

The demand must be filed directly with the competent International Preliminary Examining Authority or, if two or more Authorities are competent, with the one chosen by the applicant. The full name or two-letter code of that Authority may be indicated by the applicant on the line below:

IPEA/ US

PCT DEMAND

CHAPTER II

under Article 31 of the Patent Cooperation Treaty:
The undersigned requests that the international application specified below be the subject of international preliminary examination according to the Patent Cooperation Treaty.

For International Preliminary Examining Authority use only

Identification of IPEA		Date of receipt of DEMAND	
Box No. I IDENTIFICATION OF THE INTERNATIONAL APPLICATION			
Applicant's or agent's file reference L1247-20031		International application No. PCT/US2022/012200	
International filing date (day/month/year) 12 January 2022		(Earliest) Priority date (day/month/year) 12 January 2021	
Title of invention MULTIPLE VISCOSITY OIL-IN-WATER COMPOSITION USEFUL AS AN INJECTABLE FILLER AND A SCAFFOLD FOR COLLAGEN GROWTH			
Box No. II APPLICANT(S)			
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.) LORIA PHARMACEUTICAL, LLC 10773 NW 58th Street, Suite 751 Doral, Florida 33178 UNITED STATES OF AMERICA		E-mail address* patents@crbcp.com	
		Telephone No.	
		Facsimile No.	
		Applicant's registration No. with the Office	
* E-mail authorization: Indicating an e-mail address above authorizes the International Bureau and the International Preliminary Examining Authority, if they provide such a service, to send notifications exclusively by e-mail to that address, unless the following box is marked: ☐ notifications are requested to be sent exclusively by postal mail.			
State (that is, country) of nationality: US		State (that is, country) of residence: US	
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)			
State (that is, country) of nationality:		State (that is, country) of residence:	
☐ Further applicants are indicated on a continuation sheet.			

Box No. III AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE

The following person is ☒ agent ☐ common representative
 and ☒ has been appointed earlier and represents the applicant(s) also for international preliminary examination.
☐ is hereby appointed and any earlier appointment of (an) agent(s)/common representative is hereby revoked.
☐ is hereby appointed, specifically for the procedure before the International Preliminary Examining Authority, in addition to the agent(s)/common representative appointed earlier.

Name and address: *(Family name followed by given name; for a legal entity, full official designation.
The address must include postal code and name of country.)*

TENER, David, M.
 CAESAR RIVISE, PC
 7 Penn Center, 12th Floor
 1635 Market Street
 Philadelphia, PA 19103
 United States of America

E-mail address*

patents@crbcp.com

Telephone No.

215-567-2010

Facsimile No.

215-751-1142

Agent's registration No. with the Office

37,054

* **E-mail authorization:** Indicating an e-mail address above authorizes the International Bureau and the International Preliminary Examining Authority, if they provide such a service, to send notifications exclusively by e-mail to that address, unless the following box is marked:

☐ notifications are requested to be sent exclusively by postal mail.

☐ **Address for correspondence:** Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.

Box No. IV BASIS FOR INTERNATIONAL PRELIMINARY EXAMINATION**Statement concerning amendments:***

1. The applicant wishes the international preliminary examination **to start on the basis of:**

the description ☒ as originally filed, or
☐ as amended under Article 34

the sequence listing (if any) ☐ as originally filed, or
☐ as amended under Article 34

the claims ☐ as originally filed, or
☐ as amended under Article 19, and/or
☒ as amended under Article 34

the drawings (if any) ☐ as originally filed, or
☐ as amended under Article 34

2. ☐ The applicant wishes any amendment to the claims under Article 19 to be considered as reversed.

3. ☐ Where the IPEA wishes to start the international preliminary examination at the same time as the international search in accordance with Rule 69.1(b), the applicant requests the IPEA **to postpone** the start of the international preliminary examination until the expiration of the applicable time limit under Rule 69.1(d).

4. ☐ The applicant expressly requests **to postpone** the start of the international preliminary examination until the expiration of the applicable time limit under Rule 54bis.1(a).

* Where no check-box is marked, international preliminary examination will start on the basis of the international application as originally filed or, where a copy of amendments to the claims under Article 19 and/or amendments of the international application under Article 34 are received by the International Preliminary Examining Authority before it has begun to draw up a written opinion or the international preliminary examination report, as so amended.

Language for the purposes of international preliminary examination: English

- ☒ which is the language in which the international application was filed.
☐ which is the language of a translation furnished for the purposes of international search.
☐ which is the language of publication of the international application.
☐ which is the language of the translation (to be) furnished for the purposes of international preliminary examination.

