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Datasheet for the decision of 25 March 2022

Case Number: T 3109/19 - 3.3.07

Application Number: 10726239.6

Publication Number: 2429486

IPC: A61K8/73, A61K31/738, A61Q19/08, C08J3/24, A61J1/10

Language of the proceedings: EN

Title of invention:
PROCESS FOR PREPARING A CROSSLINKED GEL

Patent Proprietor:
Teoxane

Opponent:
Laboratoires Fill-Med Manufacturing/Laboratoires Fill-Med

Headword:
Crosslinked gel/TEOXANE

Relevant legal provisions:
EPC Art. 123(2), 83, 54, 56, 113(1)
RPBA Art. 12(4)
RPBA 2020 Art. 12(4), 11

Keyword:

Amendments - allowable (yes)
Sufficiency of disclosure - (yes)
Novelty - (yes)
Inventive step - closest prior art - non-obvious modification
Right to be heard - violation (no)
Late filed evidence and request - submitted with the statement of grounds of appeal
Late-filed evidence - submitted with the reply to the appeal
Amendment to case
Remittal - (no)
Postponement decision pending G 2/21 - (no)

Decisions cited:

T 0116/18

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Case Number: T 3109/19 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 25 March 2022

Appellant: (Patent Proprietor)	Teoxane Les Charmilles Rue de Lyon 105 1203 Geneva (CH)
Representative:	Nony 11 rue Saint-Georges 75009 Paris (FR)
Respondent: (Opponent)	Laboratoires Fill-Med Manufacturing/Laboratoires Fill-Med Bd Paepsem 18/2-4 rue de Lisbonne 1070 Anderlecht/75008 Paris (BE)
Representative:	Bandpay & Greuter 30, rue Notre-Dame des Victoires 75002 Paris (FR)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 7 October 2019 revoking European patent No. 2429486 pursuant to Article 101(3)(b) EPC.**

Composition of the Board:

Chairman	A. Usuelli
Members:	M. Steendijk
	L. Basterreix

Summary of Facts and Submissions

I. European patent 2 429 486 ("the patent") was granted on the basis of fifteen claims.

Independent claim 1 as granted related to

"Process for preparing a crosslinked gel of at least one polysaccharide or one of its salts, comprising at least the steps that consist in:
a) providing an aqueous medium containing said polysaccharide,
b) forming a homogeneous gel from the medium from step a),
c) bringing the gel obtained in step b) into contact with an effective amount of at least one crosslinking agent;
d) crosslinking said mixture formed in step c); and
e) recovering said crosslinked hydrogel,
wherein
- at least said steps a) to d) are carried out within a hermetic cavity delimited at least partially by a deformable wall, said cavity being made within a deformable pouch, the mixture present in the cavity being exposed, in step d), to conditions conducive to crosslinking;
- the homogenization, considered in step b) is carried out by optionally successive, mechanical deformations of the outer face of the deformable wall or of the pouch."

II. The patent was opposed on the grounds that its subject-matter lacked novelty and inventive step, that the claimed invention was not sufficiently disclosed and

that the patent comprised subject-matter extending beyond the content of the application as filed.

The appeal was filed by the patent proprietor against the decision of the opposition division to revoke the patent.

The decision was based on the appellant's main request and auxiliary requests 1-3 filed on 5 July 2019 and auxiliary requests 4-7 filed on 3 September 2019.

III. In its decision the opposition division cited *inter alia* the following documents:

D1 : EP 1818344 A1
D2 : US 2003/0148995 A1
D3 : US 2005/0142152 A1
D4 : US 2005/0281880 A1
D5 : WO 2008/068297 A1
D6 : WO 00/15328 A1
D7 : DE 4014051 A1
D8 : DE 102004021731 A1
D9 : US 5618105
D10 : EP 0695575 B1
D11 : FR 2152618
D12 : Experimental report filed 15 May 2018
D13 : Experimental report filed 6 December 2018
D16 : Experimental report filed 11 June 2019
D17 : Experimental report filed 5 July 2019
D18 : Experimental report filed 20 August 2019

IV. The opposition division came to the following conclusions:

(a) Claim 1 of the main request, which corresponded to claim 1 as granted, defined a process for preparing

a crosslinked gel of a polysaccharide based on independent claim 1 as filed, which defined the formation of the crosslinked gel in a hermetic cavity delimited at least partially by a deformable wall, and dependent claim 6 as filed, which defined that this cavity was made within a deformable pouch. Claim 1 of the main request further defined homogenisation of the polysaccharide in an aqueous medium by mechanical deformations of the outer face of the deformable wall or the pouch as described on page 9 lines 23-30 of the application as filed. Any incompatibility of the definition of a partially deformable cavity with the definition of the pouch, which according to page 5 lines 23-30 of the original description was entirely deformable, concerned at most an issue of clarity. The degree of deformability to allow homogenization as described on page 9 lines 23-30 was implicitly defined in claim 1 of the main request.

