

The Safety and Efficacy of Laser Assisted Liposuction and Facial Autologous Fat Grafting with the LipoLife™ System

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SPONSOR

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Revision History:

Revision	Description of Change	Amendment	Effective Date
1.0	Original	-	04-July-18
2.0	Adding requirement for Photo consent by subjects and minor modifications		31-July-18
2.1	Adding a facial MRI evaluation, after a facial fat grafting procedure at Sanctuary Plastic Surgery, Boca Raton site		25-Oct-18

STUDY ACKNOWLEDGMENT / CONFIDENTIALITY

By signing this Protocol, the Investigator(s) acknowledges and agrees:

The Protocol contains all necessary details for conducting the study. The Investigator will conduct this study as detailed herein, in compliance with Good Clinical Practice (GCP) and the applicable regulatory requirements, and will make every reasonable effort to complete the study within the time designated.

The Protocol and all relevant information on the device relating to pre-clinical and prior clinical experience, which was furnished by the Sponsor, Alma Lasers Ltd., will be made available to all physicians, nurses and other personnel who participate in the conducting of this study. The Investigator will discuss this material with them to assure that they are fully informed regarding the device(s) and the conduct of the study.

This is indicated as privileged or confidential.

Alma Lasers Ltd. will have access to any source documents from which Case Report Form information may have been generated. The Case Report Forms and other data pertinent to this study are the sole property of, Alma Lasers Ltd., which may utilise the data in various ways, such as for submission to government regulatory authorities, or in publication of the results of the study.

The conduct and results of this study will be kept confidential. The results of this study may be published. Upon completion of the Study it is the intention of the parties to prepare a joint publication regarding or describing the Study and all the results there from and both parties shall co-operate in this regard.

PRINCIPAL INVESTIGATOR

Name: _____

Signature: _____

Date: _____

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ABBREVIATIONS AND DEFINITIONS OF TERMS

AE	Adverse Event
BMI	Body Mass Index
CBC	Complete Blood Count
CFR	Code of Federal Regulations
CRF	Case Report Form
CW	Continuous Wave
DoB	Date of Birth
EKG	Electrocardiography
GCP	Good Clinical Practice
FU	Follow Up
ICH	International Conference on Harmonisation
MC	Medical Center
MRI	Magnetic Resonance Imaging
NSAIDs	Non-Steroidal Anti-Inflammatory Drugs
PI	Principal Investigator
SAE	Serious Adverse Event
SD	Standard Deviation

1 Protocol Synopsis

Protocol Number	ALM-Lipo-002	
Study Title	The Safety and Efficacy of Laser Assisted Liposuction and Facial Autologous Fat Grafting with the LipoLife™ System	
Projected Study Period	Initiation Date: October 2018	Completion Date: October 2019
Study Device	Alma Lasers LipoLife™ system	
Study Sites and Participants	Sanctuary Plastic Surgery Boca Raton FL, US and Assaf Harofeh MC, Israel\ 20 participants	
Device Description	<p>The Alma Lasers LipoLife™ system consist of FDA cleared LipoDiode 1470 system (K160952) and LipoFlow system (K171242).</p> <p>The LipoDiode 1470 system is intended for use in dermatology and general surgery procedures and indicated, among other indications, for laser assisted lipolysis. The Alma LipoFlow System is used in the aspiration, harvesting, filtering and transferring of autologous adipose tissue and infiltration for aesthetic body contouring.</p> <p>The LipoLife™ system will be used in this study for laser assisted liposuction and facial fat grafting.</p>	
Study Design and Duration	<p>Multi-center, prospective, open label, single arm study.</p> <p>Following the screening visit, eligible subjects will be enrolled into the study. Each subject will undergo laser assisted liposuction surgery w/wo facial fat grafting (5-20 subjects), using the LipoLife™ system. Pre-surgery evaluation visit will be carried out 1 week prior to the surgery. Follow up visits to evaluate safety and efficacy will take place at 1, 3 and 6 months after the surgery.</p> <p>Study duration from first subject enrollment to the last subject completion is expected to be up to 11 months.</p>	
Study Objectives	<p>Primary objectives</p> <ul style="list-style-type: none"> To evaluate the efficacy of Laser Assisted Liposuction procedure with the LipoLife™ system. <p>Secondary objectives</p> <ul style="list-style-type: none"> To evaluate the efficacy of facial fat grafting procedure using autologous fat harvested with the LipoLife™ system. To evaluate subjects' satisfaction. To evaluate procedure related safety. To evaluate fat vitality of the harvested fat with the LipoLife™ system (optional). 	