Box No. V ELECTION OF STATES

The filing of this demand constitutes the election of all Contracting States which are designated and are bound by Chapter II of the PCT.

Box No. VI CHECK LIST

The demand is accompanied by the following elements, in the language referred to in Box No. IV, for the purposes of international preliminary examination:

- | | | | |
|---|---|--------------------------|--------|
| 1. translation of international application | : | | sheets |
| 2. amendments under Article 34 | : | 3 | sheets |
| 3. amended sequence listing under Article 34 | : | ☐ | |
| 4. letter accompanying the amendments under Article 34 (Rule 66.8) | : | 8 | sheets |
| 5. copy (or, where required, translation) of amendments under Article 19 | : | | sheets |
| 6. copy of the letter accompanying the amendments under Article 19 (Rules 46.5(b) and 53.9) | : | | sheets |
| 7. copy (or, where applicable, translation) of any statement under Article 19 (Rule 62.1(ii)) | : | | sheets |
| 8. other (<i>specify</i>) | : | | sheets |

For International Preliminary
Examining Authority use only

received	not received
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☐	☐
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The demand is also accompanied by the item(s) marked below:

- | | |
|--|---|
| 1. ☒ fee calculation sheet | 5. ☐ sequence listing for the purposes of international preliminary examination (Rule 13 <i>ter</i>) |
| 2. ☐ original separate power of attorney | 6. ☐ a statement to the effect that the sequence listing does not go beyond the disclosure in the international application as filed |
| 3. ☐ original general power of attorney | 7. ☐ other (<i>specify</i>): _____ |
| 4. ☐ copy of general power of attorney; reference number, if any: _____ | |

Box No. VII SIGNATURE OF APPLICANT, AGENT OR COMMON REPRESENTATIVE

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the demand).

/david m tener/
David M. Tener, Registration No. 37,054
Agent for Applicant

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1. Date of actual receipt of DEMAND:

2. Adjusted date of receipt of demand due to CORRECTIONS under Rule 60.1(b):

3. ☐ The date of receipt of the demand is AFTER the expiration of 19 months from the priority date and item 4 or 5, below, does not apply.

☐ The applicant has been informed accordingly.

4. ☐ The date of receipt of the demand is WITHIN the time limit of 19 months from the priority date as extended by virtue of Rule 80.5.

5. ☐ Although the date of receipt of the demand is after the expiration of 19 months from the priority date, the delay in arrival is EXCUSED pursuant to Rules 82 or 82*quater*.

6. ☐ The date of receipt of the demand is AFTER the expiration of the time limit under Rule 54*bis*.1(a) and item 7 or 8, below, does not apply.

7. ☐ The date of receipt of the demand is WITHIN the time limit under Rule 54*bis*.1(a) as extended by virtue of Rule 80.5.

8. ☐ Although the date of receipt of the demand is after the expiration of the time limit under Rule 54*bis*.1(a), the delay in arrival is EXCUSED pursuant to Rules 82 or 82*quater*.

For International Bureau use only

Demand received from IPEA on:

