NCT 03796728

Study ID: CMO-MA-FAS-0512

Title: LIPS: A Prospective, Open-label Study to Evaluate the Effectiveness of Juvéderm® VOLIFT™ with Lidocaine for Lip Augmentation

Protocol Date: 10-OCT-2019

Clinical Study Protocol

LIPS: A Prospective, Open-label Study to Evaluate the Effectiveness of Juvéderm® VOLIFT™ with Lidocaine for Lip Augmentation

CMO-MA-FAS-0512

Development Phase:	Phase IV, Post-marketing
Product:	Juvéderm® VOLIFT™ with Lidocaine injectable gel
Indication:	Lip Augmentation
Sponsor:	Allergan Pharmaceuticals International Limited Clonshaugh Industrial Estate Coolock, Dublin 17, Ireland
Version and Date	Version 3, 10th October 2019
Serious Adverse Event Reporting Information: JUVÉDERM® VOLIFT® with Lidocaine	[redacted]

[redacted]

PRINCIPAL INVESTIGATOR'S AGREEMENT

I have read and understand the contents of this clinical protocol for Study No. CMO-MA-FAS-0512 Version 3 dated 10th October 2019 and will adhere to the study requirements as presented, including all statements regarding confidentiality

I agree to:

- Implement and conduct this study diligently and in strict compliance with the protocol, good clinical practices and all applicable laws and regulations.
- Maintain all information supplied by Allergan in confidence and, when this information is submitted to an Independent Ethics Committee (IEC) or another group, it will be submitted with a designation that the material is confidential.

I have read this protocol in its entirety and I agree to all aspects.

Signature **Date**

Name of Principal Investigator:

Name of Clinic

SPONSOR'S REPRESENTATIVE:

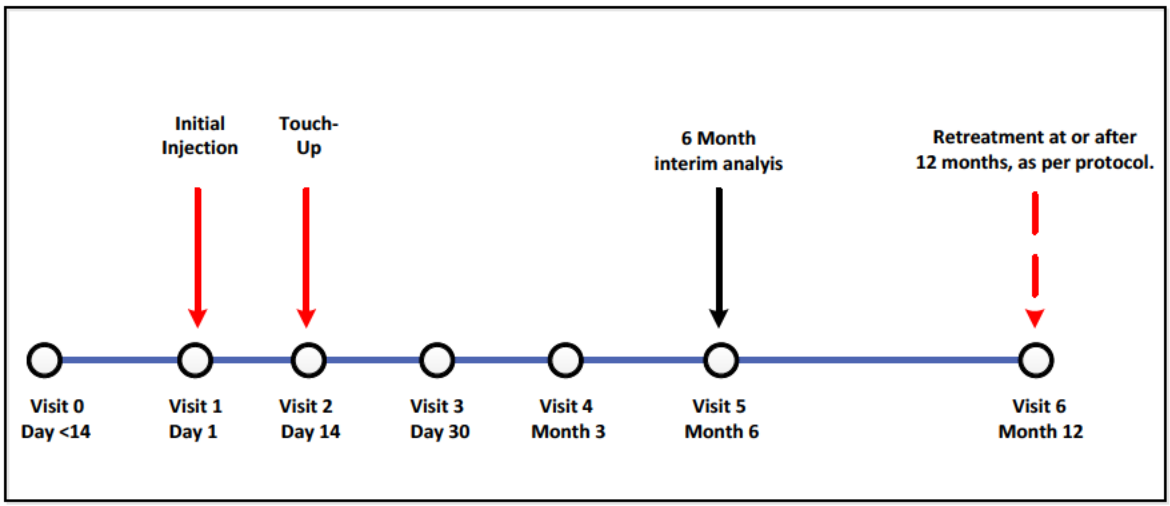
[redacted]

DATE: 10th October 2019

PROTOCOL SUMMARY

Sponsor: Allergan Pharmaceuticals International Limited, Clonshaugh Industrial Estate, Coolock, Dublin 17, Ireland	**Investigational Products:** Juvéderm® VOLIFT™ with Lidocaine	**Developmental Phase:** Phase IV, Post-marketing
Title of Study: LIPS: Prospective, open-label study to evaluate the effectiveness of Juvéderm® VOLIFT™ with Lidocaine for lip augmentation		
Protocol Number: CMO-MA-FAS-0512		
Number of Subjects: 60 subjects		
Indication: Lip augmentation		
Primary Study Objective: To evaluate the effectiveness of Juvéderm® VOLIFT™ with Lidocaine for lip augmentation. **Secondary Study Objectives:** To quantify the Investigators' and subject's assessment of aesthetic improvement of their lips.		
Methodology: This is a prospective, open-label, multi-centre, interventional, medical device, post-marketing study. Each subject will act as his/her own control. Eligible subjects will undergo treatment with Juvéderm® VOLIFT™ with Lidocaine injected into the lips for lip augmentation. All subjects will sign an informed consent form, and begin at the Screening Visit (V0). Filler treatment (Juvéderm® VOLIFT™ with Lidocaine) will be performed at V1 (Initial Treatment visit) and data will be collected at this visit for all relevant parameters as per the *Schedule of Study Procedures, Treatments and Assessments* (*Table 1.1*). Fourteen days after the initial treatment, subjects will return to the clinic and the Investigator will assess whether a Touch-up treatment is to be performed at this visit (V2). Follow-up visits will occur at V3, V4, V5, and V6 at 1, 3, 6, 12 months after the last treatment.		

Study Schema



[redacted]

Criteria for Evaluation:

Primary Endpoint

The primary endpoint will be the responder rate for lip fullness on the Lip Fullness Scale (LFS2), which is defined as the proportion of subjects who show ≥ 1-point improvement on the LFS2 compared to baseline assessment at Day 30 (after last treatment received) as assessed by the Investigator.

Secondary Endpoints

- Investigator assessment of oral commissures lines as measured by the 4-point Oral Commissures Severity Scale (OCSS) change in mean from baseline to V3, V4, V5, and V6.
- Subject's assessment of overall satisfaction with lips as measured by the FACE-Q Lips Questionnaire change in mean from baseline to V3, V4, V5, and V6.
- Investigator's assessment of global facial aesthetic improvement as measured by the 5-point Global Aesthetic Improvement Scale (GAIS) at V2, V3, V4, V5, and V6.

- Subject's assessment of global facial aesthetic improvement as measured by the 5-point GAIS at V3, V4, V5, and V6.
- Subject's assessment of natural look, feel and smoothness of their lips as measured on a 5-point Lickert scale after each treatment and at V3, V4, V5, and V6.
- Investigator's assessment of product smoothness as measured on a 5-point Lickert scale after each treatment and at V3, V4, V5, and V6.
- Investigator's assessment of dynamic lip lines upon animation at V3, V4, V5, and V6.

Key Criteria for Inclusion:

1. Male or female, 18 years of age or older
2. Signed the Institutional Independent Ethics Committee (IEC)-approved informed consent form prior to any study-related procedures being performed
3. Accept the obligation not to receive any other facial procedures or treatments anywhere in the lower face (below the orbital rim), neck, and oral cavity at any time during the study that are not related to the study
4. [redacted]
5. Women of childbearing potential must have a negative urine pregnancy test before each injectable treatment and practice a reliable method of contraception throughout the study
6. Ability to follow study instructions and likely to complete all required visits and assessments, as assessed by the Investigator.

Key Criteria for Exclusion:

1. [redacted]
2. Has lip tattoos or is planning lip tattoos during the course of the study, piercings, facial hair, or scars that would interfere with visualization of the lips and perioral area
3. Has dentures or any device covering all or part of the upper palate, and/or severe malocclusion or dentofacial or maxillofacial deformities
4. Has undergone oral surgery (e.g., tooth extraction, orthodontia, or implantation) within 6 weeks before enrollment or is planning to undergo any of these procedures during the study
5. Has ever undergone facial plastic surgery or received permanent facial implants (e.g., polymethylmethacrylate, silicone, polytetrafluoroethylene) anywhere in the face or neck, or is planning to be implanted with any of these products during the study

6. Has undergone semi-permanent dermal filler treatment (e.g., hyaluronic acid, calcium hydroxylapatite, poly-L-lactic acid) in the lower face (below the orbital rim) within 24 months before enrollment or is planning to undergo such treatment during the study
7. Has undergone mesotherapy or cosmetic resurfacing (laser, photo-modulation, intense pulsed light, radiofrequency, dermabrasion, chemical peel, or other ablative or non-ablative procedures) anywhere in the face or neck, or Botulinum toxin injections in the lower face (below the orbital rim) within 6 months before enrollment or is planning to undergo any of these procedures during the study
8. Has used any lip plumping products within 10 days before enrollment or is planning to use such products during the study (study treatment may be delayed as necessary to accommodate this 10-day washout period)
9. Has begun using any over-the-counter or prescription, oral or topical, anti-wrinkle products for the lips or around the mouth within 90 days before enrollment or is planning to begin using such products during the study (subjects who have been on a regimen of such products for at least 90 days are eligible for the study if they intend to continue their regimen throughout the study)
10. Is on an ongoing regimen of anti-coagulation therapy (e.g., warfarin) or non-steroidal anti-inflammatory drugs (NSAIDs) (e.g., aspirin, ibuprofen) or other substances known to increase coagulation time (e.g., herbal supplements with garlic or gingko) within 10 days of undergoing study device treatment (study treatment may be delayed as necessary to accommodate this 10-day washout period)
11. Is on a concurrent regimen of lidocaine or structurally related local anesthetics (e.g., bupivacaine)
12. Has a history of anaphylaxis, atopy, or allergy to lidocaine, hyaluronic acid (HA) products, or Streptococcal protein, or is planning to undergo desensitization therapy during the study
13. Has an active inflammation, infection, cancerous or precancerous lesion, or unhealed wound in the mouth area
14. Has porphyria
15. Has epilepsy
16. Has impaired cardiac conduction, severely impaired hepatic function, or severe renal dysfunction
17. Has any uncontrolled disease
18. Females who are pregnant, nursing, or planning a pregnancy
19. Current enrollment in an investigational drug or device study, participation in such a study within 6 weeks before enrollment, or be planning to participate in another investigation during the course of this study
20. Is an employee (or immediate relative of an employee) of the Investigator, Allergan, or a representative of Allergan

21. [redacted]
Products, Dose, and Mode of Administration: [redacted] Juvéderm® VOLIFT™ with Lidocaine is indicated for the treatment of deep skin depressions, face contouring, and volume restoration via deep dermis or lips mucosa injection. The Investigator will determine the appropriate volume of Juvéderm® VOLIFT™ with Lidocaine to be injected to augment the lips It is anticipated that the volume of Juvéderm® VOLIFT™ with Lidocaine to be injected for lip augmentation [redacted]
Concomitant Medications: Therapy considered necessary for the subject's welfare may be given at the discretion of the Investigator, including but not limited to medications for other conditions (i.e., hypertension, diabetes, etc.), and treatment of adverse events (AEs). All medications or treatments (including any dermal or facial aesthetic procedures) received by the subject within 30 days before the Initial Treatment visit and throughout the study, must be recorded in the study source documents and electronic case report form (eCRF).
Study Duration: Each subject will participate in the study for up to approximately 6 months.
Statistical Methods: The primary efficacy endpoint is the responder rate for lip fullness on the LFS2, which is defined as the proportion of subjects who show ≥ 1-point improvement on the LFS2 at the Day 30 visit compared to baseline assessment, as determined by the Investigator at the clinic visit. As there is no formal statistical hypothesis testing in this study descriptive statistics will be provided only. Details of the analyses for all other efficacy endpoints will be documented in the Statistical Analysis Plan (SAP).

[redacted]

[redacted]

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LIST OF ABBREVIATIONS

Abbreviation	Definition
AE	adverse event
ADE	adverse device effect
CFR	Code of Federal Regulations
DFU	Directions For Use
eCRF	electronic case report form
FDA	Food and Drug Administration
GAIS	global aesthetic improvement scale
GCP	Good Clinical Practice
HA	hyaluronic acid
ICF	informed consent form
ICH	International Conference on Harmonisation
IEC	Independent Ethics Committee
IRB	Institutional Review Board
ISR	injection site reaction
LFS2	lip fullness scale
NSAIDs	non-steroidal anti-inflammatory drugs
OCSS	oral commissures severity scale
POLSS	perioral lines severity scale
SAE	serious adverse event
SADE	serious adverse device effect
UADE	unanticipated adverse device effect
US	United States

1 INTRODUCTION

1.1 BACKGROUND

As a key aesthetic feature of the face, fullness and voluptuousness of the lips are associated with attractiveness, sensuality, and youth. Similar to the skin, however, the lips are prone to intrinsic and extrinsic factors that can dramatically change their appearance over time.

Repetitive and underlying action of the orbicularis oris muscle leads to the formation of visible, fine, vertical rhytides surrounding the lips. The tolls of gravity coupled with the loss of lip volume and support cause the upper lip to lengthen and the lip to fall vertically. As collagen production diminishes, the Cupid's bow and vermilion border lose their distinction.[1] The morphological changes of the lips over time become an obvious sign of aging. Unfortunately, because the connotation with youth is the ability to be an active and productive member of society, the pressure on individuals to conceal the signs of aging is tremendous. The inability to do so is correlated with increased anxiety and depression.[2]

Treatment with temporary dermal fillers can provide volume to the lips and perioral area, three-dimensionally restoring the natural contour of the region to which it is applied and thereby reducing some of the signs of aging lips. Several technologies have been developed for cosmetic augmentation of the lips, including injection of paraffin, oils, silicone, polymethylmethacrylate beads, autologous fat, and injectable collagen. However, allergic reactions, inadequate duration effects, and logistics of the treatment (e.g., separate surgeries) have made them impractical.[3,4] The development of cross-linked hyaluronic acid (HA)-based dermal fillers has since provided a safe, effective, and long-lasting option to volume enhancement of the lips. Currently, lip augmentation is recognized as one of the most common uses for dermal fillers, especially HA products.[5,6,7,8,9,10,11]

Restoration of aging lips is an intricate endeavor in which the physician must take into account the multiple changes that have contributed to their overall aged appearance. The areas of injection for lip augmentation include the cutaneous (white) and red lips, i.e., vermilion (body of the red lip), vermilion borders (often in the potential space between the skin and the orbicularis oris muscle), Cupid's bow and philtral columns, perioral rhytides (vertical "lipstick" lines), and oral commissures (marionette folds). Injection into the vermilion and vermilion borders may indirectly cause improvement in perioral line severity. Treatment of the perioral lines and oral commissures may not be indicated in all patients, and treatment to accentuate the Cupid's bow and/or philtral columns may not be desired by many. Ideally, usage of a product with the malleability and range to treat different areas of the lips and perioral complex would provide the most realistic and satisfactory aesthetic result.