<p>Study Endpoints</p>	<p>Primary endpoint</p> <ul style="list-style-type: none"> Improvement in aesthetic appearance as determined by blinded comparison of before and after 2D or 3D (at the Israeli site)/ 3D (at US site) digital photographs, at 3 months follow up visit compared to baseline. <p>Secondary endpoint</p> <ul style="list-style-type: none"> Improvement in aesthetic appearance as determined by blinded comparison of before and after 2D or 3D (Israel)/ 3D (US) digital photographs, at 1 and 6 months follow up visits compared to baseline. Improvement in facial aesthetic appearance in subjects that had a procedure of facial fat grafting, as determined by blinded comparison of before and after 2D or 3D (Israel)/ 3D (US) digital photographs at 1, 3 and 6 months follow up visits compared to baseline. Reduction in body weight measurement at 1, 3 and 6 months follow up visits compared to baseline. Reduction in abdominal fat thickness, among five (5) subjects that had a procedure of abdominal liposuction, as assessed by Magnetic Resonance Imaging (MRI) at 3 months follow up visit compared to baseline. This test will be held at the US site. Increase in facial fat volume, among five (5) subjects that had a procedure of facial fat grafting, as assessed by Magnetic Resonance Imaging (MRI) at 3 months follow up visit compared to baseline. This test will be held at the US site. Subject's satisfaction, following liposuction procedure, as evaluated by subject's satisfaction questionnaire (based on 5 point Likert scale) at 1, 3 and 6 months follow up visits. Subject's satisfaction, following facial fat grafting procedure, as evaluated by subject's satisfaction questionnaire (based on 5 point Likert scale) at 1, 3 and 6 months follow up visits. Safety endpoints will include adverse events (AE's) and serious adverse events (SAE's) occurring at any time during the trial or follow-ups. Fat vitality, as evaluated by cell viability assessment of 10 samples of the harvested fat (optional).
<p>Study Population</p>	<p>Twenty (20) subjects, Ten (10) with excessive fat in the lower abdomen (w/wo flanks) and Ten (10) with excessive fat in the outer thighs (w/wo inner thighs), that are willing to undergo laser assisted liposuction. Five- Twenty (5-20) subjects out of this study group should also be eligible for facial fat grafting.</p> <p>Five (5) subjects will be recruited at Dr. Pozner's clinic in Sanctuary Plastic Surgery Boca Raton FL, US and will undergo abdominal liposuction and facial fat grafting. The rest fifteen (15) subjects will be recruited at Prof. Heller's at Assaf Harofeh Medical Center in Israel. Facial fat grafting will be optional in the Israeli site.</p>

<p>Inclusion Criteria</p>	<ul style="list-style-type: none"> • Subjects with excessive fat in the lower abdomen w/wo flanks or subjects with excessive fat in the outer thighs w/wo inner thighs that are willing to undergo laser assisted liposuction. • Estimated fat harvesting of 1-3 liters. • Subjects (5-20) eligible for facial fat grafting of at least 5 cc for each cheek. • Between 18 and 70 years of age. • Provided written Informed Consent.
<p>Exclusion Criteria</p>	<ul style="list-style-type: none"> • Body Mass Index (BMI) >35. • Sever skin laxity. • Positive pregnancy test. • Current smoker. • Presence of known malignancy. • Active infection in the treatment area. • History of autoimmune disorder (e.g., Systemic Lupus Erythematosus [SLE]). • History of connective, metabolic or atrophic skin disease. • History of keloid scarring. • Chronic use (>7 consecutive days) of anticoagulants (such as aspirin) or NSAIDs within 15 days prior to enrollment. • Subjects with immune system diseases. • Subject unable to follow post treatment instructions. • Any other reason that in the opinion of the investigator, prevents the subject from participating in the study or compromise the subject safety.