Dependent claim 14 of the main request defined the homogenization to be carried out by palpitation followed by use of a mechanical device or by using such means alternately in line with page 10 lines 20-31 of the original description. The defined manual palpitation resulted in mechanical deformations of the pouch and was thus compatible with the definition of the deformation in claim 1.

Claims 1 and 14 of the main request therefore complied with the provision of Article 123(2) EPC.

Dependent claim 13 of the main request defined the homogenization with a system of side-by-side blades pressing alternately the deformable wall back and forth as described on page 10 lines 2-5 of the

original description. This passage referred to the "paddle mill" type device mentioned on page 9 line 31 to page 10 line 1, from which the feature of claim 13 could not be isolated.

Claim 13 of the main request therefore contravened Article 123(2) EPC.

(b) Auxiliary request 1, which corresponded to the main request except for the deletion of claim 13, complied with the provision of Article 123(2) EPC.

The process as defined in claim 1 of auxiliary request 1 was new over the teaching in document D1, because it involved homogenization prior to contacting the gel with a crosslinking agent, whereas in the process of document D1 the crosslinking agent was mixed with the hyaluronic acid prior to gel formation.

Documents D1-D5 all concerned the preparation of hydrogels for injection. Document D1 represented the closest prior art as it shared the most relevant technical features with the claimed subject-matter, including the use of a deformable bag as described in its examples 4-1 and 4-2.

No convincing evidence of any advantage of the defined homogenization prior to the crosslinking had been presented. The results reported in examples 1-3 of the patent and in documents D12 and D13 (test 1) did not involve a comparison with the process of examples 4-1 and 4-2 of document D1. Documents D13 (test 2), D16, D17 and D18 presented contradictory results. In view of these contradictory results it could not be concluded

that the claimed process generally provided any advantage over the process of document D1 in the preparation of a hyaluronic acid gel, let alone in the preparation of gels of any type of polysaccharide.

Merely as an alternative process for preparing a crosslinked polysaccharide gel the claimed process would be obvious to the skilled person, because homogenization to form a gel prior to crosslinking represented a common design procedure as evidenced by documents D3-D5.

The subject-matter defined according to auxiliary request 1 therefore lacked an inventive step.

(c) The amendments in accordance with auxiliary requests 1-7 were not suitable to support an inventive step.

V. The following additional documents were submitted during the appeal procedure:

D18a: Addendum to report D18
D19: TEOXANE "Experimental report n°3"
D20 : Experimental report "Technical effect of pre-homogenization of NaHA within a deformable pouch before addition of the crosslinking agent".

Document D19 was filed by the appellant with the statement of grounds of appeal. Documents D18a and D20 were filed by the respondents (opponents) with the reply to the appeal.

The appellant further presented data regarding the variation in elastic modulus between different batches

of commercially available products from FILORGA in its letter of 15 October 2020 (see page 6).

VI. With the statement of grounds of appeal the appellant filed a new main request and auxiliary requests 1-6.

Claim 1 of this main request corresponds to claim 1 of the patent as granted except for the definition of the following additional feature:

"wherein the polysaccharide is hyaluronic acid or one of its salts."

Dependent claim 12 of the main request further defined the process of claim 1 by the feature:

"wherein said homogenization of the step b) is carried out by virtue of a system of two blades side-by-side which alternately press the deformable wall or at least one of the deformable walls following a back and forth motion."

Dependent claim 13 of the main request further defined the process of claim 1 by the feature:

"wherein said homogenization of the step b) is carried out firstly by palpation, then using a mechanical device, or by using these homogenization means alternately."

VII. Oral proceedings were held on 25 March 2022 by videoconference.

VIII. The arguments of the appellant relevant to the present decision are summarized as follows:

(a) Admission of evidence

Document D18 was filed only 17 days prior to the oral proceedings before the opposition division and well after the time limit for further written submissions set under Rule 116 EPC. This left no opportunity to challenge the content of document D18, which should therefore not have been admitted.

Document D19 should be admitted as a legitimate response to the decision under appeal relying on document D18.

Documents D18a and D20 were only filed in response to the filing of document D19 and should not be admitted if document D19 were not admitted.

(b) Right to be heard / Request for remittal

The opposition division violated in its decision the appellant's right to be heard by admitting the late filed document D18 and considering that without a repeat of the experiment the appellant had not shown that the claimed method leads to the advantageous effects mentioned in the patent. Following the filing of document D18 only 17 days prior to the oral proceedings before the opposition division it was evidently impossible for the appellant to provide any repeat of the experiment to contest the results reported in document D18.

The opposition division had furthermore not taken an essential difference between the claimed process and the teaching of document D1 into account, namely the homogenisation by mechanical instead of manual deformation of the pouch. Remittal to the

first instance for a renewed debate on inventive step allowed for due assessment of inventive step by two instances.