1.2 JUVÉDERM® PRODUCTS

As described below, the investigations assessing the safety and effectiveness of HA-based dermal fillers for volume restoration of the lips have demonstrated treatment success and high patient satisfaction. Longevity of treatment with HA fillers has been reported to be longer than treatment with collagen[12,13] although the longevity of effect is relatively short-lived compared to treatment of other facial areas.

- In a multi-center European post-marketing study of the safety and effectiveness of Juvéderm® VOLBELLA without lidocaine for lip enhancement, 60 subjects desiring lip enhancement and who met eligibility criteria were treated. Interim results 3 months post-treatment show that 93.2% of subjects displayed ≥1-point improvement on the 4-point Lip Fullness Scale and 100% of Investigators and 98.3% of subjects affirmed that the pre-established lip fullness goal had been achieved (Study S15-002).
- In a multi-center clinical feasibility study for lip enhancement using Juvéderm® Ultra conducted in the United States (US) (Study JD-003), lip fullness and effectiveness of treatment was evaluated in 50 subjects who had established lip fullness goals. A separate, blinded Independent Evaluator and the subject assessed lip fullness, perioral lines, and oral commissures using validated scales. Standardized 3D images were taken to measure lip volume changes. Results showed that 71% of subjects ($p < 0.0001$) achieved their lip fullness goals and improved ≥ 1-point on the 4-point Lip Fullness Scale at the 12-week primary endpoint. Perioral line severity improved for up to 63% of subjects. Subject overall satisfaction at the 12-week endpoint was 82%, and 78% of subjects were willing or very willing to undergo study treatment again.[14]
- A post-marketing surveillance study assessed treatment comfort and aesthetic effect in 57 patients treated with Juvéderm® Ultra Smile. The most common site for injection was the vermilion border, and 95% of injectors found the gel easy to inject. Furthermore, 99% of injectors rated improved aesthetic compared to baseline. Patient satisfaction with the product was 96%.[15]

As with any dermal treatment injection, pain during administration is a possible side effect. Importantly, pain experienced during injection may compromise the physician's ability to perform the procedure with precision.[12] Physicians typically use pain-relieving agents concomitant with injection, such as a nerve block, topical anesthesia, or a local anesthetic. The inclusion of lidocaine in the HA formulation itself is intended to reduce the patient's pain during the procedure and reduce or eliminate the need for additional pain-relieving agents. As described below, pain scores have consistently been reduced with HA-based dermal fillers containing a standard amount of lidocaine (0.3%) without compromising the aesthetic result. Furthermore, lidocaine in the formulation did not affect the rheology, duration of effect, or frequency of adverse events.[16,17,18,19]

Juvéderm® VOLIFT™ with Lidocaine, included in the Juvéderm® range of products, is a malleable product capable of fitting the physical constraints that would be experienced with injection and volume expansion of the lips. The addition of lidocaine (0.3% w/w) is to increase patient comfort during treatment. Thus, the characteristics of Juvéderm® VOLIFT™ with Lidocaine should render it effective for lip volume restoration and enhancement, with increased patient comfort during treatment and a long-lasting duration.

The Juvéderm® family of non-animal HA gel implants was first CE marked and marketed in Europe in 2000, introduced into Canada in 2002, and US Food and Drug Administration (FDA)-approved in 2006. The Juvéderm® family is now approved in numerous countries throughout the world, including Korea (2004), Australia (2006), Mexico (2006), Brazil (2007), Columbia (2007), Hong Kong (2009), India (2009), and Taiwan (2009). Juvéderm®

products have not been withdrawn from any country for any reason related to safety and effectiveness of the device.

Juvéderm® VOLIFT™ with Lidocaine gained CE mark in October 2011. The product label is as follows: medical devices for the treatment of cutaneous depressions and the restoration of volumes.

Refer to the *Juvéderm® VOLIFT™ with Lidocaine Directions for Use (Appendix 1)* for further details of the mitigation of risks of Juvéderm® VOLIFT™ with Lidocaine.

2 STUDY OBJECTIVES AND CLINICAL HYPOTHESIS

2.1 STUDY OBJECTIVES

2.1.1 Primary Study Objective

To evaluate the effectiveness of Juvéderm® VOLIFT™ with Lidocaine for lip augmentation.

2.1.2 Secondary Study Objectives

To quantify the Investigators' and subject's assessment of aesthetic improvement of their lips.

2.2 CLINICAL HYPOTHESIS

The clinical hypothesis of this study is that a significant proportion of subjects treated with Juvéderm® VOLIFT™ with Lidocaine will achieve at least a 1-point improvement in the 5-point Lip Fullness Scale (LFS2) at 30 days post last treatment. Additionally, subjects will have a significantly higher satisfaction with lip appearance at post-treatment study visits when compared with baseline pre-treatment satisfaction scores, as measured by the mean change from baseline on the Satisfaction with Lips FACE-Q questionnaire. For subjects who additionally receive treatment for oral commissures a significant proportion of subjects will achieve an improvement in Oral Commissures Severity Scale (OCSS) score(s) at post-treatment study visits when compared with baseline pre-treatment scores. Investigators' and subjects' global satisfaction with the aesthetic outcome will also be assessed.

3 STUDY DESIGN

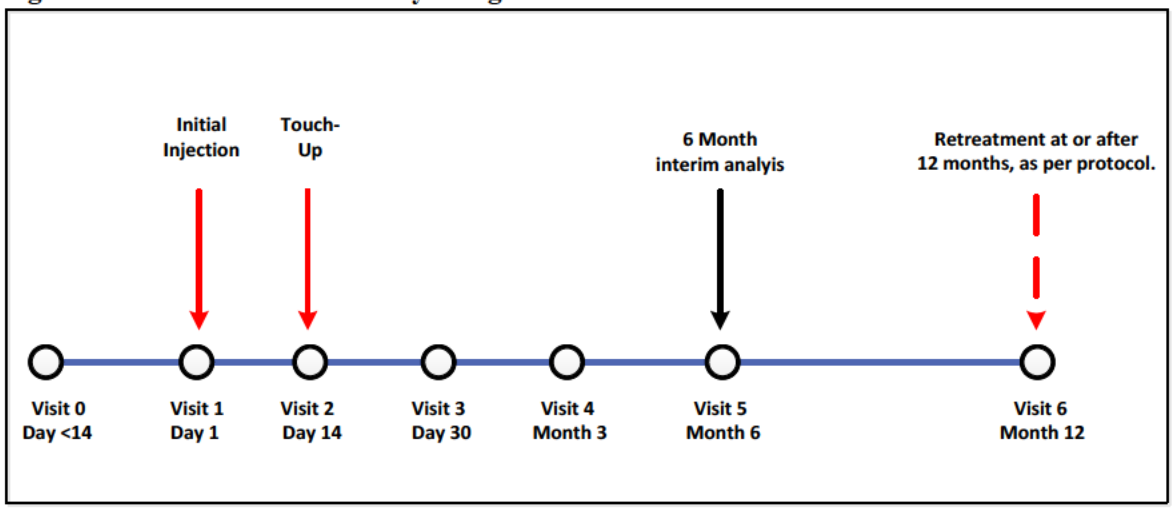
This is a prospective, open-label, multi-centre, interventional, medical device, post-marketing study evaluating the effectiveness of Juvéderm® VOLIFT™ with Lidocaine for lip augmentation. Subjects will attend up to 7 visits: Screening, Initial Treatment, Day 14 (Touch-up, if required), Day 30, Month 3, Month 6, and Month 12. (Study Exit) (see *Figure 3.1*). 60 subjects will be enrolled.

Eligible subjects will undergo treatment with Juvéderm® VOLIFT™ with Lidocaine administered via injection for enhancement as per the current DFU. Fourteen days after the initial treatment, subjects will return to the clinic and the Investigator will assess the effectiveness of treatment. If the Investigator judges that optimum correction has not been achieved, an optional Touch-up treatment may be performed during the Day 14 visit.

Subjects who receive Touch-up treatment at the Day 14 visit will attend their Day 30 visit 30 days after their last treatment (ie, after Touch-up). Similarly, subsequent follow-up visits for those subjects who undergo Touch-up treatment will occur at 3 and 6, and 12 months after the last treatment received.

At 12 months the subject will return to clinic and carry out all assessments. If eligible for treatment as per the VOLIFT Directions For Use and have had no other treatments / medications as described in the Inclusion / Exclusion since 6 months, the subject will be offered a free retreatment injection of Juvéderm® VOLIFT™ with Lidocaine. If the decision is made to not retreat at 12 months, but a later retreatment is planned, then the subject can be treated outside the study with free treatment.

Figure 3.1 Overall Study Design



Note if touch-up treatment administered, V3, V4, V5, and V6 will be +14 days.

4 STUDY POPULATION AND ENTRY CRITERIA

4.1 NUMBER OF SUBJECTS

60 subjects will be treated in this study. Subjects who "drop out" after receiving treatment on Day 1 will not be replaced.

4.2 INCLUSION CRITERIA

The following are requirements for entry into the study.

1. Male or female, 18 years of age or older
2. Signed the Institutional Review Board (IRB)/Independent Ethics Committee (IEC)-approved informed consent form prior to any study-related procedures being performed

3. Accept the obligation not to receive any other facial procedures or treatments anywhere in the lower face (below the orbital rim), neck, and oral cavity at any time during the study that are not related to the study
4. [redacted]
5. Women of childbearing potential must have a negative urine pregnancy test before each injectable treatment and practice a reliable method of contraception throughout the study
6. Ability to follow study instructions and likely to complete all required visits and assessments, as assessed by the Investigator.

4.3 EXCLUSION CRITERIA

1. [redacted]
2. Has lip tattoos or is planning lip tattoos during the course of the study, piercings, facial hair, or scars that would interfere with visualization of the lips and perioral area
3. Has dentures or any device covering all or part of the upper palate, and/or severe malocclusion or dentofacial or maxillofacial deformities
4. Has undergone oral surgery (e.g., tooth extraction, orthodontia, or implantation) within 6 weeks before enrollment or is planning to undergo any of these procedures during the study
5. Has ever undergone facial plastic surgery or received permanent facial implants (e.g., polymethylmethacrylate, silicone, polytetrafluoroethylene) anywhere in the face or neck, or is planning to be implanted with any of these products during the study
6. Has undergone semi-permanent dermal filler treatment (e.g., hyaluronic acid, calcium hydroxylapatite, poly-L-lactic acid) in the lower face (below the orbital rim) within 24 months before enrollment or is planning to undergo such treatment during the study
7. Has undergone mesotherapy or cosmetic resurfacing (laser, photo-modulation, intense pulsed light, radiofrequency, dermabrasion, chemical peel, or other ablative or non-ablative procedures) anywhere in the face or neck, or Botulinum toxin injections in the lower face (below the orbital rim) within 6 months before enrollment or is planning to undergo any of these procedures during the study
8. Has used any lip plumping products within 10 days before enrollment or is planning to use such products during the study (study treatment may be delayed as necessary to accommodate this 10-day washout period)
9. Has begun using any over-the-counter or prescription, oral or topical, anti-wrinkle products for the lips or around the mouth within 90 days before enrollment or is planning to begin using such products during the study (subjects who have been on a regimen of such products for at least 90 days are eligible for the study if they intend to continue their regimen throughout the study)
10. Is on an ongoing regimen of anti-coagulation therapy (e.g., warfarin) or non-steroidal anti-inflammatory drugs (NSAIDs) (e.g., aspirin, ibuprofen) or other substances known to increase coagulation time (e.g., herbal supplements with garlic or gingko) within 10 days of undergoing study device treatment (study treatment may be delayed as necessary to accommodate this 10-day washout period)

11. Is on a concurrent regimen of lidocaine or structurally related local anesthetics (e.g., bupivacaine)
12. Has a history of anaphylaxis, atopy, or allergy to lidocaine, HA products, or Streptococcal protein, or is planning to undergo desensitization therapy during the study
13. Has an active inflammation, infection, cancerous or precancerous lesion, or unhealed wound in the mouth area
14. Has porphyria
15. Has epilepsy
16. Has impaired cardiac conduction, severely impaired hepatic function, or severe renal dysfunction
17. Has any uncontrolled disease
18. Females who are pregnant, nursing, or planning a pregnancy
19. Current enrollment in an investigational drug or device study, participation in such a study within 6 weeks before enrollment, or be planning to participate in another investigation during the course of this study
20. Is an employee (or immediate relative of an employee) of the Investigator, Allergan, or a representative of Allergan
21. [redacted]

4.4 PERMISSIBLE AND PROHIBITED MEDICATIONS/TREATMENTS

4.4.1 Permissible Medications and/or Treatments

Therapy considered necessary for the subject's welfare may be given at the discretion of the Investigator, including but not limited to medications for other conditions (i.e., hypertension, diabetes, etc.), and treatment of adverse events (AEs). Medications should be taken consistently throughout the study and at the Investigator's discretion.

4.4.1.1 Anesthesia

Local anesthesia may be used in the area of treatment at the discretion of the Investigator/ Injector. Since the product contains lidocaine no other injectable anesthesia is expected to be used. The type of anesthesia used and dose of anesthesia during the treatment is at the clinical judgment of the Investigator/Injector. Anesthesia use elsewhere is prohibited.

The type, drug, dose and administration method of anesthesia shall be recorded. Anesthesia is to be administered according to local site practice.

4.4.1.2 Rescue Medications

Although several authors have reported that hyaluronidase (Vitrase™ or Amphadase®) is effective to reverse the effects of misplaced or excess HA-based dermal fillers, no product has been approved for this indication. Administration of hyaluronidase is considered to be

"off-label" and has not been provided as a part of the study regimen and should not be performed during this study. However, if in the Investigator's judgment it is deemed to be necessary to inject hyaluronidase for the safety of the subject, then the Investigator may inject at his/her discretion, capturing this information as a concomitant medication.

4.4.1.3 Acceptable Contraceptive Methods

Women of childbearing potential are required to practice a reliable method of contraception throughout the study. The following methods of contraception, if properly used, are generally considered reliable: oral contraceptives, patch contraceptives, injection contraceptives, male condom with intra-vaginal spermicide, diaphragm or cervical cap with spermicide, vaginal contraceptive ring, intrauterine device, surgical sterilization (bilateral tubal ligation), vasectomized partner, or sexual abstinence.

