composition containing hyaluronic acid and a local anesthetic would be due to some interaction between both active agents. It follows that, to achieve the claimed effect, the ascorbic acid derivative would have to interfere in the interaction between local anesthetic and hyaluronic acid. As a result, the obtained viscosity and/or G' values in the presence of the claimed ascorbic acid derivative could at best be

as low as in the absence of lidocaine. However some compositions of the examples of the patent in suit (compositions 1d, 1g, 2c, 3c, 3d, 6c and 14c of examples 1, 2, 3, 6 and 14 referred to by the party as of right - opponent 2 and example 1 referred to by the appellant - opponent 1) would lead to viscosity/G' values even below the one of the corresponding compositions in the absence of local anesthetic and ascorbic acid derivative. This would substantiate that the ascorbic acid derivative had actually a "competitive" role by directly lowering the viscosity/ G' values independently of the action of the local anesthetic and thus no interfering role. The claimed effect would thus not be achieved.

6.2 The Board cannot follow this approach. The claims specify that the ascorbic acid derivative prevents or reduces "the effect on the viscosity and/or elastic modulus G' of the composition caused by the local anesthetic upon sterilization by heat" (emphasis added). It is undisputed that the mentioned effect caused by the local anesthetic is an increase of the viscosity and/or G' values. It follows that the claims merely define that the ascorbic acid has to reduce or prevent said increase in the viscosity and/or G' values. The Board cannot recognise in the wording used in the claims any limitation regarding the mechanism by which this is achieved. The interpretation made by the appellant - opponent 1 goes beyond the wording of the present claims and cannot be followed. As argued by the appellant - patent proprietor, the patent in suit provides several examples wherein the viscosity/G' values are reduced in the presence of various ascorbic acid derivatives for compositions containing different local anesthetics (see *inter alia* formulations 1c and 1f in example 1 and formulation 10c in example 10). The

patent thus provides ample examples, wherein the claimed effect (*i.e.* reduction of the viscosity/G' values) is achieved. The fact that, in individual cases, compositions containing an ascorbic acid derivative at a concentration within the claimed range might have viscosity/G' values even below the one of the corresponding compositions in the absence of local anesthetic and ascorbic acid (*i.e.* going beyond the claimed effect) is not *per se* a reason to deny sufficiency of disclosure. Furthermore, as explained by the appellant - patent proprietor during the oral proceedings, the skilled person would have learned from the examples of the patent (in particular example 1 and the results obtained for formulation 1c compared to formulation 1d), that by reducing the concentration of ascorbic acid derivative the reduction of viscosity/G' values can be lowered. The Board considers therefore that the patent in suit provides sufficient information to achieve the claimed effect.

6.3 Thus, auxiliary request 6 complies with the requirements of Article 83 EPC.

7. Novelty

7.1 During oral proceedings, the appellant - opponent 1 stated that, in view of the conclusion of the Board regarding the priority issue, they had no novelty attack against auxiliary request 6.

7.2 Concerning the objections of lack of novelty raised by the party as of right - opponent 2 during the written proceedings, the Board observes the following:
- the reasoning developed under point 2. regarding novelty over D1 for the main request applies equally to auxiliary request 6,

- the passages of D2 relied upon by the party as of right - opponent 2 are the same as those of D1 (from which D2 claims priority), so that the same reasoning also applies over D2, and
- the claims of auxiliary request 6 were limited to subject-matter entitled to priority (see point 3.1), so that D3 does not form part of prior art relevant to the assessment of novelty.

7.3 Accordingly, auxiliary request 6 meets the requirements of Article 54 EPC.

8. Inventive step

8.1 The claims of auxiliary request 6 were limited to subject-matter entitled to priority (see points VII and 3.1), so that D1 no longer forms part of prior art relevant to the assessment of inventive step. Either D5 or D12 was considered to represent the closest prior art by the parties.

The purpose of the patent in suit is as detailed under point 3.2.1.

Both D12 and D5 relate to injectable formulations containing hyaluronic acid and a local anesthetic. The Board considers that D12 has more features in common with the claimed subject-matter than D5. In particular, the features relating to a hyaluronic acid gel and heat sterilisation, which are disclosed in D12 (see *e.g.* examples 12 and 21), are not disclosed in D5. In this context, the Board notes that:

- the reference to a gel among various final galenic formulation types in paragraph [0015] of D5 cannot be understood as the disclosure of a hyaluronic gel within the final composition, and

- even if it may be implicit that the final compositions of D5 would have to be sterilised before any medical application thereof, it remains that the rheological properties of the compositions upon heat sterilisation are not an issue considered in D5.