(c) Request for suspension pending G 2/21

The questions in the referral pending as G 2/21 were not pertinent to the present appeal and did not justify any suspension of the appeal proceedings.

(d) Admission main request

The restriction of claim 1 of the main request to a process involving hyaluronic acid was a justified response to the decision under appeal.

(e) Article 123(2)

Claim 1 of the main request was based on the original claims 1, 6 and 10 in combination with the definition of homogenisation by mechanical deformations described on page 9, lines 23-26 of the application as filed.

Claim 12 was based on page 10 lines 2-5 of the application as filed. The described system of two blades was not restricted to the "paddle mill" type device, which was only described in the preceding passage as an example.

Claim 13 of the main request was based on page 10, lines 29-31, where the homogenisation by combination of manual palpitation and use of a mechanical device was described.

(f) Sufficiency

The respondents' argument regarding the requirement of sufficiency was not to be admitted, because it was first introduced during the appeal proceedings and did not respond to the findings in the decision under appeal.

The argument lacked merit in substance taking account of the examples in the patent.

(g) Novelty

Document D1 described the addition of the hyaluronic acid to the crosslinking agent prior to any homogenisation. In contrast, claim 1 required in step b) homogenisation followed by the addition of a crosslinking agent in step c).

(h) Inventive step

The patent aimed at providing crosslinked gels with improved homogeneity and consequently improved injectability with respect to conventionally prepared gels. Document D2 represented the closest prior art, as it equally aimed at providing hydrogels devoid of flakes and local overcrosslinking having optimized injectability. Documents D1 and D3-5 did not address the problem of injectability.

The claimed process differed from the conventional type of process described in documents D2-D5 in the use of a pouch for the homogenisation and the crosslinking. The experimental results reported in the patent, in particular figures 5-7, demonstrated

that the use of a pouch allowed for the preparation of gels with improved injectability. This was confirmed by the experiments reported in document D13 and not effectively challenged by the experimental results reported in document D12. Document D1 described a process in which the hyaluronic acid and a crosslinking agent were combined and gently mixed in a pouch prior to gel formation. The process of document D1 involving gentle mixing without prior gel formation differed critically from the conventional type of process involving prior gel formation described in documents D2-D5, which was according to document D2 at risk of local overcrosslinking and flake formation and which required according to document D3 vigorous agitation after gel formation for the mixing with the crosslinking agent. Documents D6-D11 were of no relevance, as these documents did not relate to the problem of providing homogenous gels of crosslinked hyaluronic acid. The prior art did therefore not suggest to modify the conventional type of process of documents D2-D5 by carrying it out in a pouch as solution to the problem of providing an alternative, let alone to the problem of improving homogeneity and injectability.

The claimed process differed from the process described in document D1 in that it required homogenisation and gel formation of the hyaluronic acid prior to crosslinking and involved mechanical instead of manual homogenisation. The experimental results reported in the patent indicated that the claimed process using a pouch allowed for the preparation of gels with a favourable injectability profile, which was confirmed by the experimental

data in documents D13, D17 and D19. This was not effectively challenged by the contrasting experimental results reported in documents D16, D18 and D20 taking account of the different homogenisation times and the likely variations between different batches of hyaluronic acid used in the experiments. The skilled person had no motivation to modify the process of document D1 by allowing conventional gel formation prior to crosslinking, which risked local overcrosslinking and required vigorous agitation for the mixing with the crosslinking agent. The claimed process was therefore not obvious as solution to the problem of providing an alternative to the process of document D1, let alone to the problem of improving homogeneity and injectability.

IX. The arguments of the respondents relevant to the present decision are summarized as follows

(a) Admission of evidence

Document D18, which was filed in reaction to the filing of document D17, was correctly admitted by the opposition division.

Document D19 was not to be admitted into the appeal proceedings in accordance with Article 12(4) RPBA, because the introduction of document D19 would cause unnecessary complication, contravene procedural economy and not be pertinent for evaluating the decision under appeal.

The filing of documents D18a and D20 was justified as response to the filing of document D19.

(b) Right to be heard / Request for remittal

The appellant had not contested the admission of document D18 during the proceedings before the opposition division. The opposition division considered in its decision correctly that in view of the available evidence, including document D18, it had not been convincingly demonstrated that the claimed method leads to the advantageous effects mentioned in the patent. The opposition division had not required a repeat of the experiments of document D18.

The argument that the claimed matter additionally differed from the teaching in document D1 in the mechanical instead of manual deformation of the pouch represented an unjustified amendment to the appellant's appeal case. This amendment did not in any way justify a remittal to the first instance.

(c) Request for suspension pending G 2/21

The referral G 2/21 was relevant to present appeal and justified a suspension of the appeal proceedings if the Board were minded to set aside the decision under appeal taking account of the post-published evidence in documents D13, D17 and D19.