The Investigator and each subject will determine the appropriate method of contraception for the subject during the participation in the study.

4.4.2 Prohibited Medications/Treatments

The decision to administer a prohibited medication/treatment will be made with the safety of the study participant as the primary consideration. When possible, the Sponsor or Sponsor's representative should be notified before a prohibited medication/treatment is administered.

Prior to attending study visits, subjects must not apply facial cosmetics.

For information regarding medications requiring washout prior to treatment, see *Section 6.1.3: Washout of Prohibited Medications/Treatments*.

4.4.2.1 Anticoagulant Medications

Subjects must not initiate a regimen of anti-coagulation therapy (e.g., warfarin), NSAIDs or other substances known to increase coagulation time (e.g., herbal supplements with garlic or ginkgo biloba) for 3 days following the procedure.

4.4.2.2 Facial Procedures/Treatments

Subjects must not undergo any type of facial plastic or reconstructive surgery, dental or cosmetic procedure [e.g., dental implant, new dentures, face-lift, resurfacing (laser, photomodulation, intense pulsed light, radio frequency, dermabrasion, chemical peel, or other ablative or non-ablative procedures), tissue augmentation with dermal fillers or fat injections, BOTOX® Cosmetic injections, or mesotherapy] anywhere in the lower face (below the orbital rim), neck, and oral cavity at any time during the study.

4.4.2.3 Special Diet or Activities

Within the first 24 hours after filler treatment, on V1, if a Touch-up treatment is performed on V2, or retreatment at V6, subjects should avoid strenuous exercise, extensive sun or heat exposure and alcoholic beverages. Exposure to any of the above may cause temporary redness, swelling, and/or itching at the injection sites.

5 TREATMENT

5.1 INVESTIGATIONAL PRODUCT

Juvéderm® VOLIFT™ with Lidocaine injectable gel is a sterile, biodegradable, non-pyrogenic, viscoelastic, clear, colorless, homogeneous gel implant (dermal filler). It consists of [redacted] formulated to a concentration of 17.5 mg/mL and [redacted] lidocaine in a physiologic buffer.

Commercial grade product will be provided by Allergan for use in this study, at no cost to the subject

5.1.1 Blinding and Randomization

This is an open-label, single-arm study. Thus, blinding and randomization methods will not be implemented.

5.2 STORAGE, HANDLING AND DESTRUCTION

5.2.1 Storage

[redacted]

5.3 TREATMENT ADMINISTRATION

The Investigator will determine the appropriate volume of Juvéderm® VOLIFT™ with Lidocaine to be injected to augment the lips (e.g., add fullness). It is anticipated that the volume of Juvéderm® VOLIFT™ with Lidocaine to be injected for lip augmentation will not exceed 3.0mL total per patient.

Full details for the injection of Juvéderm® VOLIFT™ with Lidocaine will be provided in the *Juvéderm® VOLIFT™ with Lidocaine Directions for Use (Appendix 1).*

For information on use of local anesthesia and use of rescue medications, refer to *Section 4.6.1.1* and *Section 4.6.1.2*, respectively.

6 STUDY VISIT SCHEDULE AND PROCEDURES

6.1 PATIENT ENTRY PROCEDURES

Prospective patients as defined by the criteria in *Sections 4.2 (Inclusion Criteria)* and *4.3 (Exclusion Criteria)* will be considered for entry into this study.

6.1.1 Informed Consent

The study will be discussed with the patient. The subject must give written informed consent subject prior to the performance of any study-related procedures, inclusive of screening procedures, or change(s) in treatment, e.g. washout of medications.

See *Section 11.6: Informed Consent* for additional information and requirements regarding informed consent.

Informed Consent Extension to Follow-up

[redacted]

6.1.2 Subject Number

All subjects who provide informed consent will be assigned a subject number [redacted]

6.1.3 Washout of Prohibited Medications/Treatments

If washout of any medications is required, the subject must provide written informed consent before the washout can commence.

Table 6.1 lists the medications/treatments that are prohibited during the study and the length of time that must pass between the medication/treatment and treatment in the study.

For additional information/examples of specific treatment/procedures, refer to *Section 4.3 (Exclusion Criteria)*.

Study treatment may be delayed as necessary to accommodate the washout period. If treatment is delayed beyond the 14-day screening period (see *Table 1.1: Schedule of Study Procedures, Treatments, and Assessments*), screening procedures are to be repeated as necessary to confirm participation eligibility. The inclusion/exclusion criteria must be reassessed and the patient eligibility confirmed prior to study treatment.

Table 6.1 Washout Periods of Medications/Treatment

6.1.4 Subject Enrollment

A subject is considered "entered" into the trial after the subject has signed the Informed Consent Form (ICF) and a subject number has been assigned.

A subject is considered "enrolled" after confirmation of participation eligibility and treatment has occurred.

6.2 DESCRIPTION OF STUDY VISITS

[redacted]

6.2.2 Treatment

The Treatment visit is considered as Day 1. Subjects confirmed to be eligible for participation during the screening period will receive study treatment as described in *Section 5.3: Treatment Administration*

6.2.2.1 Prior to Study Treatment

[redacted]

[redacted]

6.2.2.2 Study Treatment

Administer study treatment as described in *Section 5.3: Treatment Administration*

6.2.2.3 Post Study Treatment

[redacted]

6.2.3 Day 14 Visit (Touch-up Treatment, if required)

[redacted]

6.2.3.1 For All Subjects

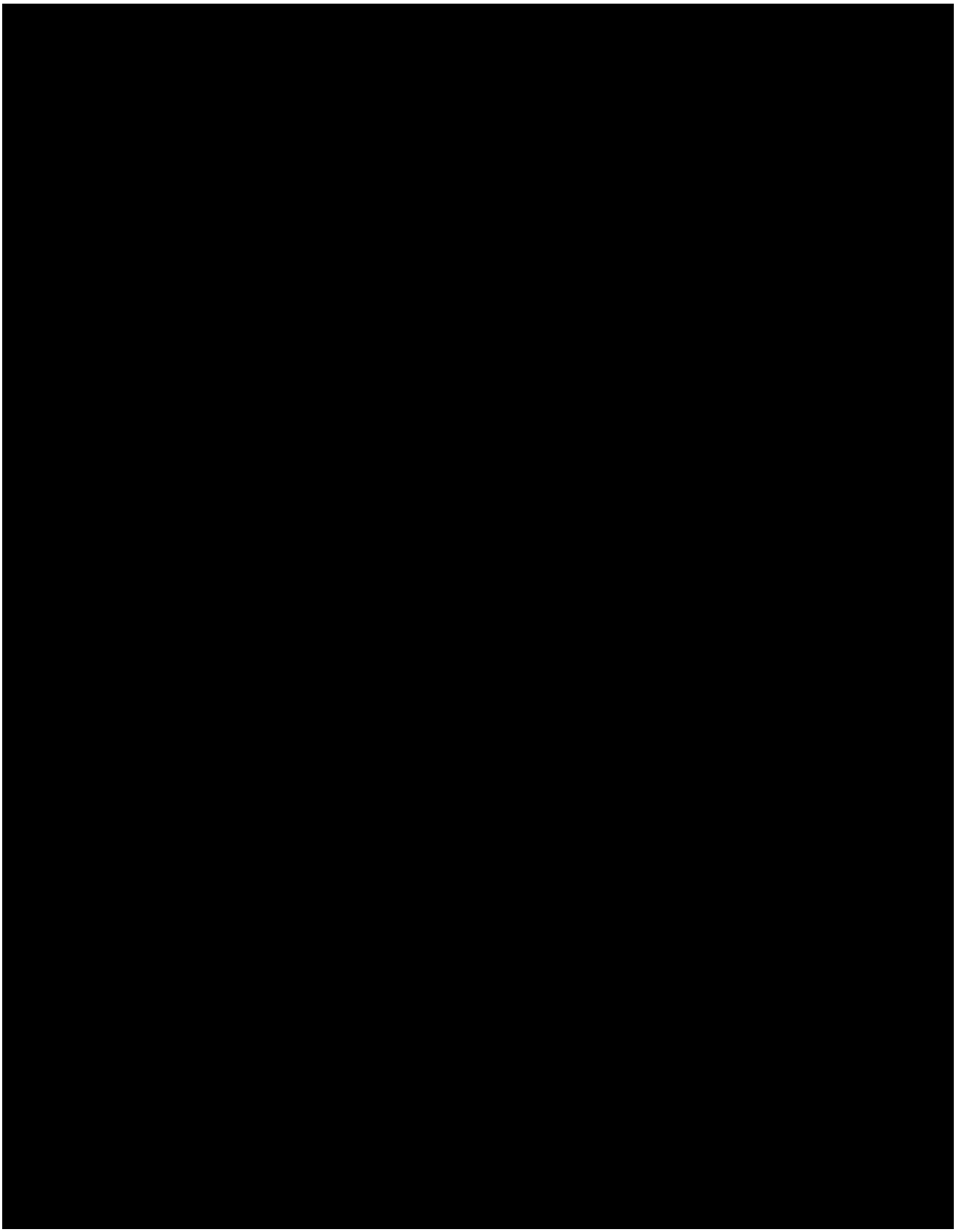
- Record concomitant medications/procedures.
- Record AEs.

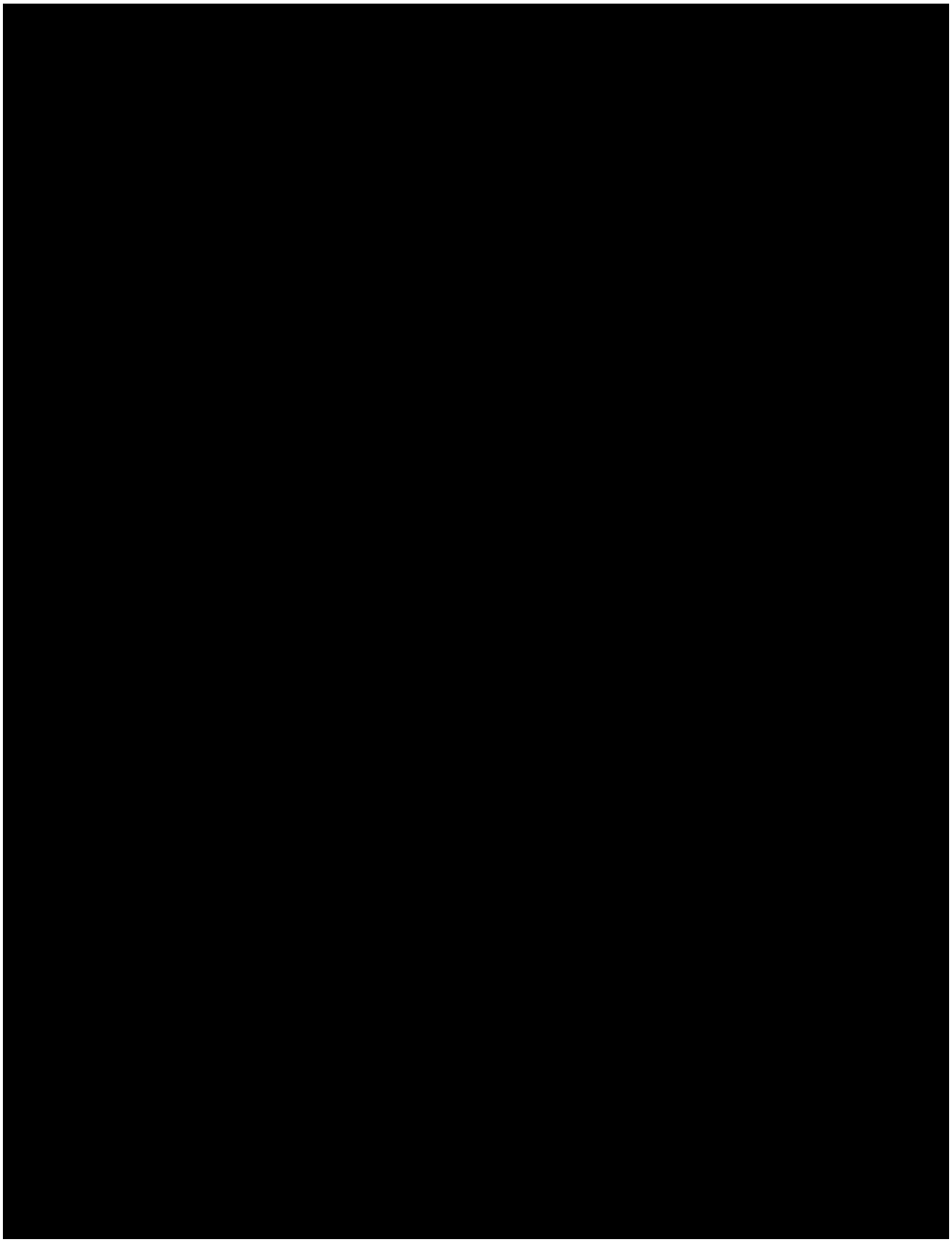
[redacted]

- Investigator and subject determine if Touch-up Treatment is required.

6.2.3.2 For Subjects Receiving Touch-Up Treatment

6.2.4 Day 30 Visit





[redacted]

6.2.8 Unscheduled Visits

Each time the subject returns to the study site, the Investigator (or designee) will solicit and record information about ISRs, AEs, and concomitant medications/procedures. An interim or unscheduled visit may replace a scheduled visit if it occurs within the acceptable visit window for a scheduled visit or if the scheduled visit was missed. All applicable procedures should be performed.

6.2.9 Early Discontinuation

Subjects may withdraw consent for participation or be withdrawn from the study at any time without jeopardy to future medical care. See *Section 8: Discontinuation Criteria* regarding reasons for discontinuations.

If a subject exits the study prior to month 6, the subject will be asked to attend an end of study visit and have all assessments performed and clinical data collected as required by the month 6 visit. If a subject does not consent to the extension of the study at completion of their 6-month visit, this will be recorded in the database.

Participation eligible subjects who withdraw before any treatment is given may be replaced by another suitable subject. The subject number will not be reassigned to a different subject.

6.3 POST-TREATMENT INSTRUCTIONS FOR SUBJECTS

Prior to leaving the study site, the subject's next study visit should be scheduled and a reminder card provided to the subject. If possible, the remainder of the visits should be scheduled at the end of the Day 14 visit.