PCT

CHAPTER II

FEE CALCULATION SHEET

Annex to the Demand

<table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="padding: 5px;">International application No. PCT/US2022/012200</td> </tr> <tr> <td style="padding: 5px;">Applicant's or agent's file reference L1247-20031</td> </tr> </table>	International application No. PCT/US2022/012200	Applicant's or agent's file reference L1247-20031	For International Preliminary Examining Authority use only										
International application No. PCT/US2022/012200													
Applicant's or agent's file reference L1247-20031													
Applicant LORIA PHARMACEUTICAL, LLC													
CALCULATION OF PRESCRIBED FEES <i>(Applicants may be entitled to a reduction of the preliminary examination fee and the handling fee as indicated in the PCT Fee Tables (www.wipo.int/pct/en/fees.pdf))</i> <table style="width: 100%; margin-top: 10px;"> <tr> <td style="width: 60%;">1. PRELIMINARY EXAMINATION FEE</td> <td style="width: 20%; text-align: right; border: 1px solid black;">320.00</td> <td style="width: 20%; text-align: center; border: 1px solid black;">P</td> </tr> <tr> <td>2. HANDLING FEE</td> <td style="text-align: right; border: 1px solid black;">216.00</td> <td style="text-align: center; border: 1px solid black;">H</td> </tr> <tr> <td>3. TOTAL OF PRESCRIBED FEES Add the amounts entered at P and H and enter total in the TOTAL box</td> <td style="text-align: right; border: 1px solid black;">536.00</td> <td></td> </tr> <tr> <td></td> <td colspan="2" style="text-align: center; border: 1px solid black;">TOTAL</td> </tr> </table>		1. PRELIMINARY EXAMINATION FEE	320.00	P	2. HANDLING FEE	216.00	H	3. TOTAL OF PRESCRIBED FEES Add the amounts entered at P and H and enter total in the TOTAL box	536.00			TOTAL	
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2. HANDLING FEE	216.00	H											
3. TOTAL OF PRESCRIBED FEES Add the amounts entered at P and H and enter total in the TOTAL box	536.00												
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MODE OF PAYMENT <i>(Not all modes of payment may be available at all IPEAs)</i> <table style="width: 100%; margin-top: 10px;"> <tr> <td>☒ credit card <i>(details should not be included on this sheet)</i></td> <td>☐ postal money order</td> </tr> <tr> <td>☐ authorization to charge deposit or current account with the IPEA (see below)</td> <td>☐ check</td> </tr> <tr> <td>☐ bank transfer</td> <td>☐ revenue stamps</td> </tr> <tr> <td>☐ cash</td> <td>☐ other <i>(specify)</i>: _____</td> </tr> </table>		☒ credit card <i>(details should not be included on this sheet)</i>	☐ postal money order	☐ authorization to charge deposit or current account with the IPEA (see below)	☐ check	☐ bank transfer	☐ revenue stamps	☐ cash	☐ other <i>(specify)</i> : _____				
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☐ bank transfer	☐ revenue stamps												
☐ cash	☐ other <i>(specify)</i> : _____												
AUTHORIZATION TO CHARGE (OR CREDIT) DEPOSIT OR CURRENT ACCOUNT <i>(This mode of payment may not be available at all IPEAs)</i> <table style="width: 100%; margin-top: 10px;"> <tr> <td style="width: 50%; vertical-align: top;"> ☐ Authorization to charge the total fees indicated above. ☒ <i>(This check-box may be marked only if the conditions for deposit or current accounts of the IPEA so permit)</i> Authorization to charge any deficiency or credit any overpayment in the total fees indicated above. </td> <td style="width: 50%; vertical-align: top;"> IPEA/ <u>US</u> Deposit or Current Account No.: <u>03-0075</u> Date: <u>November 11, 2022</u> Name: <u>David M. Tener</u> Signature: _____ /david m tener/ </td> </tr> </table>		☐ Authorization to charge the total fees indicated above. ☒ <i>(This check-box may be marked only if the conditions for deposit or current accounts of the IPEA so permit)</i> Authorization to charge any deficiency or credit any overpayment in the total fees indicated above.	IPEA/ <u>US</u> Deposit or Current Account No.: <u>03-0075</u> Date: <u>November 11, 2022</u> Name: <u>David M. Tener</u> Signature: _____ /david m tener/										
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**IN THE UNITED STATES PATENT OFFICE
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY**

Applicant: LORIA PHARMACEUTICAL, LLC
International App. No.: PCT/US2022/012200
International Filing Date: 12 January 2022
Earliest Priority Date: 12 January 2021
Attorney Reference No.: L1247/20031
Authorized Officer: Kari Rodriquez
For: MULTIPLE VISCOSITY OIL-IN-WATER COMPOSITION
USEFUL AS AN INJECTABLE FILLER AND A SCAFFOLD
FOR COLLAGEN GROWTH

AMENDMENT UNDER ARTICLE 34

Mail Stop PCT
Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Commissioner:

INTRODUCTORY COMMENTS

In response to the Written Opinion mailed from the International Searching Authority on 1 April 2022, please replace original sheets 21-23 with attached replacement sheets 21-23 to effect the claim amendments identified below.

AMENDMENTS TO THE CLAIMS

The following listing of amended claims shows the amendments made to the original set of claims by Replacement Sheets 21-23.

Listing of Amended Claims:

1. A filler composition comprising:

1-80 vol.% of a first silicone oil having a first viscosity of 12,500 to 20,000,000 cSt;

15-98 vol.% of water;

1-3 wt.% of a transport medium;

0.05-10 vol.% of a surfactant; and optionally

a second silicone oil having a second viscosity lower than the first viscosity,

wherein:

the filler composition is free of collagen;

the filler composition is a pharmaceutically acceptable oil-in-water emulsion;

~~the second silicone oil is provided in an amount of 1-80 vol.% when the first viscosity is 30,000 cSt or less;~~

~~the second silicone oil is provided in an amount of 0-80 vol.% when the first viscosity is greater than 30,000 cSt;~~

at least one of the first silicone oil and the second silicone oil is dispersed in the water as droplets having an average diameter of less than 30 microns; and

the transport medium is sufficiently biodegradable when implanted intradermally or subcutaneously in a human to provide a temporary scaffold for collagen growth between the droplets.