(d) Admission main request

The main request corresponded to auxiliary request 3 as filed before the opposition division, but included as amendment the additional dependent claims 12 and 13. As this modification was not justified in the statement of grounds of appeal the

main request was not to be admitted into the appeal proceedings in accordance with Article 12(4) RPBA.

(e) Article 123(2) EPC

Claim 1 of the main request defined a cavity in the form of a pouch which may be partially delimited by a deformable wall, whereas the original disclosure only mentioned a pouch in the context of an entirely deformable cavity. Moreover, the mechanical deformations had originally only been disclosed with respect to the pouch as such (not its deformable wall) and only in the context of its degree of deformability allowing the homogenization by mechanical deformations.

Claim 12 defined the homogenization by means of a system of two blades side-by-side alternately pressing the deformable wall following a back and forth motion, which had originally only been disclosed in the context of a device of the "paddle mill" type.

Claim 13 of the main request additionally defined that the homogenization by mechanical deformation is carried out by combination of manual palpitation and use of a mechanical device, whereas the original application consistently distinguished between mechanical and manual homogenization.

(f) Sufficiency

The patent only described the homogenization in a fully deformable pouch and failed to teach how the mechanical homogenization can be realized in a partially deformable pouch.

(g) Novelty

Document D1 described the preparation of a crosslinked gel of hyaluronic acid by providing an aqueous mixture of hyaluronic acid in a deformable pouch, wherein the mixture is homogenized and crosslinked by mechanical deformations of the pouch. Claim 1 of the main request did not define any duration for the steps b) and c) nor require any interruption of the homogenisation by the crosslinking or exclude the presence of a crosslinking agent during step b). The order of the formation of a gel of the hyaluronic acid in step b) and the crosslinking according to step c) defined in claim 1 did therefore not represent a difference with the teaching of document D1.

(h) Inventive step

Document D1 could not be disqualified by document D2 as suitable starting point in the prior art, because document D1 equally aimed at providing uniformly crosslinked hyaluronic acid gels suitable for cosmetic applications. In as far as novel, the process defined in claim 1 could only differ from the teaching in document D1 in the gel formation prior to mixing the crosslinking agent with the hyaluronic acid. As no particular effect of this difference was addressed in the patent, any effect allegedly demonstrated in documents D13, D17 and D19 could not be relied upon for a reformulation of the technical problem. Moreover, in view of the contrasting results presented in documents D16, D18 and D20 no such effect had been convincingly shown to result from this difference within the whole

scope of the claim. Merely as solution to the problem of providing an alternative process, irrespective of the resulting quality of the gels, the claimed process would be obvious to the skilled person. Document D1 did not indicate the order of gel formation and addition of the crosslinking agent to be critical. Gel formation prior to crosslinking was conventional and had been described in each of documents D2-D5. The mention of flake formation in document D2 did not amount to a general prejudice against the claimed process. Moreover, it had not been demonstrated that flake formation was actually prevented within the whole scope of the claim.

The process of claim 1 differed from the conventional type of process in documents D2-D5 in that the gel formation and the crosslinking are carried out in a pouch. Examples 1-3 of the patent and the experiments in document D13 were not suitable to show an advantageous effect of the use of a pouch, because additional differences influenced the results, in particular differences in the time for homogenisation and the temperature during crosslinking. The results reported in document D12 further confirmed that no unexpected effect could be attributed to the use of a pouch within the whole scope of the claim. As solution to the problem of providing a mere alternative process the defined homogenisation and crosslinking in a pouch was obvious in view of the use of a pouch for gel formation described in document D3, the use of a pouch for gel formation and crosslinking described in document D1 and the use of a pouch for convenient mixing described in documents D6-D11.

X. The appellant requested that the decision under appeal be set aside and that the patent be maintained on the basis of requests No. 1-7 filed with the statement of grounds of appeal, referred to by the Board as the main request and auxiliary requests 1-6.

The appellant further requested that the respondents' new objections under Article 83 EPC be disregarded and that the case be remitted to the opposition division for a renewed debate on inventive step.

The appellant also requested that documents D18 and D20 be excluded from the debate and that document D19 be admitted in the event that document D18 were admitted.

XI. The respondents requested that the appeal be dismissed.

The respondents further requested that the new main request and new auxiliary requests 1-6 not be admitted.

The respondents also requested that document D19 not be admitted and that document D20 be admitted in the event that document D19 were admitted.

Subsidiarily, the respondents requested that the proceedings be suspended until the referral G 2/21 has been decided by the Enlarged Board of Appeal.

Reasons for the Decision

1. Admission of evidence

The appellant did not contest the admission of document D18 during the proceedings before the opposition

division. The Board finds therefore no ground to overturn the discretionary admission of document D18 by the opposition division.