[redacted]

7 METHODS OF ASSESSMENT AND ENDPOINTS

7.1 STUDY PROCEDURES

7.1.1 Demographic Data

Subject demographic data will be collected at the Screening Visit.

These data include age, gender, and Fitzpatrick type.

7.1.2 Medical History

Medical history will be obtained from each subject at the Screening Visit.

Medical history includes pertinent surgical history and a detailed history of prior aesthetic procedures with start and stop dates, if applicable, as well as any discontinuations due to intolerability or toxicity.

7.1.3 Concomitant Medications/Procedures

Concomitant medication/procedure status shall be collected at all visits. Concomitant medications include prescription medications, dietary supplements, over-the-counter medications, and oral herbal preparations.

A list of concomitant medications/procedures will be collected at the screening visit. Data collected shall be medication/treatment name, dose, frequency, start date, stop date (if applicable). All medications or treatments received within 30 days before the screening visit shall be recorded. Medications/procedures received more than 30 days before screening and in the Investigators judgment is pertinent to this study, should also be recorded.

Following treatment at Day 1, subjects will be asked at each subsequent study visit whether any new medication/procedures have been administered or of any changes in dosage or frequency, have occurred since the previous visit. All concomitant medications and procedures will be recorded on eCRFs.

7.1.4 Fitzpatrick Skin Phototype

The subject's Fitzpatrick skin phototype will be determined at the screening visit using the parameters listed in *Table 7.1.*

Table 7.1 Fitzpatrick Skin Phototype

Skin type	Typical Features	Tanning ability
I	Pale white skin, blue/green eyes, blond/red hair	Always burns, does not tan
II	Fair skin, blue eyes	Burns easily, tans poorly
III	Darker white skin	Tans after initial burn
IV	Light brown skin	Burns minimally, tans easily
V	Brown skin	Rarely burns, tans darkly easily
VI	Dark brown or black skin	Never burns, always tans darkly

7.1.5 Urine Pregnancy Test

The urine pregnancy test will be performed at the screening visit and prior to administration of any study treatment (Day 1 and Day 14, if applicable and at retreatment at Month 12). The urine pregnancy test will be performed only for women of childbearing potential. The woman's childbearing status must be clearly reported in the source documentation.

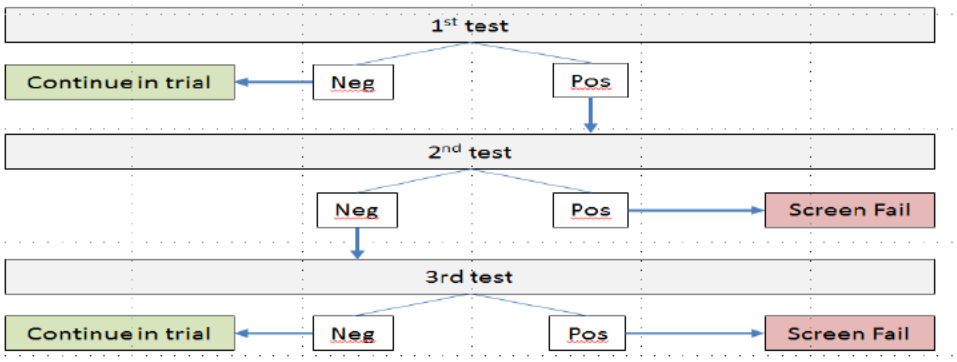
[redacted] Women of childbearing potential must have a negative pregnancy test before any study treatments are given. See *Figure 7.1* to determine pregnancy status.

Women who are determined to have negative pregnancy test results may continue in the study and receive study treatments as applicable.

- Women who are determined to have positive pregnancy test results prior to initial treatment must be informed of their pregnancy status and discontinued from the study as screen failures.
- Women who are determined to have positive pregnancy test results after receiving the initial treatment must be withdrawn from the study and have their pregnancy followed and reported per *Section 9.2.4: Pregnancy*.

- Women who are determined to have positive pregnancy test at re-treatment will not be eligible for the retreatment, and have their pregnancy followed and reported per *Section 9.2.4: Pregnancy*.

Figure 7.1 Pregnancy Test Results



Neg=negative; Pos=positive

7.1.6 Photographs

Facial photographs will be captured prior to study treatments and immediately after. Additional images will be captured at the Day 30, Month 3, Month 6, Month 12 and any subsequent visits. Images will be used by the investigator and subject for the facial assessments. [redacted]

[redacted]

[redacted] 3D photographs will also be taken for each subject to aid in facial assessments and measure the volume change in the lips.

Equipment and training for the capturing of images will be provided by a vendor selected by Allergan.

7.1.7 Injection Site Reaction (ISR) 30-Day Diary

The ISR 30-Day Diary will be completed by the subject beginning on the day of treatment and for 30 consecutive days. [redacted]

7.1.7.1 Day 1 Visit (Treatment)

The subject will be provided with an ISR Diary on the day of the study treatment. [redacted]

7.1.7.2 Day 14 Visit (Touch-up, if required)

[redacted]

7.1.7.3 Day 30 Visit

[redacted]

7.2 EFFICACY MEASURES

7.2.1 Lip Fullness Scale (LFS2)

The Lips Fullness Scale 2 (LFS2) is an Investigator assessment of overall lip fullness measured by a 5-point scale (see *Appendix 3: Lip Fullness Scale 2 (LFS2)*). The Investigator will use the LFPS2 to perform a live assessment of the subject at the visits specified in *Table 1.1: Schedule of Study Procedures, Treatments, and Assessments*. Photographic images will be collected to capture the subject status at the time of the live assessments.

7.2.2 Oral Commissures Severity Scale (OCSS)

The Oral Commissure Severity Scale (OCSS) is an Investigator assessment measured on a 4-point scale (see *Appendix 4: Oral Commissure Severity Scale (OCSS)*). The Investigator will use the OCSS to perform a live assessment of the subject at the visits specified in *Table 1.1: Schedule of Study Procedures, Treatments, and Assessments*. Photographic images will be collected to capture the subject status at the time of the live assessments.

7.2.3 FACE-Q Satisfaction with Lips

The subject will assess satisfaction using the 10 items on the Satisfaction with Lips questionnaire of the FACE-Q (see *Appendix 5)*. The responses to the items are combined to create a scale score that ranges from 0 to 100. This FACE-Q was designed to assess the impact of treatment from the subject's perspective.

7.2.4 Global Aesthetic Improvement Scale (GAIS) Questionnaires

7.2.4.1 GAIS Investigator

Investigator's assessment of global facial aesthetic improvement as measured by the 5-point GAIS (see *Appendix 6: Global Aesthetic Improvement Scale (GAIS)*).

7.2.4.2 GAIS Subject

Subject's assessment of global facial aesthetic improvement as measured by the 5-point GAIS (see *Appendix 6: Global Aesthetic Improvement Scale (GAIS)*).

8 DISCONTINUATION CRITERIA

8.1 DISCONTINUATION OF THE STUDY

The Investigator or Allergan, may terminate the Investigator's participation in this study after submission of a written notice. Allergan may terminate the study at any time for any reason.

8.2 DISCONTINUATION OF SUBJECTS

A subject may voluntarily withdraw or the Investigator may withdraw the subject at any time without prejudice to the subjects' future medical care by the investigator or institution. It is the responsibility of the site Investigator to discontinue a subject's participation when the subject's health or wellbeing is threatened by continuation in the study.

For any subjects who withdraw from the study, the date and reason for withdrawal should be recorded on the eCRF. If an AE or ISR is ongoing at the time of the withdrawal, the Investigator will attempt to follow the subject until the AE or ISR has resolved or stabilized.

8.2.1 Withdrawal Criteria

The following circumstances shall result in a subject's discontinuation from the study:

- the subject undergoes repeat treatment other than Touch-up at Day 14 or study retreatment
- If subject is administered any of the prohibited procedures listed as exclusionary in Section 4.3
- Subject is lost to follow-up. Subjects may be withdrawn if they do not return for follow-up visits. If a subject fails to return for one or more scheduled study visits, the Investigator will attempt to contact the subject to determine and document the reason the subject has failed to return and to encourage compliance with the study visit schedule.

The following circumstances may result in a subject's discontinuation from the study:

- AEs or serious adverse events (SAEs) that render the subject unable to continue study participation
- Protocol violation
- Non-compliance with study requirements
- Discretion of Investigator (must document reason on eCRF)
- Progressive injury (at the discretion of the Investigator)
- There are changes in the subject's condition that render the subject unacceptable for further participation in the judgment of the Investigator
- A subject is unable to physically or mentally tolerate the use of the test treatment

9 ADVERSE EVENTS

Throughout the course of the study (from the date of informed consent), all AEs will be monitored and recorded in source documents and on the AE eCRF. If an AE occurs, the first concern will be the safety of the study participant. All AEs related to study treatments or procedures will be followed until resolved or stabilized based on the Investigator's clinical judgement.

9.1 DEFINITIONS

9.1.1 Adverse Events (AE)

The reference safety data will be the current VOLIFT with Lidocaine instructions for use.

According to EN ISO 14155:2011 an AE is any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device or the comparator device.

NOTE 1: This definition includes events related to the investigational medical device or the comparator.

NOTE 2: This definition includes events related to the procedures involved.

NOTE 3: For users or other persons, this definition is restricted to events related to investigational medical devices.

Adverse advents are collected once informed consent has been obtained, regardless of whether or not the subject has been administered study treatment. Disease signs and symptoms that existed prior to the study treatment are not considered AEs unless the condition recurs after the subject has recovered from the pre-existing condition or the condition worsens in intensity or frequency during the study.

All AEs ongoing at the exit visit must be followed until resolved or stable, based on the investigator's clinical judgment.

9.1.2 Serious Adverse Events (SAE)

According to EN ISO 14155:2011 an SAE is an AE that:

- Led to death,
- Led to a serious deterioration in the health of the subject that
  - resulted in a life-threatening illness or injury, or
  - resulted in a permanent impairment of a body structure or a body function, or
  - required in-subject hospitalisation or prolongation of existing hospitalisation, or
  - resulted in medical or surgical intervention to prevent permanent impairment to body structure or a body function.

- Led to foetal distress, foetal death or a congenital abnormality or birth defect.

NOTE: Planned hospitalisation for a pre-existing condition, or a procedure required by the CIP, without serious deterioration in health, is not considered an SAE. Allergan considers all cancer AEs as SAEs. Abortion is also considered an SAE except for elective abortion of a normal fetus.

(See *Section 9.3: Procedures for Reporting an SAE/SADE*).

Any pre-planned surgery or procedure should be clearly documented in the site source documents by the medically qualified Investigator at the time of the subject's entry into the study.

9.1.3 Adverse Device Effect (ADE)

According to EN ISO 14155:2011 any AE related to the use of an investigational medical device, including those events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device.

NOTE 1: This definition includes AEs resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device.

NOTE 2: This definition includes any event resulting from use error or from intentional misuse of the investigational medical device.

9.1.4 Serious Adverse Device Effect (SADE)

According to EN ISO 14155:2011 a SADE is an ADE that resulted in any of the consequences characteristic of an SAE or that might have led to an SAE if

a) suitable action had not been taken, or

b) intervention had not been made, or

c) circumstances had not been less fortunate.

SADEs will be handled under the SAE reporting system.

9.1.5 Unanticipated Serious Adverse Device Effect (USADE)

According to EN ISO 14155:2011 a USADE is a serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the current version of the risk analysis report

NOTE: Anticipated serious adverse device effect (ASADE) is an effect which by its nature, incidence, severity or outcome has been identified in the risk analysis report.

9.1.6 Device Deficiency

A device deficiency is defined in accordance with ISO 14155 as "inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety, or performance." Device deficiencies include malfunctions, use errors, and inadequate labeling.

If a device deficiency occurs, the Investigator will notify the Sponsor by email at the email address provided on the cover page of this protocol. Allergan shall review all device deficiencies and determine/document in writing whether they could have led to a SADE. These shall be reported to the regulatory authority as required by national regulations.

9.1.7 Injection Site Reaction (ISR)

ISRs following treatment with dermal fillers include redness, pain after injection, tenderness to touch, firmness, swelling, lumps/bumps, bruising, itching, discoloration, and other specified events. Subjects will maintain a diary record of the presence, location, frequency, severity, and duration of any ISR for 30 days after treatment (initial and Touch-up). (See *Section 7.1.7: Injection Site Reaction (ISR) 30-Day Diary* for further details).

ISRs that persist longer than 30 days (i.e., ongoing at the end of the diary period) will be reported as AE and followed as described in *Section 9.2: Procedure for Reporting Adverse Events*. If an ISR is ongoing or appears 30 days after the patient's last study visit, it will be followed up by Allergan Product Surveillance separate from this study protocol.

9.1.8 Incident

The Medical Device Directive (MDD) article 10 and MED DEV defines an incident as: any malfunction or deterioration in the characteristics and/or performance of a device, as well as any inadequacy in the labelling or the Instructions for use which, directly or indirectly, led to or might have led to the death of a subject, or USER or of other persons or to a serious deterioration in their state of health (see definition of SAE).

As per applicable Medical Device Guidance Document, MEDDEV 2.12-1 rev. 8, all events that the Sponsor determines fulfil the criteria of incidence must be reported to applicable Competent Authorities (CAs).

9.2 PROCEDURE FOR REPORTING ADVERSE EVENTS

All AEs and ADEs must be recorded in source documents and on the appropriate eCRF. All AEs that are related and unexpected (not listed as treatment-related in the current package insert or Directions for Use) must be reported as required by the ethics committee, local regulations, and the governing health authorities.

9.2.1 Timelines for Reporting

The Investigator is to adhere to the following schedule (*Table 9.1*) in reporting different types of AEs.

Table 9.1 Adverse Events Reporting Timelines

Adverse Event Type	Reporting to Allergan	Start of Collection	End of Collection
AEs, ADEs	Record on AE eCRF upon awareness for review by the Clinical Monitor	Immediately after IC signed	last subject visit

SAEs, SADEs	Record on SAE Form and fax / e-mail to Allergan within 24 hours of awareness	Immediately after IC signed	30 days after last subject visit

9.2.2 Severity

The Investigator will determine the severity classification based on the following definitions, his/her experience in the use of dermal fillers and/or the subject's description of the event. ISR severity is defined on the ISR 30-Day Diary.

The term "severe" is used to describe the intensity of an AE; the event itself could be of relatively minor clinical significance (e.g., 'severe' headache). This is not the same as "serious". Seriousness of AEs is defined in *Section 9.1.2: Serious Adverse Events (SAE)*.