2. The filler composition of claim 1, which comprises 3 vol.% of the second silicon oil and 27 vol.% of the first silicone oil, wherein the second viscosity is 1,000 cSt and the first viscosity is 12,500 cSt.

3. The filler composition of claim 1, which comprises 5 vol.% of the second silicon oil and 25 vol.% of the first silicone oil, wherein the second viscosity is 12,500 cSt and the first viscosity is 100,000 cSt.

4. The filler composition of claim 1, which comprises 30 vol.% of the first silicon oil and none of the second silicone oil, wherein the first viscosity is 100,000 cSt.

5. The filler composition of claim 1, wherein ~~the first viscosity is from 12,500 cSt to 20,000,000 cSt and~~ the second viscosity is from 65 cSt to 5000 cSt.

6. The filler composition of any one of claims 1-5, wherein the first silicone oil and the second silicone oil are polydimethylsiloxane.

7. The filler composition of any one of claims 1-5, wherein the transport medium is a water-soluble polymer.

8. The filler composition of any one of claims 1-5, wherein the transport medium is at least one member selected from the group consisting of carboxymethylcellulose (CMC), hyaluronic acid, hydroxyethyl cellulose, methyl cellulose, hydroxypropylmethyl cellulose, polyvinylpyrrolidone, polyvinylalcohol, guar gum, hydroxypropyl guar gum, xanthan gum, croscarmellose sodium, and alginic acid.

9. The filler composition of claim 8, wherein the transport medium is CMC.

10. The filler composition of claim 9, wherein the CMC is cross-linked.

11. The filler composition of any one of claims 1-5, wherein the temporary scaffold dissolves in 7 to 35 days.

12. The filler composition of any one of claims 1-5, wherein the surfactant is lidocaine.

13. The filler composition of any one of claims 1-5, wherein the average diameter of the droplets is from 1 nanometer to 1 micron.

14. The filler composition of any one of claims 1-5, wherein:

the first silicone oil and the second silicone oil are polydimethylsiloxane;

the transport medium is an optionally cross-linked water-soluble polymer selected from the group consisting of carboxymethylcellulose (CMC), hyaluronic acid, hydroxyethyl cellulose, methyl cellulose, hydroxypropylmethyl cellulose, polyvinylpyrrolidone, polyvinylalcohol, guar gum, hydroxypropyl guar gum, xanthan gum, croscarmellose sodium, and alginic acid;

the temporary scaffold dissolves in 7 to 35 days;

the surfactant is lidocaine; and/or

the average diameter of the droplets is from 1 nanometer to 1 micron.

15. A method for preparing the filler composition according to any one of claims 1-5, comprising the steps of:

(i) preparing an oil phase comprising the steps of:

(a) providing at least one silicone oil~~an active ingredient~~ that is substantially sterile and substantially free of pyrogen, wherein the at least one silicone

oil comprises active ingredient is the first silicone oil and optionally the second silicone oil ~~or the first silicone oil when there is no second silicone oil~~;

(b) mixing the at least one silicone oil ~~active ingredient~~ with 1-5 volumes of sterile injectable water for 4 to 6 minutes at 1200 to 1500 rpm;

(c) allowing the ~~active ingredient~~ at least one silicone oil and water mixture to separate into a lower water layer and an upper layer containing the ~~active ingredient~~ at least one silicone oil;

(d) removing the lower water layer and collecting the upper layer; and

(e) repeating steps (b) through (d) on the ~~active ingredient~~ at least one silicone oil at least once to obtain the oil phase;

(ii) preparing a water phase solution comprising the sequential steps of:

(a) dissolving with stirring a transport medium in a sterile solvent selected from the group consisting of injectable water, normal saline, Ringer's solution, and lactated Ringer's solution, to form a preliminary water phase solution;

(b) sterilizing the preliminary water phase solution to form a sterilized water phase solution; and

(c) optionally freezing and thawing the sterilized water phase solution; and

(iii) preparing an oil-in-water emulsion by combining 35-45 parts by volume of the oil phase with 55-65 parts by volume of the water phase solution with agitation to form an emulsion of the ~~active ingredient~~ at least one silicone oil within the water.