In the decision under appeal an inventive step was denied taking account of the results in the late-filed document D18. Document D19 presents experimental evidence intended to explain the results reported in document D18. The filing of document D19 with the statement of grounds of appeal by the appellant therefore represents a legitimate reaction to the decision under appeal. Documents D18a and D20 present further experimental evidence contrasting the results reported in document D19. The filing of documents D18a and D20 with the reply to the appeal by the respondent therefore represents a legitimate response to the statement of grounds of appeal. Documents 18a, D19 and D20 are therefore not disregarded under Article 12(4) RPBA 2007 and thus part of the appeal proceedings.

The respondents have not objected to the admission of the data regarding the variation of the elastic modulus of different batches of commercially available products from FILORGA reported in the appellant's letter of 15 October 2020. The respondents have actually taken up these data to argue that the experimental results relied upon by the appellant are not reproducible. This evidence is therefore admitted into the appeal proceedings under Article 13(1) RPBA 2020.

2. Right to be heard / Request for remittal

2.1 Rather than requiring a repeat of the experiments of document D18 from the appellant, the opposition division considered in the reasons for its decision (see page 24, first paragraph) that in view of the

available evidence, including document D18, it had not been convincingly demonstrated that the claimed method leads to the advantageous effects mentioned in the patent. As the appellant did not contest the admission of document D18 during the proceedings before the opposition division, the Board does not recognize any violation of the appellant's right to be heard in this matter.

2.2 The Board observes that in requesting remittal for a renewed debate on inventive step before the opposition division the appellant relies on an argument presented for the first time during the appeal proceedings with the letter of 15 October 2020, namely that the opposition division failed to take a further difference with respect to the prior art into account. Such an amendment to the appellant's appeal case is not considered to represent a special reason within the meaning of Article 11 RPBA 2020 that justifies a remittal.

Main request

3. Admission of the main request

The respondents have contested the main request filed with the statement of grounds of appeal as an inadmissible amendment of the appellant's appeal case under 12(4) RPBA 2020. The Board observes that Article 12(4) RPBA 2020 is not applicable in view of the transitional provision of Article 25(2) RPBA 2020.

The amendment of the main request merely concerns the definition in claim 1 of hyaluronic acid or one of its salts as the polysaccharide to be used. As a result, claim 1 of the main request corresponds to claim 1 of

auxiliary request 3 on which the decision under appeal was based. The Board considers this amendment, which does not present the respondents with any new aspects of the case, a legitimate response to the finding in the decision under appeal that the presented results obtained with hyaluronic acid could not be extrapolated to polysaccharides in general. Accordingly, the Board finds no reason not to admit the main request under Article 12(4) RPBA 2007.

4. Added subject-matter

4.1 The respondents objected that claim 1 of the main request comprised subject-matter extending beyond the original disclosure due to the introduction in claim 1 as originally filed of the features of the cavity being made within a deformable pouch and the homogenization in step b) as carried out by mechanical deformations of the outer face of the deformable wall or of the pouch (see section IX(e) above).

Dependent claim 6 of the application as originally filed defines:

"*Process according to any of the preceding claims,* ***wherein the cavity is made within a deformable pouch***. [highlighting by the Board]

Furthermore, the application as originally filed describes on page 9, lines 23-26:

"*According to one particular embodiment, the deformable wall, or even the pouch has a degree of deformability such that* ***the homogenization, considered in step b), may be carried out by optionally successive, mechanical***

deformations of the outer face of the deformable wall, or even of the pouch."[highlighting by the Board]

The contested features of claim 1 (see sections I and VI above) are thus practically word by word based on the disclosure in the application as filed. In this context the Board agrees with the finding in the decision under appeal, that the remaining reference to a delimitation at least partially by a deformable wall represents at most an ambiguity in the patent as granted and that the degree of deformability mentioned in the cited passage on page 9 is implicit in the requirement of claim 1 of the main request that the homogenization is carried out by the mechanical deformations.

The contested amendments in claim 1 of the main request do therefore not introduce any subject-matter extending beyond the content of the application as filed.

4.2 The respondents further contested the definition of the feature concerning manual palpation in claim 13 in view of its dependence on claim 1 defining homogenization by mechanical deformations (see section IX(e) above).

The application as originally filed describes on page 10, lines 29-31:

"According to one particular embodiment, ***the homogenization may be carried out firstly by palpation, then using a mechanical device.***
According to yet another embodiment, ***these various homogenization means may be used alternately.***"[highlighting by the Board]

The Board agrees with the decision under appeal that mechanical deformations of the pouch as described on page 9 lines 23-26 of the application as filed and defined in claim 1 of the main request do not exclude manual palpitations as described in the cited passage of page 10. The definition of the deformation involving such palpation in claim 13 (see section VI above) does therefore not define subject-matter extending beyond the content of the application as filed.