Severity will be assessed as:

- **Mild** The AE does not interfere in a significant manner with the subject's normal functioning level. It may be an annoyance.
- **Moderate** The AE produces some impairment of function but not hazardous to health. It is uncomfortable and/or an embarrassment.
- **Severe** The AE process significant impairment of functioning or incapacitation and/or it is a hazard to the subject.

If an AE changes in severity, the worst severity should be reported.

9.2.3 Causality

Relationship to a device refers to a determination of the relationship (if any) between an AE and the device. A causal relationship is present if a determination is made that there is a reasonable possibility that the AE may have been caused by the device.

An AE could be considered procedure-related when, in the judgment of the Investigator, it is reasonable to believe that the event is associated with the procedure, regardless of the relationship to the study device. Procedure-related causes that contribute to the occurrence of the event can be attributed to other products, surgical techniques, or medications required specifically for the procedure.

Relationship to the device or procedure must be determined by the Investigator and cannot be delegated to other study staff.

Causality will be assessed as:

01 Not related: relationship to the device or procedures can be excluded when:

- the event is not a known side effect of the product category the device belongs to or of similar devices and procedures;
- the event has no temporal relationship with the use of the investigational device or the procedures.
- the serious event does not follow a known response pattern to the medical device (if the response pattern is previously known) and is biologically implausible;
- the discontinuation of medical device application or the reduction of the level of activation/exposure - when clinically feasible – and reintroduction of its use (or increase of the level of activation/exposure), do not impact on the serious event;
- the event involves a body-site or an organ not expected to be affected by the device or procedure;
- the serious event can be attributed to another cause (e.g. an underlying or concurrent illness/ clinical condition, an effect of another device, drug, treatment or other risk factors);
- the event does not depend on a false result given by the investigational device used for diagnosis, when applicable;
- harms to the subject are not clearly due to use error;
- in order to establish the non-relatedness, not all the criteria listed above might be met at the same time, depending on the type of device/procedures and the serious event.

02 Unlikely: the relationship with the use of the device seems not relevant and/or the event can be reasonably explained by another cause, but additional information may be obtained.

03 Possible: the relationship with the use of the investigational device is weak but cannot be ruled out completely. Alternative causes are also possible (e.g. an underlying or concurrent illness/ clinical condition or/and an effect of another device, drug or treatment). Cases were relatedness cannot be assessed or no information has been obtained should also be classified as possible.

04 Probable: the relationship with the use of the investigational device seems relevant and/or the event cannot reasonably explained by another cause, but additional information may be obtained.

05 Causal relationship: the serious event is associated with the investigational device or with procedures beyond reasonable doubt when:

- the event is a known side effect of the product category the device belongs to or of similar devices and procedures;
- the event has a temporal relationship with investigational device use/application or procedures;
- the event involves a body-site or organ that the investigational device or procedures are applied to;
- the investigational device or procedures have an effect on;

- the serious event follows a known response pattern to the medical device (if the response pattern is previously known);
- the discontinuation of medical device application (or reduction of the level of activation/exposure) and reintroduction of its use (or increase of the level of activation/exposure), impact on the serious event (when clinically feasible);
- other possible causes (e.g. an underlying or concurrent illness/ clinical condition or/and an effect of another device, drug or treatment) have been adequately ruled out;
- harm to the subject is due to error in use;
- the event depends on a false result given by the investigational device used for diagnosis, when applicable;
- in order to establish the relatedness, not all the criteria listed above might be met at the same time, depending on the type of device/procedures and the serious event.

9.2.4 Pregnancy

If a female of childbearing potential becomes pregnant during the study, the Investigator will notify the Sponsor immediately by completing the Pregnancy Surveillance Form after the pregnancy is confirmed. The Investigator shall (1) instruct the subject to notify her physician of the presence of the medical device and (2) follow the progress of the pregnancy to term.

Pregnancy by itself will not be considered an AE or serious adverse event (SAE). Hospitalization for a normal delivery does not constitute an SAE. However, the occurrence of an adverse pregnancy outcome for the mother or child may constitute an AE or SAE, and these should be reported as described in *Section 9.2: Procedure for Reporting Adverse Events*. Allergan considers any abortion (spontaneous or not spontaneous) as a SAE and should be reported as described in *Section 9.3: Procedures for Reporting an SAE/SADE.*

9.3 PROCEDURES FOR REPORTING AN SAE/SADE

The investigator is required to document AEs (non-serious and serious), device deficiencies, and incidents that occur during the duration of the study on the forms provided by Allergan.

All SAEs, device deficiencies, and incidents from consent to 30 days after the last treatment, or last study visit (whichever is later) are to be immediately (within 24 hours) reported to Allergan.

[redacted]

All subjects with a SAE, device deficiency, and incident must be followed up and the outcomes reported. The investigator is to supply Allergan and the EC with any additional requests for information.

An AE that continues beyond the end of the study final database lock will be followed independently from this study by the relevant Allergan safety department.

Both the investigator and Allergan will comply with all Medical Device Reporting requirements.

10 STATISTICAL METHODS

10.1 GENERAL STATISTICAL CONSIDERATIONS

A brief summary of the general statistical analysis methods is provided below; full details will be provided in a separate Statistical Analysis Plan (SAP), which will be finalized prior to database lock.

Data will summarized using descriptive statistics (number of observations (n), mean, standard deviation (SD), median, minimum, and maximum for continuous variables; and n and percent for categorical variables.

Baseline is defined as the latest assessment prior to any study treatments for each subject. End of study is the last clinical visit an enrolled subject has in this study. For subjects who complete this study, the end of study visit will be their V5 visit; for subjects who drop out early, they will be asked to come back for the last clinical visit for end of study data collection.

10.1.1 Analysis Populations

The following analysis populations will be used:

1. **Full Analysis Set**: Consists of all subjects who were consented and enrolled into this study and treated with the investigational product Juvederm VOLIFT with Lidocaine during the study.
2. **Safety Analysis Set**: Identically defined as the Full Analysis Set.
3. **Evaluable Set:** Consists of subjects in the Full Analysis Set who have had at least a baseline and a Day 30 (Visit 3) post-treatment efficacy assessment.
4. **Per Protocol Set:** Consists of subjects in the Evaluable Set who had not had any major protocol deviations.

10.1.2 Subgroups

As males and females may have differing expectations / perceptions of aesthetic improvement, data will be analysed by gender separately.

Additional subgroup analysis will be discussed in the study SAP.

10.2 DEMOGRAPHICS AND BASELINE CHARACTERISTICS

Subject disposition, demographics and baseline characteristics will be summarized using descriptive statistics.

10.3 EXPOSURE AND CONCOMITANT THERAPIES

Subject study product exposure and compliance will be summarized using descriptive statistics.

The latest version of the *World Health Organization Drug Dictionary* will be used to classify prior and concomitant medications and therapies by therapeutic class and drug/device name. Prior medication/therapy is defined as those started by enrolled subjects before the date of first study treatment. Concomitant medication/therapy is defined as those taken on or after the date of first treatment. Prior and concomitant medications/therapies will be summarized using descriptive statistics.

10.4 STUDY ENDPOINTS

10.4.1 Primary Endpoint

The primary endpoint will be the responder rate for lip fullness on the LFS2, which is defined as the proportion of subjects who show ≥ 1-point improvement on the LFS2 compared to baseline assessment, at Day 30 after last treatment received.

10.4.2 Secondary Endpoints

10.4.2.1 Oral Commissures Severity Scale (OCSS)

Change from baseline in OCSS will be determined at each post-treatment visit.

10.4.2.2 FACE-Q – Satisfaction with Lips Questionnaire

- Subject's assessment of satisfaction with treatment of their lips as measured by the change from baseline in the FACE-Q Satisfaction with Lips questionnaire at all post-treatment visits.

10.4.2.3 Global Aesthetic Improvement Scales (GAIS)

- Investigator's assessment of global facial aesthetic improvement as measured by the 5-point GAIS at post-treatment visits beginning at Day 30 after last treatment received.
- Subject assessment of global facial aesthetic improvement as measured by the 5-point GAIS at post-treatment visits beginning at Day 30 after last treatment received.

10.4.2.4 Natural Look and Feel/Product Smoothness/Dynamic lip lines

- Subject's assessment of natural look and feel of their lips as measured by the 5-point Likert scale at post-treatment visits beginning at Day 30 after last treatment received.
- Investigator's assessment of product smoothness as measured by the 5-point Likert scale at post-treatment visits beginning at Day 30 after last treatment received.
- Investigator assessment of dynamic lip lines upon animation at post-treatment visits beginning at Day 30 after last treatment received

10.5 EFFICACY ANALYSES

Unless stated otherwise, all efficacy analyses will compare post-treatment assessment values to the subject's corresponding baseline assessment value.

10.5.1 Primary Efficacy Analysis

The primary efficacy endpoint is the responder rate for lip fullness on the LFS2, which is defined as the proportion of subjects who show ≥ 1-point improvement on the LFS2 compared to baseline assessment, at Day 30 after last treatment received.

10.5.2 Analysis of All Other Efficacy endpoints

Details of the analyses for all other efficacy endpoints will be documented in the SAP.

10.5.3 Missing Data

Missing data strategy will be documented in the study SAP.

10.5.4 Adverse Events

Adverse events (AEs) will be coded using MedDRA version 20.1 or higher, and presented by System Organ Class (SOC) and Preferred Term (PT). Treatment-emergent AEs will also be summarized by serious AEs (SAE), AE severity, AE leading to treatment or study early termination, and relationship to study drugs/devices.

10.6 INTERIM ANALYSES AND DATA MONITORING

An interim analysis will be performed when all patients complete their 6 months visit (or discontinue early), full details will be described in the SAP.

10.7 DETERMINATION OF SAMPLE SIZE

It is expected that the responder rate for this study is approximately 80% based on the results of a pivotal study of a similar investigational product Juvéderm Volbella XC. [redacted] The margin of error (associated with 95% CI) for estimating an 80% expected responder rate is 10%, which is desirable to attain by having a sample size of 60 subjects for the study. Patients' dropout rate is expected to be negligibly small at Day 30 post-treatment when the primary efficacy assessment is collected, thus 60 subjects will be recruited into the study.

10.8 CHANGES IN THE CONDUCT OF THE STUDY OR PLANNED ANALYSIS

Any changes to the conduct or planned analyses will be handled via protocol or SAP amendment, respectively.

11 REGULATORY, ETHICAL, AND LEGAL OBLIGATIONS

11.1 DECLARATION OF HELSINKI

The Investigator will ensure that this study is conducted in accordance with the most recent revision of the Declaration of Helsinki.

11.2 GOOD CLINICAL PRACTICE

The study will be conducted according to the study protocol and to the principles of good clinical practice ISO14155:2011.

11.3 INDEPENDENT ETHICS COMMITTEES

Before implementing this study, the protocol, the proposed subject informed consent forms, and other information for the subjects must be reviewed by a properly constituted committee or committees responsible for approving clinical studies. The IEC written, signed approval letter/form must contain approval of the designated Investigator, the protocol (identifying protocol title, date and version number), the subject informed consent form (date, version), and any other subject facing documents.

11.4 REGULATORY AUTHORITY APPROVAL

The study is utilizing all products as per their licensed usage and indications. Regulatory approval will be in place as required by participating countries.

11.5 PROTOCOL COMPLIANCE

The Investigator is responsible for compliance with the protocol at the investigational site. The Investigator is also responsible for reporting all issues of protocol non-compliance to the respective IEC and to the Sponsor. A representative of the Sponsor will make frequent contact with the Investigator and his/her research staff and will conduct regular monitoring visits at the site to review subject and study device accountability records for compliance with the protocol, e.g., subject eligibility criteria, volume of product injected, procedures performed, and follow-up visit schedule.

11.6 INFORMED CONSENT

Written informed consent is to be obtained from the subject prior to any study-related procedures or change in treatment. Privacy-related documentation will also be obtained from each subject prior to enrolment into the study, in accordance with relevant country and applicable local privacy requirements.

All subjects will be required to participate in the consent process. During the consent process, the person obtaining consent will inform the subject of all elements of informed consent. The Investigator must ensure that the subject is given full and adequate oral and written information about the nature, purpose, possible risk and benefit of the clinical trial. Subjects must also be notified that they are free to withdraw from the clinical trial at any time without prejudice to future care. The subject should be given the opportunity to ask questions and allowed time to consider the information provided.

If the ICF is revised for any reason (e.g., protocol amendment or new safety data), the revised ICF must be reviewed and approved by the IEC. The revised ICF is not considered effective until approved by the IEC. All subjects currently enrolled in the clinical trial must sign the revised ICF. Subjects enrolled in the clinical trial after the revised ICF has been approved by the IEC will sign the revised version.

11.7 SUBJECT CONFIDENTIALITY AND DISCLOSURE

A report of the results of this study may be published or sent to the appropriate health authorities as appropriate but the subject's name will not be disclosed in these documents. The subject's name may be disclosed to the Sponsor of the study, Allergan, or the governing health authorities if they inspect the study records. Appropriate precautions will be taken to maintain confidentiality of medical records and personal information.

11.8 SPONSOR MONITORING OF STUDY DOCUMENTATION

A representative of the Sponsor will monitor the study on a periodic basis. The determination of the extent and nature of monitoring will be based on considerations such as the objective, purpose, design, complexity, size, and endpoints of the study. This will be detailed in the Study Monitoring Plan.

Authorized representatives of Allergan or regulatory authority representatives will conduct on-site visits to review, audit and copy study-related documents. These representatives will meet with the Investigator(s) and appropriate staff at mutually convenient times to discuss study-related data and questions.

11.9 STUDY DOCUMENTS

The Investigator must maintain source documents for each subject in the study, including all demographic and medical information etc., and keep a copy of the signed and dated informed consent forms. All information on the eCRFs must be traceable to these source documents in the subject's file.

11.10 COLLECTION OF STUDY DATA

The Investigator is responsible for ensuring that study data are properly recorded on each subject's eCRFs and related documents. An Investigator who has signed the protocol signature page should sign off for the eCRFs (as indicated in the eCRFs) to attest that the observations and findings are recorded on the eCRFs correctly and completely. The eCRFs are to be submitted to Allergan in a timely manner at the completion of the study, or as otherwise specified by Allergan.

The data reported on the eCRFs shall be derived from source documents and be consistent with these source documents, and any discrepancies shall be explained in writing. Any change or correction to data reported on an eCRF shall be dated, initialed and explained, if necessary, and shall not obscure the original entry (i.e., an audit trail shall be maintained); this applies to both written and electronic changes and corrections.