Furthermore, while the possible addition of ascorbic acid derivative as radical interceptor agent is generally mentioned in D5, D5 does not disclose any preferred embodiment or specific example actually containing an ascorbic acid derivative. D5 does therefore not disclose any specific embodiment structurally closer to the presently claimed combinations than D12, which does indeed not disclose the addition of any ascorbic acid derivative. Finally, no effect of either lidocaine or ascorbic acid derivative on the rheological properties is identified in D5. On the other hand, D12 describes the effect of addition of lidocaine on G' upon sterilization of compositions comprising hyaluronic acid gel particles (see example 21 and Figure 7) and generally mentions the issue related to a too high viscosity of hyaluronic acid compositions for injection through thin needles (see page 2, first paragraph). Thus D12 relates to a similar issue as the one underlying the presently claimed subject-matter.

Hence, the Board considers that D12 represents the closest prior art.

8.2 During oral proceedings, the attending parties agreed that the closest embodiment of D12 was the composition of example 21. It was also undisputed that the present compositions differ from the one of this example in that they contain a given ascorbic acid derivative.

8.3 The main point of dispute concerned the presence of a technical effect linked to this distinguishing feature compared to the closest prior art and in its occurrence over the whole scope of the claims.

The Board notes that the experimental data provided in the patent in suit substantiate that the addition of the present ascorbic acid derivatives leads to a reduction of the viscosity/G' increase upon sterilization due to the local anesthetic.

Moreover, this effect is actually part of the claims, so that it is *de facto* achieved by compositions falling under the claims (compositions not achieving said effect would not fall under the claims). Regarding the data of table 6 of D14 cited by the opposition division and the party as of right - opponent 2, the Board considers that they are not sufficient to throw doubts on the results of the patent in suit because:

- as argued by the appellant - patent proprietor, D14 itself mentions that the results in table 6 differ from the knowledge from the prior art, and
- the argument of the appellant - patent proprietor relating to variable pH conditions amongst the compositions of Table 6 is credible, so that the comparison of the results within the table 6 is not meaningful.

In this context, the appellant - opponent 1 argued that, to be taken into account, the effect must be one of the final product. The effect of ascorbic acid derivative would only be relevant in the preparation of the final compositions and would not have a relevance for the final compositions. This argument is not convincing. The reduction of the viscosity/G' in comparison to compositions not containing any ascorbic

acid (such as the closest prior art composition) is indeed relevant for the final composition as it is credible that it will facilitate the injection of the compositions through fine needles. Finally the fact that the claims do not define the viscosity of the final composition, *i.e.* the level of the effect achieved by the addition of the ascorbic acid derivative, is irrelevant for the assessment of inventive step in the present case. The reduction of the viscosity/G' value of the final composition in comparison to the closest prior art composition is *per se* advantageous, independently of its level.

8.4 It follows that, starting from D12, the objective technical problem resides in the provision of further injectable compositions comprising a hyaluronic acid gel and a local anesthetic with reduced viscosity/G' upon heat sterilisation (independent claim 6) as well as a method to achieve these rheological properties (independent claim 1).

8.5 D12 does not teach to compensate for the increase in G’ due to lidocaine in any manner. D5 mentions the addition of ascorbic acid as radical interceptor agents but does not consider any effect on rheological properties of the compositions. The skilled person would therefore not have found in D12 whether alone or in combination with D5 an incentive to add an ascorbic acid derivative to the present compositions to solve the problem posed.

During the written proceedings, the party as of right - opponent 2 also combined the teachings of D12 with D9. As explained by the appellant - patent proprietor, the skilled person would not have combined D9 with D12 because D9 is a beauty blog focusing on skin care and

merely mentions sodium ascorbyl phosphate as antioxidant and collagen stimulator. D9 does not relate to hyaluronic acid compositions let alone injectable, sterilised ones. Even if the skilled person would have combined the teachings of D9 with D12, D9 does not provide any hint towards any effect on the viscosity of a hyaluronic acid composition.

Hence the claimed compositions as well as their preparation and the cosmetic and medical uses thereof are inventive. Furthermore, for the same reasons, the use of an ascorbic acid derivative to reduce the viscosity/G' increase due to lidocaine upon heat sterilisation is not rendered obvious by the teachings of the documents cited by the parties in the context of inventive step.

8.6 The Board finally notes that, even when starting from D5 as the closest prior art, the similar conclusion would be reached. The distinguishing feature versus the closest specific embodiments of D5, *i.e.* the examples thereof, would still be the addition of ascorbic acid. The same reasoning as developed above under 8.3 to 8.5 would thus apply.

8.7 Accordingly, auxiliary request 6 fulfills the requirements of Article 56 EPC.

Order

For these reasons it is decided that:

The decision under appeal is set aside

The case is remitted to the opposition division with the order to maintain the patent on the basis of the claims of auxiliary request 6 filed by the appellant - patent proprietor with the reply to the statement of grounds of appeal and a description to be adapted thereto.

The Registrar: The Chairman:

B. Atienza Vivancos A. Usuelli

Decision electronically authenticated