4.3 The respondents further maintained that the definition of the system for homogenization in claim 12 of the main request introduced subject-matter that was not originally disclosed (see section IX(e) above).

The application as originally filed describes on page 9 line 31 to page 10 line 5:

"*According to another alternative, the deformations may be carried out mechanically, for example using a device of "paddle mill" type, commonly used for the preparation of biological samples.*
According to one such embodiment, the receptacle is placed in the device, then ***the homogenization is carried out by virtue of a system of two blades side-by-side which alternately press the deformable wall or at least one of the deformable walls following a back and forth motion.***" [highlighting by the Board]

The Board observes that the additionally defined feature of claim 12 (see section VI above) is described practically word by word in the cited passage of pages 9-10. The Board considers that the defined two blade system requires no further specification in terms of a "paddle mill" type device in order to comply with Article 123(2) EPC, because such a device is mentioned

in the cited passage as a mere example of a device for performing the mechanical deformations.

4.4 Accordingly, the Board concludes that the main request meets the requirement of Article 123(2) EPC.

5. Sufficiency

5.1 The Board notes that the ground of lack of sufficient disclosure had been raised in the notice of opposition, but that the requirement of sufficiency of disclosure was not addressed in the decision under appeal following the revocation of the patent on other grounds. The respondents' line of argument in the reply to the appeal, namely that the patent does not teach how the mechanical homogenization in a partially deformable pouch can be realized, is considered to represent a mere further development of the argument in the notice of opposition that the claimed invention cannot be carried out over the whole scope of the claims. The Board does therefore not recognize any ground for disregarding the respondents' line of argument (Article 14(2) RPBA 2007).

5.2 The claims define a process involving homogenization in a deformable pouch by mechanical deformation. The patent demonstrates in its examples how this homogenization may be carried out. The Board does not recognize why, with the examples in the patent at hand, the skilled person would not be able to choose deformable pouches that are suitable for the defined homogenization.

5.3 Accordingly, the Board concludes that the main request meets the requirement of sufficiency of disclosure.

6. Novelty

The Board observes that claim 1 requires the formation of a hyaluronic acid gel in step b) with subsequent addition of a crosslinking agent in step c). In contrast, according to document D1 (see paragraphs [0039] and [0062]) the hyaluronic acid starting material is brought into contact with the dissolved crosslinking agent directly without prior gel formation.

Accordingly, the Board concludes that the main request meets the requirement of novelty.

7. Inventive step

7.1 The Board recalls that the problem solution approach implies that in case an inventive step can be recognized starting from a particular item of prior art which is convincingly identified as most promising starting point and thus represents the closest prior art, attempts to argue a lack of inventive step starting from less promising starting points are bound to fail. However, in case an inventive step is apparently convincingly denied starting from a promising particular item of prior art, the mere argument that the claimed subject-matter nevertheless involves an inventive step in view of an allegedly closer prior art, may not be persuasive, because in such case the allegedly closest prior art is likely to represent a starting point that is in fact not more promising.

In the present case two types of known processes for preparing injectable gels of crosslinked hyaluronic

acid have been proposed as starting points in the prior art, namely

(a) the process for preparing a crosslinked hyaluronic acid gel described in examples 4-1/4-2 of document D1 in which a deformable pouch is used as defined in the claims, but in which the crosslinking agent is combined with the hyaluronic acid prior to gel formation

(b) the "conventional" process for preparing a crosslinked hyaluronic acid gel as described in documents D2-D5 in which the crosslinking agent is added after gel formation with the hyaluronic acid as defined in the claims, but in which the process is carried out in a conventional receptacle instead of a deformable pouch.

In view of the common objective of preparing injectable gels of crosslinked hyaluronic acid and the complementary nature of the differences of the two types of processes with the claimed process the Board considers it purposeful to assess the requirement of inventive step starting from each one of the two types of processes rather than to attempt to determine which of the two starting points is actually the more promising.

7.2 Assessment starting from document D1

7.2.1 Document D1 describes the preparation of crosslinked hyaluronic acid gels suitable for injection (see D1 paragraph [0041]) in which physical cutting of the hyaluronic acid polymer chain during stirring and mixing steps is avoided (see paragraphs [0010] and [0024]-[0025]). In examples 4-1/4-2 document D1

discloses the preparation of such a gel in which hyaluronic acid is added to a crosslinking agent in a deformable pouch with subsequent mixing by kneading for 5 minutes (see D1 paragraphs [0062]-[0063]). As explained in section 6 above, the process of claim 1 of the main request differs from this process of document D1 in the formation of a hyaluronic acid gel prior to the addition of a crosslinking agent.