11.11 ARCHIVING OF STUDY DOCUMENTS

All study-related correspondence, subject records, consent forms, subject privacy documentation, records of the distribution and use of all products, and copies of eCRFs should be maintained on file. Allergan-specific essential documents are to be retained for a period of at least 10 years after the last device covered by the EU declaration of conformity

has been placed on the market. These documents are to be retained for a longer period, however, if required by the applicable regulatory requirements or if needed by Allergan.

11.12 DISCLOSURE OF INFORMATION

This study will be registered and results posted on www.clinicaltrials.gov. Allergan, as the Sponsor, has proprietary interest in this study. Authorship and manuscript composition will reflect joint cooperation between study Investigators and Allergan personnel. Authorship will be established prior to the writing of the manuscript. As this study involves multiple centers, no individual publications will be allowed prior to completion of the final report of the multicenter study except as agreed with Allergan.

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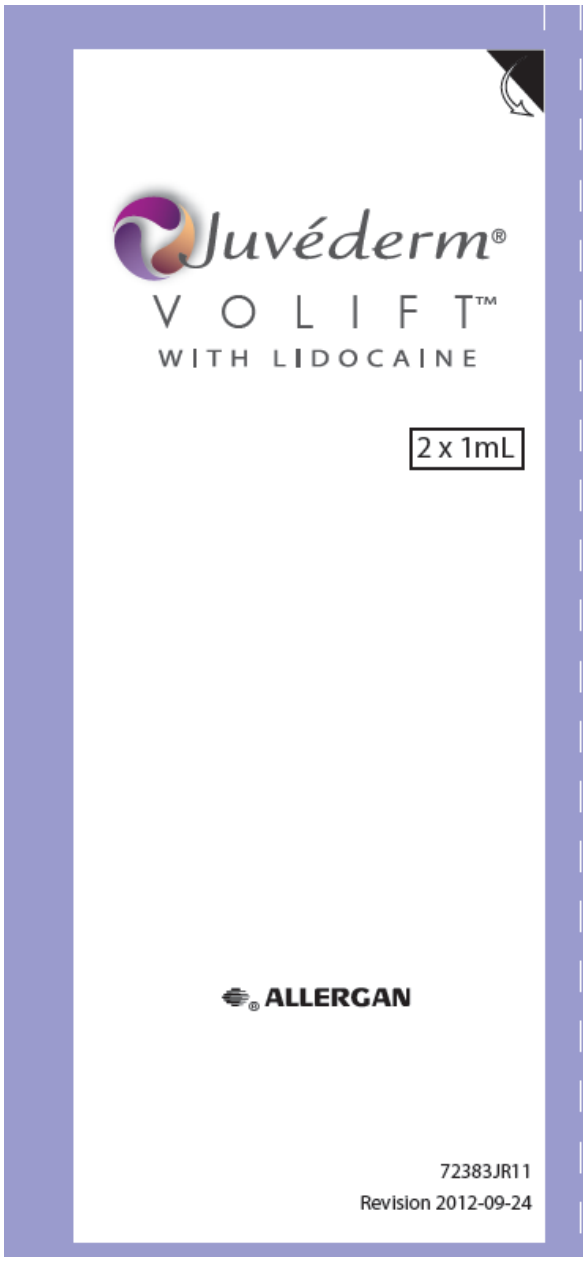
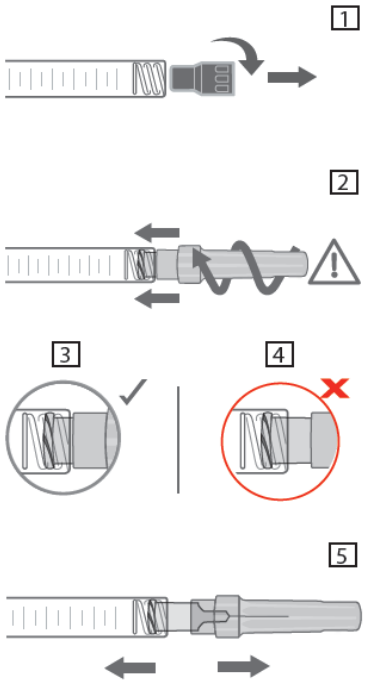
13 APPENDICES

APPENDIX 1 JUVEDERM® VOLIFT™ WITH LIDOCAINE DFU



EN Only for professional use
FR Réservé à un usage professionnel
DE Ausschließlich für die Anwendung durch Ärzte vorgesehen
ES Solo para uso profesional
IT Riservato per uso professionale
PT Reservado a uma utilização profissional
TR Yalnızca profesyonel kullanım içindir.
NO Forbeholdt profesjonell bruk.
SV Endast för professionell användning.
NL Enkel voor professioneel gebruik.
PL Wyłącznie do podawania przez profesjonalistów.
UK Тільки для професійного використання.
RU Предназначено для профессионального использования.
AR مخصص للاستعمال المهني.



EN

COMPOSITION

Hyaluronic Acid gel	17.5 mg
Lidocaine hydrochloride	3 mg
Phosphate buffer pH 7.2 q.s.	1 mL

One syringe contains 1mL of ***Juvéderm® VOLIFT™ with Lidocaine***.

DESCRIPTION

Juvéderm® VOLIFT™ with Lidocaine is a sterile pyrogen-free physiological solution of cross-linked hyaluronic acid which is not of animal origin. The gel is presented in a graduated, pre-filled, disposable syringe. Each box contains two 1mL ***Juvéderm® VOLIFT™ with Lidocaine*** syringes, 4 single-use 30G1/2" sterile needles to be used only for injecting ***Juvéderm® VOLIFT™ with Lidocaine*** , an instruction leaflet and a set of labels in order to ensure traceability.

STERILISATION

The contents of the ***Juvéderm® VOLIFT™ with Lidocaine*** syringes are sterilised by moist heat.
The 30G1/2" needles are sterilised by radiation.

INDICATIONS

- ***Juvéderm® VOLIFT™ with Lidocaine*** is an injectable gel implant intended for the treatment of any deep skin depressions due to conditions such as premature aging.
- ***Juvéderm® VOLIFT™ with Lidocaine*** can also be used for face contouring and volume restoration to correct facial structural defects such as asymmetry, contour deformities, volume loss in the lips, cheeks, chin, lower face.....
- ***Juvéderm® VOLIFT™ with Lidocaine*** is intended to be used via deep dermis or lips mucosa injection by an authorized medical practitioner.
- The presence of lidocaine is meant to reduce the patient's pain during treatment.

CONTRA-INDICATIONS

- Do not inject ***Juvéderm® VOLIFT™ with Lidocaine*** in the periorbital area (eyelids, under-eye area, crow's feet) and glabellar region.
- Do not inject into the blood vessels (intravascular).
- Do not overcorrect.
- ***Juvéderm® VOLIFT™ with Lidocaine*** must not be used in:
  - Patients suffering from untreated epilepsy;
  - Patients who tend to develop hypertrophic scarring;
  - Patients with known hypersensitivity to hyaluronic acid;
  - Patients with known hypersensitivity to lidocaine or to amide-type local anaesthetics;
  - Patients suffering from porphyria;
  - Women who are pregnant or breastfeeding;
  - Children.
- ***Juvéderm® VOLIFT™ with Lidocaine*** must not be used in areas presenting cutaneous inflammatory and/or infectious processes (acne, herpes, etc.).
- ***Juvéderm® VOLIFT™ with Lidocaine*** should not be used simultaneously with laser treatment, deep chemical peels or dermabrasion. For surface peels, it is recommended not to inject the product if the inflammatory reaction generated is significant.

PRECAUTIONS FOR USE

- ***Juvéderm® VOLIFT™ with Lidocaine*** is indicated only for intra-dermal injections and injections in the mucous membrane of the lips.
- As a matter of general principle, injection of a medical device is associated with a risk of infection.
- There is no available clinical data (efficiency, tolerance) about injection of ***Juvéderm® VOLIFT™ with Lidocaine*** into an area which has already been treated with another filling product. It is recommended not to inject it in site which has been treated with a permanent implant.
- No clinical data is available regarding the efficiency and tolerance of ***Juvéderm® VOLIFT™ with Lidocaine*** injections in patients having

a history of, or currently suffering from, autoimmune disease. The medical practitioner shall therefore decide on the indication on a case-by-case basis, according to the nature of the disease and its corresponding treatment, and shall also ensure the specific monitoring of these patients. In particular, it is recommended that these patients undergo a preliminary dual test, and to refrain from injecting the product if the disease is active.

• There is no available clinical data concerning the tolerance of the ***Juvéderm® VOLIFT™ with Lidocaine*** injection in patients presenting a history of severe multiple allergies or anaphylactic shock. The medical practitioner shall therefore decide on the indication on a case-by-case basis, according to the nature of the allergy, and shall also ensure the specific monitoring of these at-risk patients. In particular, the decision may be taken to propose a double test or suitable preventive treatment prior to any injection.

• Patients showing a history of streptococcal disease (recurrent sore throats, acute rheumatic fever) shall be subjected to a dual test before any injection is administered. In the event of acute rheumatic fever with heart complications, it is recommended not to inject the product.

• Patients on anti-coagulation medication (anticoagulants, aspirin, or nonsteroidal anti-inflammatory drugs) must be warned of the potential increased risks of haematomas and bleeding during injection.

• There is no data available regarding the safety of injecting greater amount than 20 mL of ***Juvéderm® VOLIFT™ with Lidocaine*** per 60 kg (130 lbs) body mass per year.

• The combination of ***Juvéderm® VOLIFT™ with Lidocaine*** with certain drugs that reduce or inhibit hepatic metabolism (cimetidine, beta-blockers, etc.) is inadvisable.

• ***Juvéderm® VOLIFT™ with Lidocaine*** should be used with caution in patients showing symptoms of cardiac conduction disorders.

• Please recommend that the patient not use any makeup during the 12 hours following the injection treatment and that any extended exposure to the sun, UV rays and temperatures below 0°C be avoided, as well as any sauna or hammam sessions during the two weeks following the injection treatment.

• If the needle is blocked, do not increase the pressure on the plunger rod but stop the injection and replace the needle.

• Athletes should be made aware that this product contains an active principle that may produce a positive result in anti-doping tests.

• Medical practitioners must take into account the fact that this product contains lidocaine.

• The composition of this product is compatible with fields used for magnetic resonance imaging.

INCOMPATIBILITIES

Hyaluronic acid is known to be incompatible with quaternary ammonium salts such as benzalkonium chloride.

Juvéderm® VOLIFT™ with Lidocaine should therefore never be placed in contact with these substances or with medical-surgical instrumentation which has been treated with this type of substance.

SIDE EFFECTS

The patients must be informed that there are potential side effects associated with implantation of this product, which may occur immediately or may be delayed. These include, but are not limited to:

• Inflammatory reactions (redness, oedema, erythema, etc.) which may be associated with itching or pain on pressure or both, occurring after the injection. These reactions may last for a week. In particular, it has to be noticed that injection in the mucous membrane may cause more oedema and bruising due to the specific physiology of theses tissues. Besides, a preventive anti-inflammatory treatment by a medical practitioner can be recommended.

• Haematomas.

• Induration or nodules at the injection site.

• Staining or discolouration of the injection site.

• Poor effect or weak filling effect.

• Cases of necroses in the glabellar region, abscesses, granuloma and immediate or delayed hypersensitivity after hyaluronic acid and/or lidocaine injections have been reported. It is therefore advisable to take these potential risks into account.

• Patients must report inflammatory reactions which persist for more than one week, or any other side effect which develops, to their medical practitioner as soon as possible. The medical practitioner should use an appropriate treatment.

• Any other undesirable side effects associated with injection of ***Juvéderm® VOLIFT™ with Lidocaine*** must be reported to the distributor and/or to the manufacturer.

METHOD OF USE & POSOLOGY

• This product is designed to be injected into the dermis or the mucous membrane of the lips by an authorized medical practitioner in accordance with local applicable regulation.

• Use of the supplied 30G 1/2" needle is recommended. However, depending on the medical practitioner's preferred injection technique, it is possible to use a 25G, 27G or 30G sterile cannula (please refer to the list hereunder). Choice of cannula length is determined by the user according to his/her injection technique. For lip indication, the use of 25G cannula (please refer to the list below) is not recommended.

Material Number	Description
94323/ HPC30019ACSH	Easyflow System-20* cannula 30G x 19mm.
94324/ HPC30025ACSH	Easyflow System-20* cannula 30G x 25mm.
94325 / HPC27025ACSH	Easyflow System-20* cannula 27G x 25mm.
94326 / HPC27038ACSH	Easyflow System-20* cannula 27G x 38mm.
94327/ HPC25038ACSH	Easyflow System-20* cannula 25G x 38mm.

• Contra-Indications, Method of use, Precautions for use and Warnings defined for the needle in this leaflet apply also to the cannula referenced above if used with this product.

As precision is essential to a successful treatment, the product must be used by medical practitioners who have undertaken specific training in injection techniques for filling skin depression and volume restoration.

• ***Juvéderm® VOLIFT™ with Lidocaine*** is to be used as supplied. Modification or use of the product outside the Directions for Use may adversely impact the sterility, homogeneity and performance of the product and it can therefore no longer be assured.

• Before starting treatment patients should be informed of the product's indications, contra-indications, incompatibilities and potential undesirable effects.

• The area to be treated should be disinfected thoroughly prior to the injection.

• Remove tip cap by pulling it straight off the syringe as shown in fig. 1. Then firmly push the needle provided in the box (fig. 2) into the syringe, screwing it gently clockwise. Twist once more until it is fully locked and has the needle cap in the position shown in fig. 3. If the needle cap is positioned as shown in fig. 4, it is incorrectly attached.

Next, remove the protective cap by holding the body of the syringe in one hand, the protective cap in the other, as shown in fig. 5, and pulling the two hands in opposite directions.

Inject slowly.

Failure to comply with these precautions could cause a disengagement of the needle and/or product leakage at luer-lock level.
• The amount injected will depend on the areas which are to be corrected. In particular, injection of an excessive volume can be at the origin of severe oedema.
• It is important to massage the area treated after the injection in order to ensure that the substance has been uniformly distributed.