2 Introduction

The dramatic evolution of contemporary plastic surgery has brought liposuction to become the second-most commonly performed elective aesthetic procedure performed in the USA ¹. In this minimally invasive procedure, excess fat deposits are removed, and either discarded or exploited in subsequent lipo-sculpturing procedures aiming to restore the normal appearance of a range of body regions suffering from surgical, accidental or traumatic tissue loss, or disease- or aging-related cosmetic defects ². Autologous fat tissue has become a popular filling material, particularly in the face and hands ³⁻⁵, largely due to its circumvention of complications associated with allogenic fillers and implants, high and simple accessibility, cost-effectiveness and host-compatibility ^{6,7}. Yet, relatively high resorption rates have been reported, averaging 55% within one year of transplantation, with sample composition, purity and viable adipocyte content flagged as key determinants of implanted fat longevity ⁸⁻¹⁴.

The most commonly used liposuction techniques rely on mechanical, thermal, ultrasonic or hydric forces to harvest the desired sample. Laser-assisted liposuction (LAL) induces temperature elevations that lead to liquefaction of the adipose tissue and eventual adipocytolysis, enabling removal of larger volumes of fat than traditional liposuction techniques ¹⁵. In addition, the thermal effect elicits collagen deposition and rearrangement, coagulation of vasculature, skin contraction and reduced laxity. Multiple wavelengths can be used to provide for selective photothermolysis, each providing distinct ratios of penetration and scatter, fat absorption, and tissue tightening. In general, high absorption lasers (1370, 1440 and 1470 nm) generate localized thermal damage, while the lower absorption lasers (980, 1064 and 1320 nm) lead to more diffuse tissue response ¹⁶. Overall, LAL is considered safe and tolerable, and has been associated with a lower touch-up rate and improved precision as compared to conventional liposuctioning techniques ¹⁷.

Alma Surgical's LipoLife integrates a 1470 nm diode laser, emitting light preferentially absorbed by water, rendering it ideal for gentle fat tissue collection, with reduced risk of burning and scarring. In addition, its radially emitting fiber reduces emission intensity and subsequently, the risk of burns and internal scarring. Abdominal fat samples harvested with the LipoLife device were more homogenous, demonstrated higher viable adipocyte counts and contained fewer fibrous and blood contaminants as compared to those collected via mechanical liposuctioning ¹⁸. These virtues are expected to yield more long-lasting clinical outcomes, thereby reducing the need for correction or repeat procedures. When deploying the device for Teimourian grades I-

II arm contouring in a single-session laser lipolysis procedure in 45 patients, Leclere and colleagues reported an average 4.7-5.5 cm decrease in arm circumference ($p < 0.01$), with slightly better results for grades IIa and IIb patients. Similarly, the average skin pinch decreased by 0.7 cm for grade I patients and 2.1 cm and 2.9 cm for the grade IIa and IIb patients, respectively. Patient-evaluated pain was minimal, and mean downtime was shorter than one day. Complications included prolonged edema in 11 patients¹⁹. The same group reported on a 26.6-degree reduction in cervicomental angle in patients presenting Rohrich type IV aging neck undergoing a single LipoLife treatment session; 2/10 patients requested complementary surgery 6 months following LAL²⁰. When deployed to address gynecomastia, Trelles et al. (2013) reported no complications, skin burns, edema or areolar congestion. In addition, nipple sensitivity was not compromised. Mean chest and areola diameter reductions 6 months posttreatment, were 11.93 cm and 1.80 cm, respectively ($p < 0.05$). A significant degree of skin retraction was observed among all patients and patients resumed their normal activities within three days of surgery²¹.

The present multi-center, open-label, prospective study aims to assess the safety and efficacy of LipoLife, laser-assisted liposuction of abdominal and outer thigh fat samples, as well as the efficacy of facial autologous fat grafting with the harvested fat tissue. Contouring and volumetric enhancement outcomes will be assessed up to 6 months following the procedure.

3 The Investigational Device

3.1 Indication for Use

The Alma Lasers LipoLife™ system (see Fig.1) consist of FDA cleared LipoDiode 1470 system (K160952) and LipoFlow system (K171242).



Figure 1: Alma Lasers LipoLife™ system

The LipoDiode 1470 system is intended for use in dermatology and general surgery procedures and indicated, among other indications, for laser assisted lipolysis.

The Alma LipoFlow System is used in the aspiration, harvesting, filtering and transferring of autologous adipose tissue and infiltration for aesthetic body contouring. If the harvested fat is to be re-implanted, the harvested fat is only to be used without any additional manipulation.