16. The method of claim 15, wherein the sterile solvent contains a cross-linking agent which forms cross-links in the transport medium.

17. The method of claim 16, wherein the cross-linking agent is 1,4-butanediol diglycidyl ether in an amount from 0.01 to 10% by weight of the composition.

18. A soft tissue augmentation method comprising intradermally and/or subcutaneously injecting into a patient the filler composition of any one of claims 1-5.

19. The soft tissue augmentation method of claim 18, wherein a volume of 20 to 60 ml of the filler composition is injected into a single injection site.

20. The soft tissue augmentation method of claim 18, wherein:

the filler composition stimulates collagen growth;

the transport medium forms a temporary scaffold for collagen growth between ~~the active ingredient~~ droplets; and

a collagen matrix anchors the ~~active ingredient~~ droplets in place as the temporary scaffold dissolves within 7-35 days.

21. The soft tissue augmentation method of claim 18, wherein the filler composition is injected into a penis or a scrotum for penis or scrotum enhancement.

REMARKS/ARGUMENTS

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

This response is in no way a concession as to the propriety in any or all of the designated countries of any or all of the objections.

Amendments

Original claims 1, 5, 15 and 20 are replaced with amended claims 1, 5, 15 and 20. The amendments are supported by the original disclosure as described below.

The viscosity range of 12,500-20,000,000 cSt added to claim 1 is incorporated from original claim 5 and finds further support in the specification at Paragraph 0020.

The limitation in claim 1 specifying that the filler composition is free of collagen finds support in the specification at, e.g., Paragraph 0078, which discloses that certain (not all) embodiments include collagen, and therefore implicitly discloses that other embodiments are free of collagen.

Claim 15 is amended for improved consistency with claim 1, and finds support in Paragraphs 0029 and 0046.

Claim 20 is also amended for improved consistency with claim 1, and finds support in Paragraphs 0109-0111.

No new matter is added.

Re Item V – Inventive Step

Claims 1-5 and 7-14 are novel and inventive over US 20090169615 A1 (Pinsky).

Pinsky discloses compositions and methods for administering collagen for the purpose of collagen replacement therapy used to treat conditions associated with the breakdown or loss of collagen. See, e.g., Abstract and Paragraph 0009.

Applicant's invention relates to compositions effective to elicit a foreign body reaction upon injection into the patient, such that collagen is formed. See, e.g., Paragraphs 0002 and 0057. Thus, the invention does administer collagen for collagen replacement therapy but rather relates to a different field of technology than Pinsky. Base claim 1 specifies that the filler composition is free of collagen. A person having ordinary skill in the art at the time the application was filed (a "PHOSITA") would have lacked reasonable motivation to consult, combine or modify a reference like Pinsky to provide a collagen-free filler composition not used for collagen replacement therapy.

Moreover, a PHOSITA would have lacked reasonable motivation to modify Pinsky to include a silicone oil having a viscosity of 12,500-20,000,000 cSt (and optionally a second silicone oil of lower viscosity) to elicit “an aggressive response producing collagen to surround the emulsified oil droplets while minimizing adverse reactions such as ulceration of the skin and fevers.” See Paragraph 0002 of the application. Pinsky does not disclose the viscosity of any silicone oils, but does teach that its emulsions having much lower viscosities of “about 50 centistokes or less” (Paragraph 0124). This teaching would have further dissuaded a PHOSITA from including as a substantial ingredient of the emulsion a silicone oil having a viscosity at least 250x higher.

Claims 6 and 15-21 are inventive over the combination of Pinsky and the inventor’s earlier patent, US 9993578 B1 (Loria ‘578).

For the reasons noted above, a PHOSITA would have considered Pinsky to be non-analogous art from a different field of invention than the instant invention and not reasonably pertinent to solving the problems addressed by the instant invention.

Moreover, as explained in the instant specification at Paragraph 0055, Loria ‘578 teaches away from the use of silicon droplets having an average diameter of less than 30 microns (as specified in base claim 1 of this application):

The use of an oil-in-water emulsion aids in solving the common problem of lumps and irregularities forming after injection of silicone oil droplets. Silicone oil droplets with smaller diameters (preferably from 1 nanometer to 30 microns) can be delivered both intradermally and into the subcutaneous space of and under the skin more effectively with an emulsion, avoided the irregularities that commonly form when an emulsion is not used. The emulsion permits the oil droplets to be delivered close together with minimal to no migration or coalescence, allowing for a foreign body reaction FBR to take place and each droplet be encased in collagen. When droplets less than 30 microns are used without migration and the foreign body reaction takes place, collagen is formed in a smooth, continuous sheet. **This result was unexpected in view of the previous understanding that if the silicone droplets were too small in size, i.e., under about 30 microns in diameter, the silicone oil would likely be ineffective, as the phagocytes would phagocytize the silicone oil, carrying it away before collagen production could be stimulated.** See, e.g., U.S. Patent No. 9,993,578 B1. [Emphasis added.]