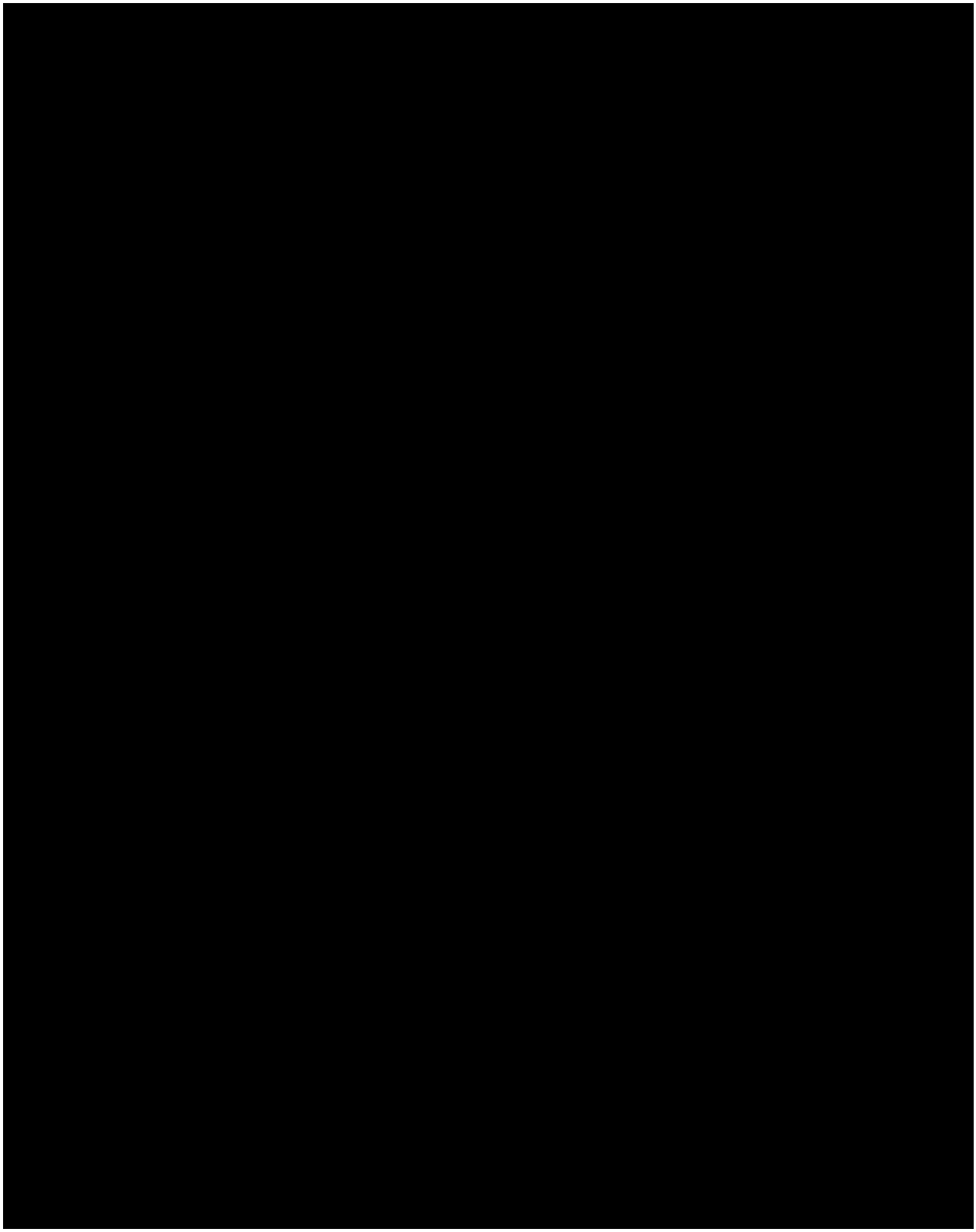
WARNINGS

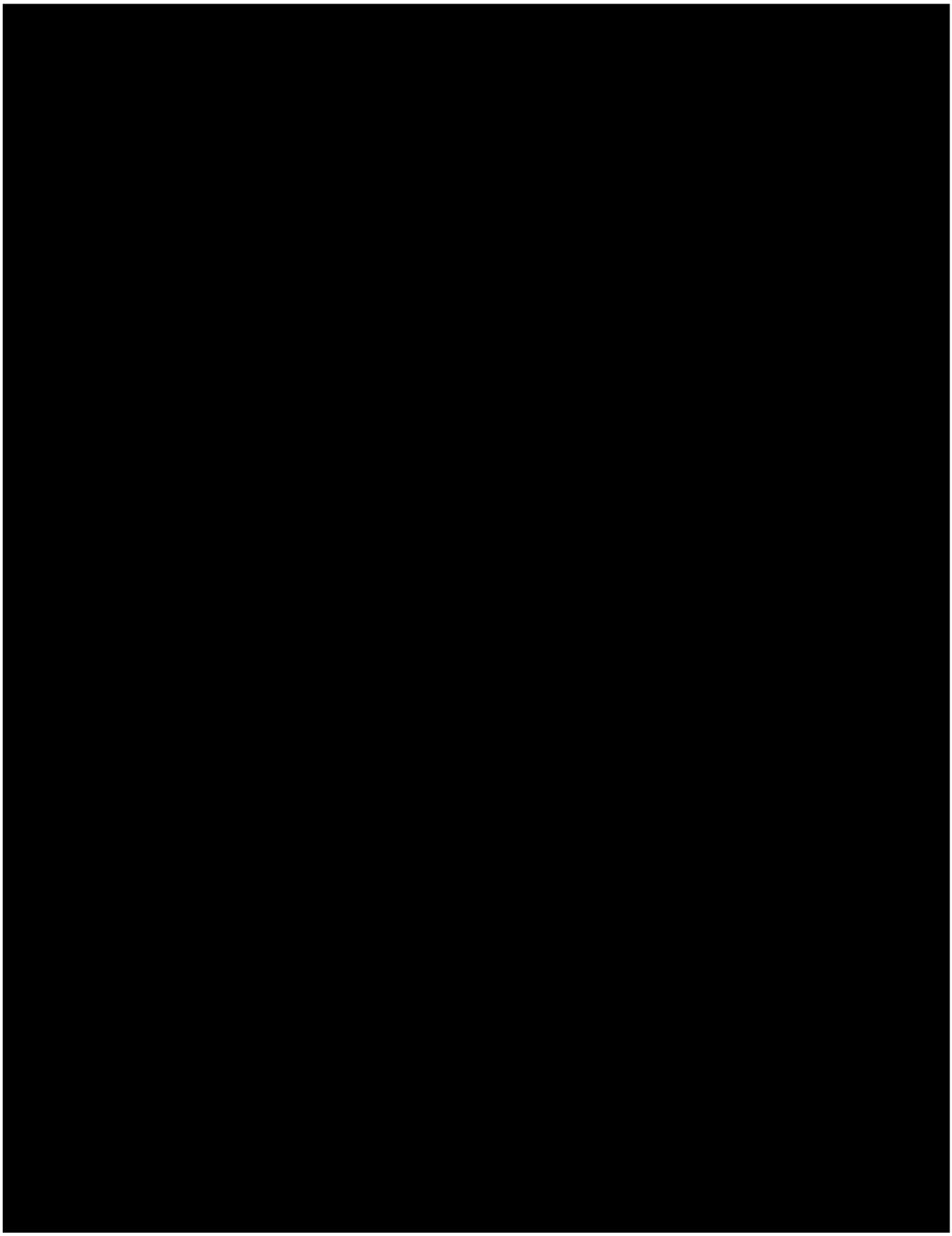
• Check the expiry date on the product label.
• Do not re-use. Sterility of this device cannot be guaranteed if the device is re-used.
• Do not re-sterilise.
• For the needles (CE 0123 TSK Laboratory, Japan):
EC- Representative : Emergo Europe
Molenstraat 15
2513 BH The Hague (NL)
- Used needles must be thrown away in the appropriate containers. Do the same for the syringes. Please consult the current applicable directives to ensure their correct elimination.
- Never try to straighten a bent needle; throw it away and replace it.

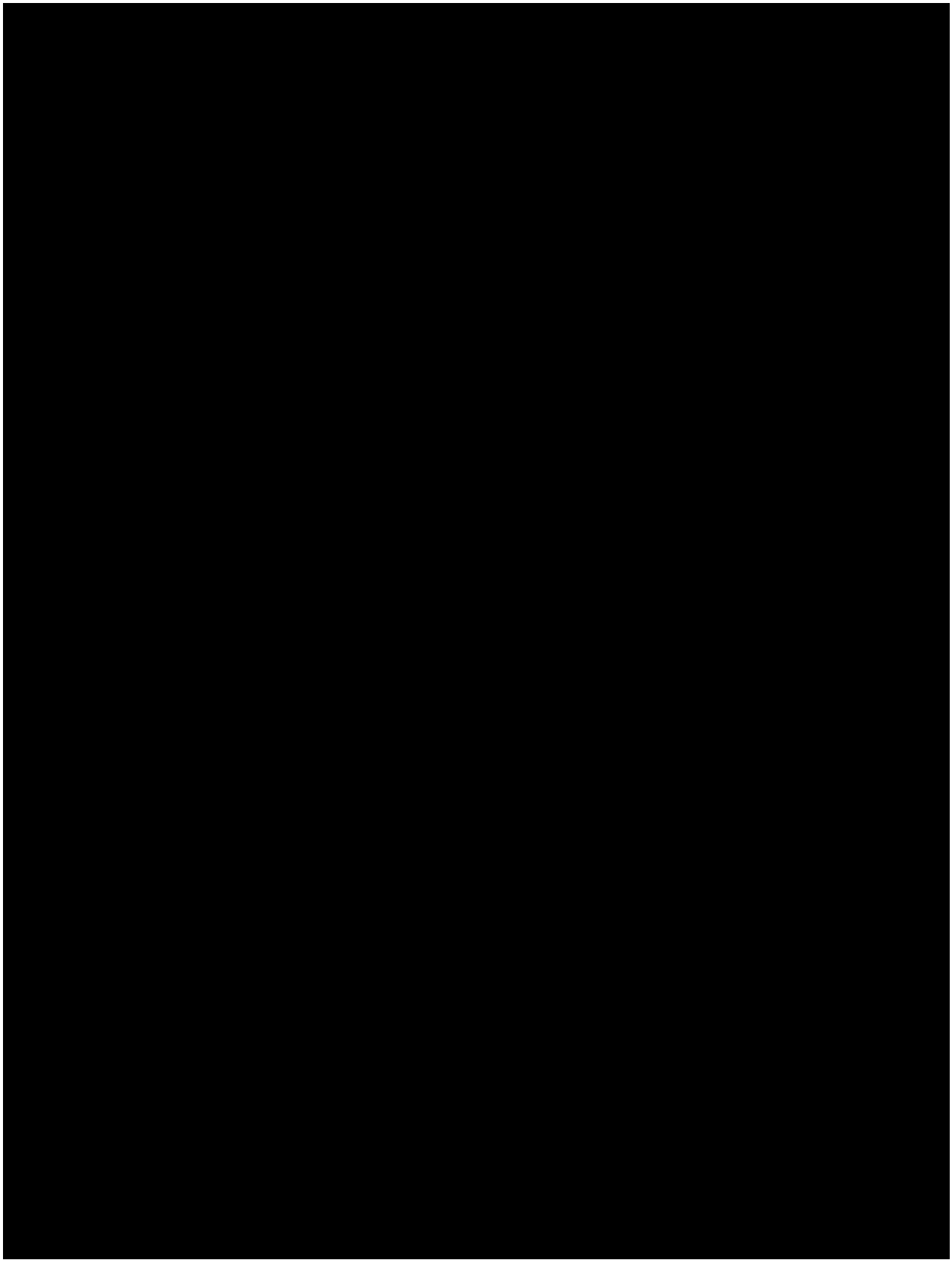
STORAGE CONDITIONS

- Store between 2°C and 25°C.
- Fragile.

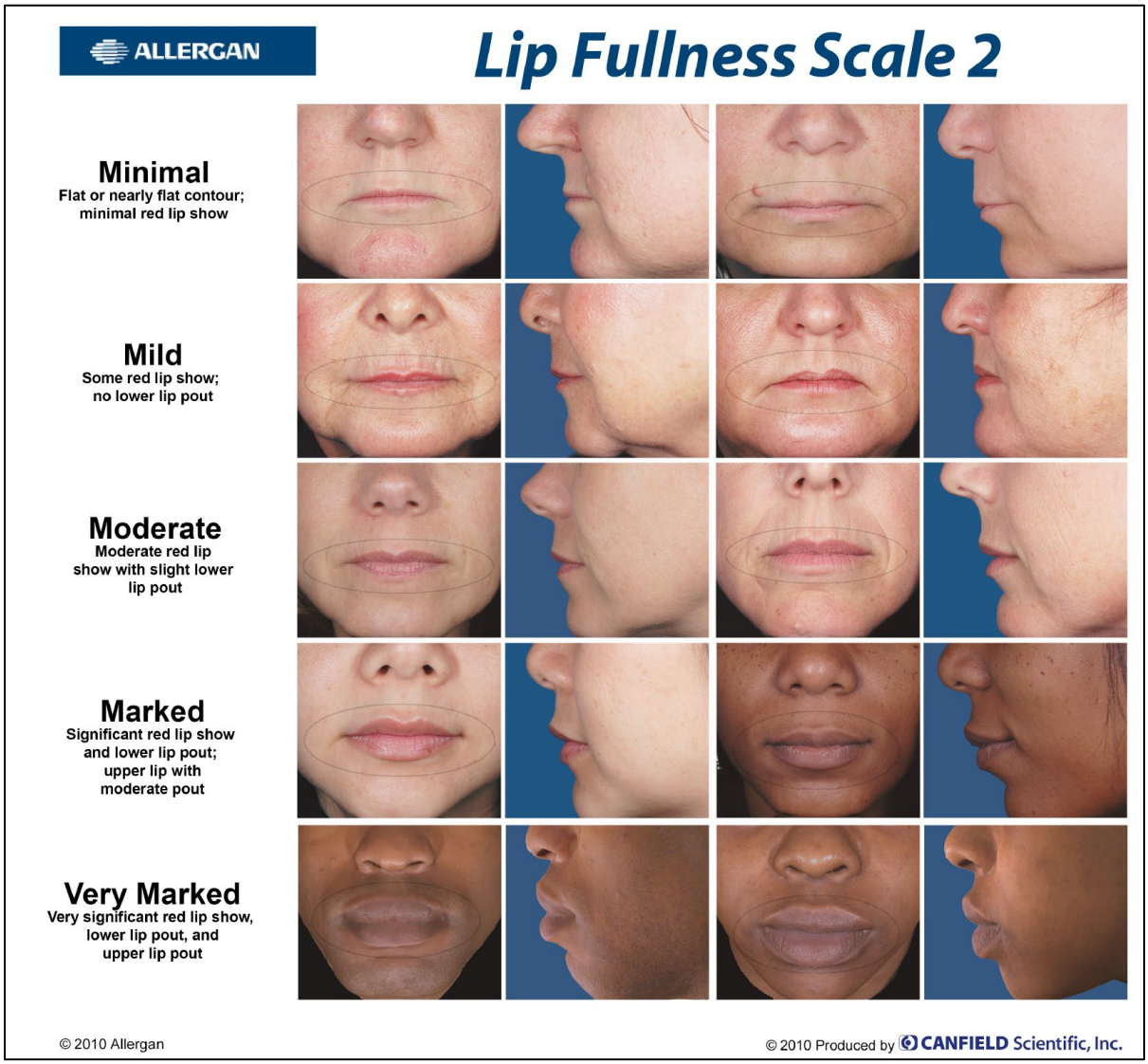
APPENDIX 2 INJECTION SITE REACTION (ISR) 30-DAY DIARY