7.2.2 The patent indicates (see paragraph [0122] with reference to Figures 5-7) that the claimed process allows for providing gels with an improved injectability profile with respect to gels which are conventionally prepared in a rigid receptacle. The injection profile in Figure 5, which was obtained with a gel prepared according to the claims, indeed shows a more regular pattern compared to Figures 6 and 7, which were obtained with a gel prepared in a rigid receptacle. Whilst the patent does not present a comparison with the process of document D1 involving the use of a pouch without gel formation prior to crosslinking, the Board acknowledges that the mentioned experimental results reported in the patent substantiate that the claimed process allows for the alternative preparation of injectable gels of crosslinked hyaluronic acid with respect to document D1.

Documents D16, D18 and D20 relied upon by the respondent present apparently less favourable injection profiles for gels prepared in accordance with the claims (see D16, pages 8-9, samples 2 and B; D18, pages 5/7, samples A/A'; D20, pages 5/6, samples A/C) than the profiles reported in the patent. The Board observes that variations in the results from separate experiments are to be expected in view of the possible

influence of differences in manual handling and homogenisation times as well as variations that may exist between different batches of hyaluronic acid as indicated by the data presented in the appellant's letter of 15 October 2020. In fact, document D16 presents for a gel prepared in line with examples 4-1/4-2 of document D1 also a rather uneven injection profile (see D16, page 9, sample A). The Board therefore considers that whilst documents D16, D18 and D20 seem to indicate suboptimal conditions for carrying out the claimed process, this process involving gel formation prior to crosslinking performed in a deformable pouch may still be considered to represent a suitable alternative process with respect to the process of examples 4-1/4-2 of document D1.

The problem to be solved starting from document D1 may therefore be seen in the provision of an alternative process allowing the preparation of injectable gels of crosslinked hyaluronic acid.

7.2.3 As mentioned in section 7.2.1 above, document D1 itself discloses the kneading of the pouch as a gentle form of mixing aimed at avoiding physical cutting of the hyaluronic acid polymer. Whilst document D1 suggests that this method of mixing the crosslinking agent with the hyaluronic acid is suitable for a mixture in the solid powder state or in a highly viscous gel state (see D1, paragraph [0039]), the process of examples 4-1/4-2 involves a procedure in which the crosslinking agent and the hyaluronic acid are combined and directly mixed to subsequently obtain a gel-like mixture. In this context the skilled person would expect that the efficient initial blending of the components is favoured by starting the mixing before the actual gel formation and that the initial blending is less

efficient if started after the gel formation, because the increased viscosity of a gel opposes such blending. This expectation finds confirmation in document D2, which indicates flake formation and local overcrosslinking from mixing a gel with a crosslinking agent. Accordingly, it would not be evident from document D1 itself that the modification of the process of examples 4-1/4-2 by performing initial gel formation prior to the addition of the crosslinking agent represents a suitable alternative.

Documents D2-D5 describe the preparation of injectable crosslinked hyaluronic acid gels involving initial gel formation and subsequent combination with a crosslinking agent in a conventional receptacle (see D2, reference Example 2, paragraphs [0075]-[0084]; D3 e.g. example 1, paragraph [0070]; D4, example 1, paragraph [0028]; D5, page 11, lines 5-11 and page 15, lines 19-27). These documents do not indicate the exchangeability of a process involving gel formation before the addition of a crosslinking agent and a process involving combination of the hyaluronic acid with the crosslinking agent before gel formation. To the contrary, document D2 specifically indicates that the conventional preparation involving gel formation before addition of the crosslinking agent is associated with the risk of formation of "flakes" and local overcrosslinking and that this risk is effectively avoided by a process in which the crosslinking is carried out during gel formation (see D2, paragraphs [0007]-[0010]). Moreover, documents D3-D5 do not mention any process involving crosslinking during the gel formation, let alone that such process could be exchanged with the conventional type of process involving gel formation prior to crosslinking.

The Board therefore concludes that the process of claim 1 of the main request would not be obvious to the skilled person starting from document D1 as closest prior art.

7.3 Assessment starting from documents D2-D5

7.3.1 As mentioned in section 7.2.3, documents D2-D5 describe the preparation of injectable crosslinked hyaluronic acid gels involving initial gel formation and subsequent combination with a crosslinking agent in a conventional receptacle.

The process of claim 1 of the main request differs from the conventional type of process as described in documents D2-D5 in the use of a deformable pouch for the gel formation and crosslinking instead of a conventional rigid receptacle.

7.3.2 As mentioned in section 7.2.2 above, the patent indicates in paragraph [0122] with reference to Figures 5-7 that the claimed process allows for providing gels with an improved injectability profile with respect to gels which are conventionally prepared in a rigid receptacle. The profile obtained with a gel prepared according to the claims (see Figure 5) indeed shows a more regular pattern compared to the profile obtained with gels prepared in a rigid receptacle (see Figures 6 and 7). The Board therefore considers that the mentioned experimental results reported in the patent substantiate that the claimed process allows for the improved preparation of injectable gels of crosslinked hyaluronic acid with respect to the conventional type of process of documents D2-D5.