Such unexpectedly good results are evidence of the inventiveness of the claimed invention.

In view of the foregoing amendments and clarifying remarks, Applicants respectfully submit that the amended claims are clearly novel and inventive over the prior art.

Conclusion

Applicant respectfully requests that the International Preliminary Examining Authority reconsider the Written Opinion in view of the amendments and above remarks, and provide a favorable opinion as to the patentability of the claims.

Respectfully submitted,
CAESAR RIVISE, PC

11 November 2022

By /david m tener/
David M. Tener
USPTO Registration No. 37054
USPTO Customer No. 03000
7 Penn Center, 12th Floor
1635 Market Street
Philadelphia, PA 19103
(215) 567-2010
Attorneys for Applicant

REPLACEMENT SHEET

CLAIMS

WHAT IS CLAIMED IS:

1. A filler composition comprising:
1-80 vol.% of a first silicone oil having a first viscosity of 12,500 to 20,000,000 cSt;
15-98 vol.% of water;
1-3 wt.% of a transport medium;
0.05-10 vol.% of a surfactant; and optionally
a second silicone oil having a second viscosity lower than the first viscosity,
wherein:
the filler composition is free of collagen;
the filler composition is a pharmaceutically acceptable oil-in-water emulsion;
at least one of the first silicone oil and the second silicone oil is dispersed in the water as droplets having an average diameter of less than 30 microns; and
the transport medium is sufficiently biodegradable when implanted intradermally or subcutaneously in a human to provide a temporary scaffold for collagen growth between the droplets.
2. The filler composition of claim 1, which comprises 3 vol.% of the second silicon oil and 27 vol.% of the first silicone oil, wherein the second viscosity is 1,000 cSt and the first viscosity is 12,500 cSt.
3. The filler composition of claim 1, which comprises 5 vol.% of the second silicon oil and 25 vol.% of the first silicone oil, wherein the second viscosity is 12,500 cSt and the first viscosity is 100,000 cSt.
4. The filler composition of claim 1, which comprises 30 vol.% of the first silicon oil and none of the second silicone oil, wherein the first viscosity is 100,000 cSt.
5. The filler composition of claim 1, wherein the second viscosity is from 65 cSt to 5000 cSt.
6. The filler composition of any one of claims 1-5, wherein the first silicone oil and the second silicone oil are polydimethylsiloxane.
7. The filler composition of any one of claims 1-5, wherein the transport medium is a water-soluble polymer.
8. The filler composition of any one of claims 1-5, wherein the transport medium is at least one member selected from the group consisting of carboxymethylcellulose (CMC), hyaluronic acid, hydroxyethyl cellulose, methyl cellulose,

REPLACEMENT SHEET

hydroxypropylmethyl cellulose, polyvinylpyrrolidone, polyvinylalcohol, guar gum, hydroxypropyl guar gum, xanthan gum, croscarmellose sodium, and alginic acid.

9. The filler composition of claim 8, wherein the transport medium is CMC.
10. The filler composition of claim 9, wherein the CMC is cross-linked.
11. The filler composition of any one of claims 1-5, wherein the temporary scaffold dissolves in 7 to 35 days.
12. The filler composition of any one of claims 1-5, wherein the surfactant is lidocaine.
13. The filler composition of any one of claims 1-5, wherein the average diameter of the droplets is from 1 nanometer to 1 micron.
14. The filler composition of any one of claims 1-5, wherein:
 - the first silicone oil and the second silicone oil are polydimethylsiloxane;
 - the transport medium is an optionally cross-linked water-soluble polymer selected from the group consisting of carboxymethylcellulose (CMC), hyaluronic acid, hydroxyethyl cellulose, methyl cellulose, hydroxypropylmethyl cellulose, polyvinylpyrrolidone, polyvinylalcohol, guar gum, hydroxypropyl guar gum, xanthan gum, croscarmellose sodium, and alginic acid;
 - the temporary scaffold dissolves in 7 to 35 days;
 - the surfactant is lidocaine; and/or
 - the average diameter of the droplets is from 1 nanometer to 1 micron.
15. A method for preparing the filler composition according to any one of claims 1-5, comprising the steps of:
 - (i) preparing an oil phase comprising the steps of:
 - (a) providing at least one silicone oil that is substantially sterile and substantially free of pyrogen, wherein the at least one silicone oil comprises the first silicone oil and optionally the second silicone oil;
 - (b) mixing the at least one silicone oil with 1-5 volumes of sterile injectable water for 4 to 6 minutes at 1200 to 1500 rpm;
 - (c) allowing the at least one silicone oil and water mixture to separate into a lower water layer and an upper layer containing the at least one silicone oil;
 - (d) removing the lower water layer and collecting the upper layer; and
 - (e) repeating steps (b) through (d) on the at least one silicone oil at least once to obtain the oil phase;
 - (ii) preparing a water phase solution comprising the sequential steps of:

REPLACEMENT SHEET

- (a) dissolving with stirring a transport medium in a sterile solvent selected from the group consisting of injectable water, normal saline, Ringer's solution, and lactated Ringer's solution, to form a preliminary water phase solution;
 - (b) sterilizing the preliminary water phase solution to form a sterilized water phase solution; and
 - (c) optionally freezing and thawing the sterilized water phase solution; and
 - (iii) preparing an oil-in-water emulsion by combining 35-45 parts by volume of the oil phase with 55-65 parts by volume of the water phase solution with agitation to form an emulsion of the at least one silicone oil within the water.
16. The method of claim 15, wherein the sterile solvent contains a cross-linking agent which forms cross-links in the transport medium.
17. The method of claim 16, wherein the cross-linking agent is 1,4-butanediol diglycidyl ether in an amount from 0.01 to 10% by weight of the composition.
18. A soft tissue augmentation method comprising intradermally and/or subcutaneously injecting into a patient the filler composition of any one of claims 1-5.
19. The soft tissue augmentation method of claim 18, wherein a volume of 20 to 60 ml of the filler composition is injected into a single injection site.
20. The soft tissue augmentation method of claim 18, wherein:
the filler composition stimulates collagen growth;
the transport medium forms a temporary scaffold for collagen growth between the droplets; and
a collagen matrix anchors the droplets in place as the temporary scaffold dissolves within 7-35 days.
21. The soft tissue augmentation method of claim 18, wherein the filler composition is injected into a penis or a scrotum for penis or scrotum enhancement.

REIVINDICACIONES

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1. Una composición de relleno que comprende:
 - 1-80 vol.% de un primer aceite de silicona que tiene una primera viscosidad;
 - 15-98 vol.% de agua;
 - 1-3 % en peso de un medio de transporte;
 - 0,05-10 vol.% de un tensioactivo; y opcionalmente un segundo aceite de silicona con una segunda viscosidad inferior a la primera viscosidad,en donde:
 - la composición de relleno no contiene colágeno;
 - la composición de relleno es una emulsión de aceite en agua farmacéuticamente aceptable;
 - al menos uno de los dos aceites de silicona se dispersa en el agua en forma de gotitas con un diámetro medio inferior a 30 micras; y
 - el medio de transporte es suficientemente biodegradable cuando se implanta por vía intradérmica o subcutánea en un ser humano para proporcionar un andamiaje temporal para el crecimiento de colágeno entre las gotitas.
2. La composición de relleno de la reivindicación 1, que comprende 3 vol.% del segundo aceite de silicona y 27 vol.% del primer aceite de silicona, en la que la segunda viscosidad es de 1.000 cSt y la primera viscosidad es de 12.500 cSt.
3. La composición de relleno de la reivindicación 1, que comprende 5 vol.% del segundo aceite de silicona y 25 vol.% del primer aceite de silicona, en la que la segunda viscosidad es 12.500 cSt y la primera viscosidad es 100.000 cSt.
4. La composición de relleno de la reivindicación 1, que comprende 30 vol.% del primer aceite de silicona y ninguno del segundo aceite de silicona, en la que la primera viscosidad es 100.000 cSt.

5. La composición de relleno de la reivindicación 1, en la que la segunda viscosidad es de 65 cSt a 5000 cSt.

6. La composición de relleno de cualquiera de las reivindicaciones 1-5, en la que el primer aceite de silicona y el segundo aceite de silicona son polidimetilsiloxano.

7. La composición de relleno de una cualquiera de las reivindicaciones 1-6, en la que el medio de transporte es un polímero soluble en agua.