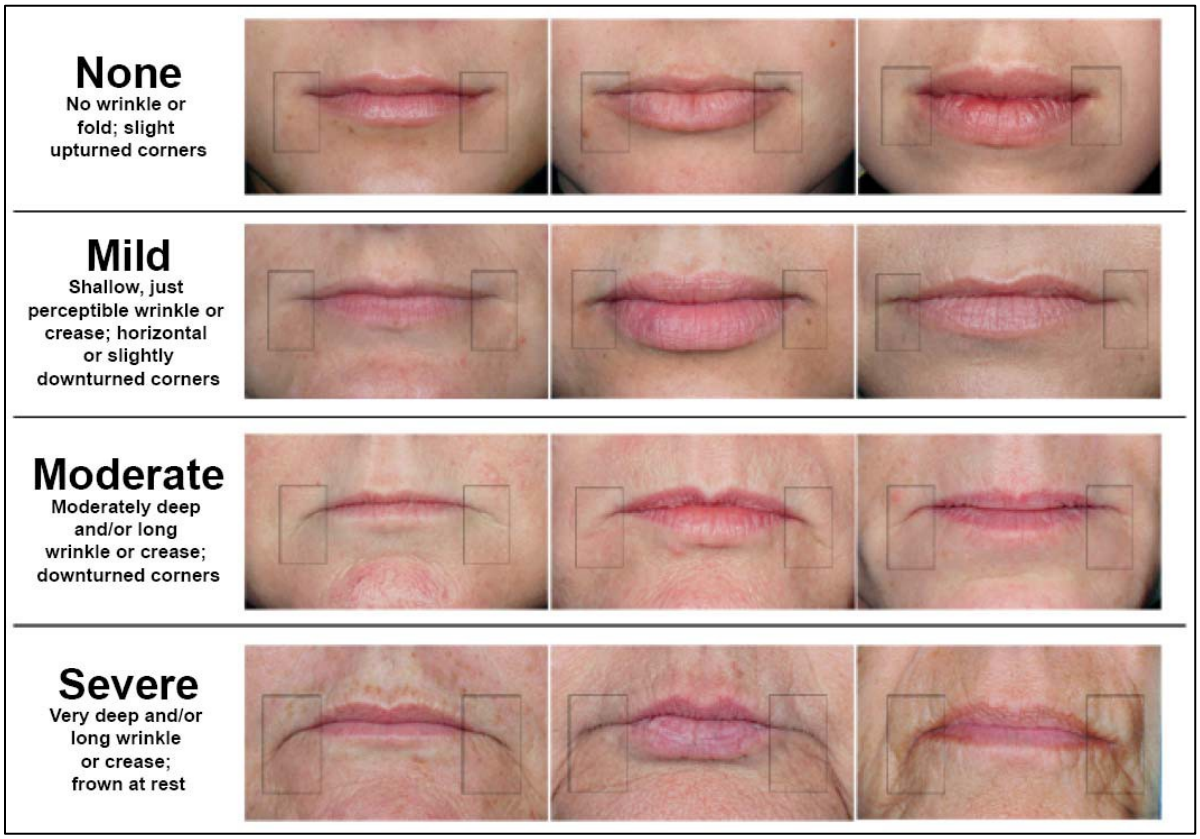


APPENDIX 3 LIP FULLNESS SCALE 2 (LFS2)

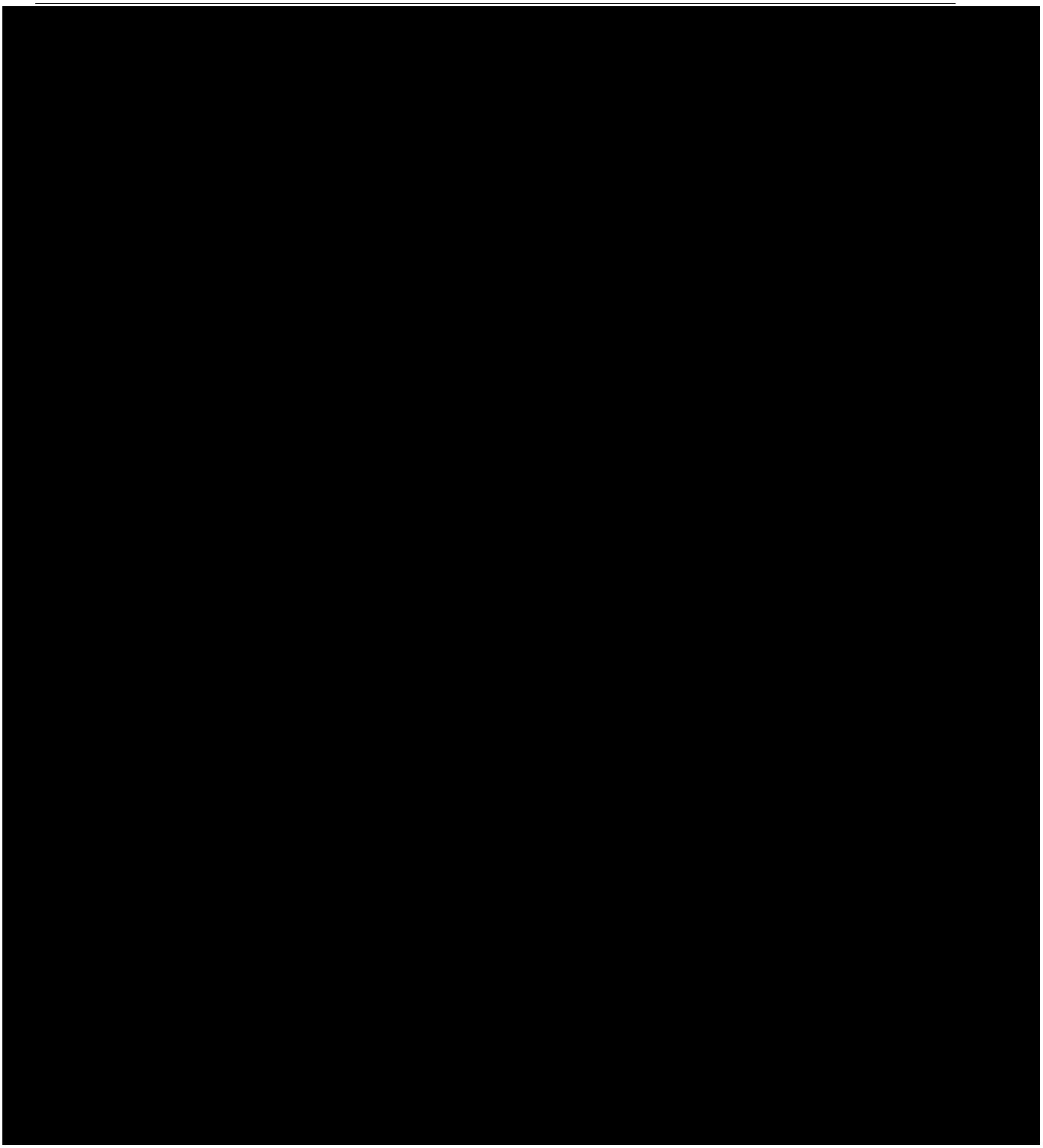


Grade	Description
Very Marked	Very significant red lip show, lower lip pout, and upper lip pout
Marked	Significant red lip show and lower lip pout
Moderate	Moderate red lip show with slight lower lip pout
Mild	Some red lip show; no lower lip pout
Minimal	Flat or nearly flat contour, minimal red lip show

APPENDIX 4 ORAL COMMISSURE SEVERITY SCALE (OCSS)



Grade	Description
Severe	Very deep and/or long wrinkle or crease; frown at rest
Moderate	Moderately deep and/or long wrinkle or crease; downturned corners
Mild	Shallow, just perceptible wrinkle or crease; horizontal or slightly downturned corners
None	No wrinkle or fold; slight upturned corners



APPENDIX 6 GLOBAL AESTHETIC IMPROVEMENT SCALE (GAIS)

INVESTIGATOR ASSESSMENT OF GLOBAL AESTHETIC IMPROVEMENT		
Using the Subject's image obtained at Baseline for reference, record your assessment of the level of improvement to the Subject's lips.		
Score (Circle one number)	**Grade**	**Description**
2	**Much Improved**	**Marked improvement in appearance**
1	**Improved**	**Improvement in appearance, but a touch-up or re-treatment is indicated**
0	**No Change**	**The appearance is essentially the same as the original condition**
-1	**Worse**	**The appearance is worse than the original condition**
-2	**Much Worse**	**The appearance is much worse that the original condition**

SUBJECT'S SELF-ASSESSMENT OF GLOBAL AESTHETIC IMPROVEMENT			
While viewing the image of you that was obtained prior to the first study treatment for reference, record your assessment of the level of improvement to your appearance.			
	Score (Circle one number)	**Grade**	
	2	**Much Improved**	
	1	**Improved**	
	0	**No Change**	
	-1	**Worse**	
	-2	**Much Worse**	

APPENDIX 7 SUBJECT ASSESSMENT OF NATURAL LOOK AND FEEL

Please answer the following questions as they relate to your lips NOW after you have been treated.

Please circle one number for each statement to indicate your agreement with each statement:

	Not at All		Somewhat		Very Much
1. My lips look natural	0	1	2	3	4
2. My lips feel natural	0	1	2	3	4

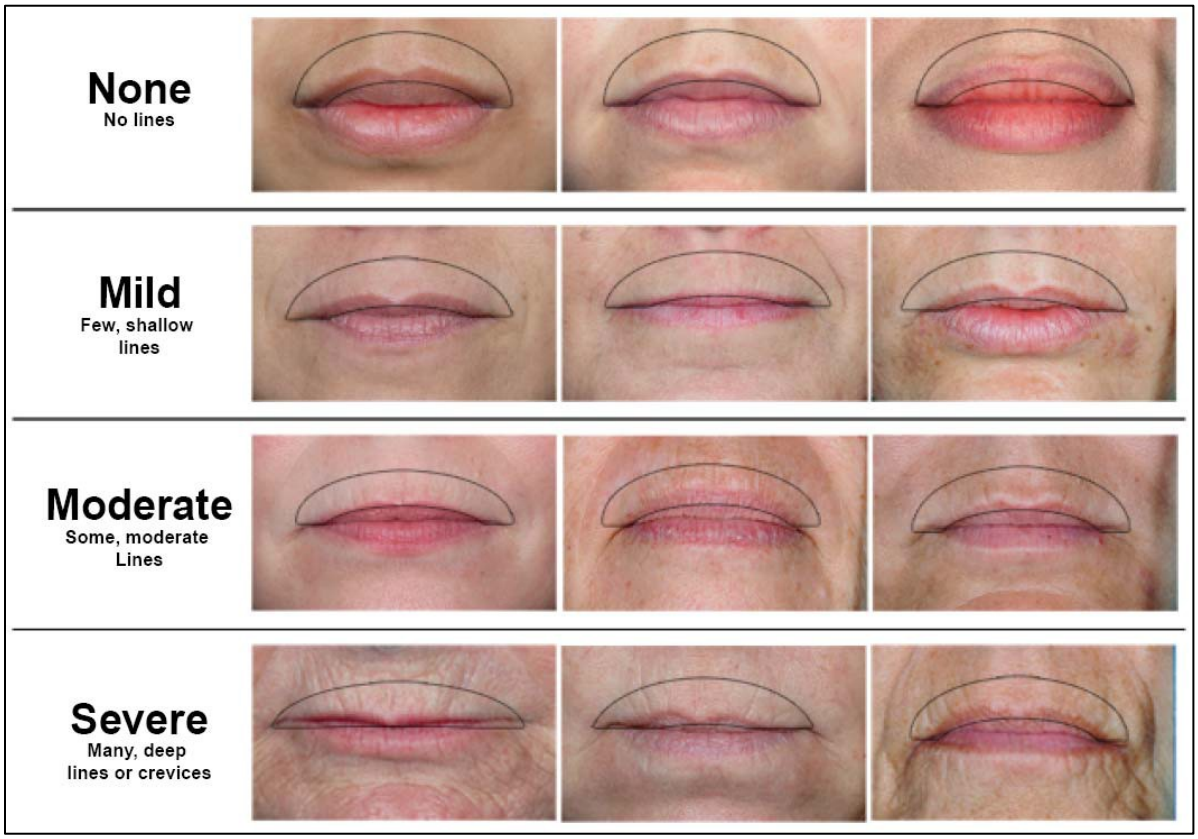
APPENDIX 8 INVESTIGATOR ASSESSMENT OF SMOOTHNESS

Please answer the following question as they relate to your patient's lips <u>NOW</u> after they have been treated.

Please circle one number to indicate the result the product gave to the smoothness of the lips after treatment:

	Lumpy/ Grainy		Somewhat Smooth		Smooth
Smoothness of lips	**0**	**1**	**2**	**3**	**4**

APPENDIX 9 PERIORAL LINES AT REST SEVERITY SCALE (POLSS)



APPENDIX 10 INVESTIGATOR ASSESSMENT OF DYNAMIC LIP LINES UPON ANIMATION

Please answer the following question as they relate to your patient's lips NOW after they have been treated.

Please circle one number to indicate the result the product gave to the dynamic lip lines upon animation (ask the patient to 'kiss' lips):

	Worse	No change	Improved	Much improved
Dynamic lip lines upon animation	**0**	**1**	**3**	**4**