The respondents' argument, that the differences in the injection profiles reported in the patent cannot be attributed to the mere use of a pouch as defined in the claims due to the further differences in homogenisation time and temperature profiles in the compared processes, is not considered convincing. According to the description of the experiments in the patent the different homogenisation times and temperature profiles already result themselves from the difference in the receptacle used (see patent, paragraphs [0158] and [0166]-[0169] with reference to Table 1 and Figures 2-4). Document D12, which has been relied upon by the respondents, does not present evidence that casts doubt on the relevance of the use of the pouch for obtaining the injection profiles reported in the patent. The numerical differences in the dissolution time, yield and injectability forces reported in document D12 (see D12, tables 1, 2 and 4) with respect to the results reported in the patent (see tables 1-3) indicate that depending on the set up of the experiments more or less fluid gels are prepared, but do not invalidate the evidence in the patent regarding the injection profiles. On the basis of the available evidence the Board therefore concludes that the use of the deformable pouch indeed allows for obtaining the improved injection profile as reported in the patent.

The problem to be solved starting from the conventional type of process as described in documents D2-D5 may therefore be seen in the provision of a process allowing the preparation of gels of crosslinked hyaluronic acid with an improved injection profile.

7.3.3 Documents D2, D4 and D5 do not make any reference to the use of a deformable pouch. Document D3 only refers to the use of a deformable pouch for preparing a

diluted sodium hyaluronate solution without mention of subsequent crosslinking. Documents D2-D5 do therefore not themselves suggest the use of a pouch as defined in claim 1 of the main request.

As mentioned in section 7.2.1 above, document D1 describes the utility of a pouch for gently mixing hyaluronic acid and a crosslinking agent to produce a gel-like mixture. However, document D1 does thereby not suggest that the conventional type of process described in documents D2-D5 involving gel formation prior to crosslinking could be improved in terms of injectability of the crosslinked hyaluronic acid product by performing the process in a deformable pouch.

Documents D6-D11 describe the use of a deformable pouch as a convenient method for mixing a variety of components, but do not refer to any use of a deformable pouch for gel formation and crosslinking. These documents provide therefore no suggestion as to the utility of a deformable pouch for improving the conventional type of process of documents D2-D5 with regard to the injection profile of the resulting crosslinked gels.

The Board therefore concludes that the process of claim 1 of the main request would not be obvious to the skilled person starting from the conventional type of process as described in documents D2-D5 as closest prior art.

7.4 Accordingly, the Board concludes that the main request meets the requirement of inventive step.

Request for suspension of the proceedings pending G 2/21

8. In T 116/18 the following questions were referred to the Enlarged Board of Appeal:

If for acknowledgement of inventive step the patent proprietor relies on a technical effect and has submitted evidence, such as experimental data, to prove such an effect, this evidence not having been public before the filing date of the patent in suit and having been filed after that date (post-published evidence):

- Should an exception to the principle of free evaluation of evidence be accepted in that post-published evidence must be disregarded on the ground that the proof of the effect rests exclusively on the post-published evidence?

- If the answer is yes (the post-published evidence must be disregarded if the proof of the effect rests exclusively on this evidence), can the post-published evidence be taken into consideration if, based on the information in the patent application in suit or the common general knowledge, the skilled person at the filing date of the patent application in suit would have considered the effect plausible (ab initio plausibility)?

- If the answer to the first question is yes (the post-published evidence must be disregarded if the proof of the effect rests exclusively on this evidence), can the post-published evidence be taken into consideration if, based on the information in the patent application in suit or the common general knowledge, the skilled person at the filing date of the patent application in suit would have

seen no reason to consider the effect implausible (ab initio implausibility)?

The referral is pending as G 2/21.

As explained in section 7 above (see in particular paragraphs 7.2.2 and 7.3.2), the Board concludes that the subject-matter of claim 1 of the main request involves an inventive step in view of a technical effect which is derivable from the patent and supported by experimental results disclosed in the patent. The referred questions are therefore not considered determinative to the outcome of the present appeal proceedings.

Moreover, the respondents denied *a priori* that in the absence of any mention of an effect with respect to the teaching of document D1 in the application as filed the appellant could rely for the reformulation of the technical problem on any alleged effect over the teaching of document D1, irrespective of the status of the post-published documents as evidence for such an effect (see section IX(h) above). In contrast, the referred questions address the status of post-published documents as evidence of an effect relied upon to support an inventive step.

Taking account of the interest of procedural economy as well as the interest of legal certainty the Board has therefore rejected the respondents' request for a suspension of the proceedings pending G 2/21.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the opposition division with the order to maintain the patent on the basis of the main request filed with the statement setting out the grounds of appeal and a description to be adapted.

The Registrar: The Chairman:

B. Atienza Vivancos A. Usuelli

Decision electronically authenticated