8. La composición de relleno de cualquiera de las reivindicaciones 1-7, en la que el medio de transporte es al menos un miembro seleccionado del grupo que consiste en carboximetilcelulosa (CMC), ácido hialurónico, hidroxietilcelulosa, metilcelulosa, hidroxipropilmetilcelulosa, polivinilpirrolidona, polivinilalcohol, goma guar, hidroxipropil goma guar, goma xantana, croscarmelosa sódica y ácido algínico.

9. La composición de relleno de la reivindicación 8, en la que el medio de transporte es CMC.

10. La composición de relleno de la reivindicación 9, en la que el CMC está reticulado.

11. La composición de relleno de cualquiera de las reivindicaciones 1-10, en la que el andamio temporal se disuelve en 7 a 35 días.

12. La composición de relleno de cualquiera de las reivindicaciones 1-11, en la que el tensioactivo es lidocaína.

13. La composición de relleno de cualquiera de las reivindicaciones 1-12, en la que el diámetro medio de las gotitas es de 1 nanómetro a 1 micra.

14. La composición de relleno de una cualquiera de las reivindicaciones 1-13, en la que:

el primer aceite de silicona y el segundo aceite de silicona son polidimetilsiloxano;

el medio de transporte es un polímero soluble en agua opcionalmente reticulado seleccionado del grupo que consiste en carboximetilcelulosa (CMC), ácido hialurónico, hidroxietilcelulosa, metilcelulosa, hidroxipropilmetilcelulosa, polivinilpirrolidona, polivinilalcohol, goma guar, hidroxipropil goma guar, goma xantana, croscarmelosa sódica y ácido algínico;

el andamio temporal se disuelve en 7 a 35 días;

el tensioactivo es lidocaína; y/o

el diámetro medio de las gotitas es de 1 nanómetro a 1 micra.

15. Método para preparar la composición de relleno según una cualquiera de las reivindicaciones 1 a 14, que comprende las etapas de:

(i) preparar una fase oleosa que comprende los pasos de:

(a) proporcionar al menos un aceite de silicona que es sustancialmente estéril y libre de pirógenos, en donde el al menos un aceite de silicona comprende el primer aceite de silicona y opcionalmente el segundo aceite de silicona;

(b) mezclar el al menos un aceite de silicona con 1-5 volúmenes de agua inyectable estéril durante 4 a 6 minutos a 1200 a 1500 rpm;

(c) dejar que la mezcla de al menos un aceite de silicona y agua se separe en una capa inferior de agua y una capa superior que contiene el al menos un aceite de silicona;

(d) retirar la capa inferior de agua y recoger la capa superior; y

(e) repetir las etapas (b) a (d) sobre el al menos un aceite de silicona al menos una vez para obtener la fase oleosa;

(ii) preparar una solución en fase acuosa que comprenda las etapas secuenciales de:

(a) disolver con agitación un medio de transporte en un disolvente estéril seleccionado del grupo que consiste en agua inyectable, solución salina normal, solución de Ringer y solución de Ringer lactato, para formar una solución de fase acuosa preliminar;

(b) esterilizar la solución en fase acuosa preliminar para formar una solución en fase acuosa esterilizada; y

(c) opcionalmente, congelar y descongelar la solución en fase acuosa esterilizada; y

(iii) preparar una emulsión de aceite en agua combinando 35-45 partes en volumen de la fase oleosa con 55-65 partes en volumen de la solución en fase acuosa con agitación para formar una emulsión del al menos un aceite de silicona dentro del agua.

16. El método de la reivindicación 15, en el que el disolvente estéril contiene un agente reticulante que forma reticulantes en el medio de transporte.

17. El método de la reivindicación 16, en el que el agente de reticulación es éter diglicidílico de 1,4-butanodiol en una cantidad de 0,01 a 10% en peso de la composición.

18. La composición de relleno de cualquiera de las reivindicaciones 1-14 para su uso en un método de aumento de tejido blando.

19. La composición de relleno de la reivindicación 18, en la que se inyecta un volumen de 20 a 60 ml de la composición de relleno en un único punto de inyección.

20. La composición de relleno de la reivindicación 18 o 19, en la que:

la composición de relleno estimula el crecimiento de colágeno;

el medio de transporte forma un andamio temporal para el crecimiento de colágeno entre las gotitas; y

una matriz de colágeno ancla las gotitas en su lugar a medida que el andamiaje temporal se disuelve en un plazo de 7 a 35 días.

21. La composición de relleno de la reivindicación 18, 19 o 20, en la que la composición de relleno se inyecta en un pene o un escroto para mejorar el pene o el escroto.