The complete operating manual describing the LipoLife™ system will be attached separately.

3.2 Device description

3.2.1 LipoDiode 1470 system

The Alma LipoDiode 1470 system operates with a wavelength of 1470nm which is absorbed in water and supports laser-Assisted liposuction.

The Alma LipoDiode 1470 system comprised of:

- Alma 1470 diode laser device
- LipoDiode kit, including: 30cm, 25cm and 15cm cannulas (see Fig.2)
- Laser optical fibers- Angel fibers 400µm/600µm
- Footswitch
- Safety eyewear
- Operator's Manual



Figure 2: LipoDiode

3.2.2 LipoFlow system

The LipoFlow system provides two modes of operation:

- Peristaltic mode: used for tumescent injection.
- Vacuum mode: used for liposuction and fat transplant procedures.

User can activate only one mode at a time.

The Alma LipoFlow system comprised of:

- LipoFlow system console
- Overflow filter
- Re-usable Canister 2000 ml
- Infiltration kit, including: 15cm and 25cm Infiltration cannulas (see Fig.3)
- LipoFlow kit, including tubes and disposable waste bags
- Fat grafting sterile kit, including: sterile canister and sterile tube (see Fig.4)
- Footswitch
- Operator's Manual



Figure 3: Infiltration Kit



Figure 4: Fat grafting sterile kit

3.2.3 Procedure and parameters

Prior to performing the liposuction procedure, local anaesthesia is administered using the LipoFlow peristaltic mode. Tumescent fluid usage is 150 cc to 500 cc for a 10 x 10 cm² area, while the anticipated total mg/kg dosage of tumescent lidocaine should not exceed 45 mg/kg.

Approximately 20–30 minutes should be allowed to enable an adequate diffusion of the tumescent solution and provide effective vasoconstriction.

Liposuction with the LipoLife™ system involves simultaneous work of laser and suction. Alma 1470 diode laser is used in Continuous Wave (CW) emission mode, Pulse mode and Repeat mode. Power settings are recommended to be selected as a function of the liposuction area: 10-13W (chin, arms and knees), 13W (abdomen, back), and 15W (thighs, hips and buttocks). The laser energy is conveyed into the fat layer using a 3mm cannula which incorporates a 400 or 600µm optical single-use fiber. The suction tube is connected directly to the cannula so laser and suction will work simultaneously.

The LipoLife™ system is designed to be operated only by licensed medical practitioners properly trained in its handling and use. Personnel operating the device must read the operator's manual.

4 Study Objectives

4.1 Primary objective:

To evaluate the efficacy of Laser Assisted Liposuction procedure with the LipoLife™ system.

4.2 Secondary objectives:

- To evaluate the efficacy of facial fat grafting procedure using autologous fat harvested with the LipoLife™ system.
- To evaluate subjects' satisfaction.
- To evaluate procedure related safety.
- To evaluate fat vitality of the harvested fat with the LipoLife™ system (optional).

5 Study Design

This is a multi-center, prospective, open label, single arm study.

The study will include 6 visits at the medical center: screening, pre-surgery evaluation visit, laser assisted liposuction surgery w/wo facial fat grafting and 3 follow up visits.

Following the screening visit, eligible subjects will be enrolled into the study. Each subject will undergo laser assisted liposuction surgery w/wo facial fat grafting (5-20 subjects), using the LipoLife™ system. Pre-surgery evaluation visit will be carried out 1 week prior to the surgery. Follow up visits to evaluate safety and efficacy will take place at 1, 3 and 6 months after the surgery (See Figure 5 for an illustration of the study design).

5.1 Study Endpoints

5.1.1 Primary endpoint

Improvement in aesthetic appearance as determined by blinded comparison of before and after 2D/3D digital photographs, at 3 months follow up visit compared to baseline (2D or 3D at Assaf Harofeh MC, Israel and 3D at Sanctuary Plastic Surgery, US).

5.1.2 Secondary endpoints

- Improvement in aesthetic appearance as determined by blinded comparison of before and after 2D/3D digital photographs, at 1 and 6 months follow up visits

compared to baseline (2D or 3D at Assaf Harofeh MC ,Israel and 3D at Sanctuary Plastic Surgery, US).

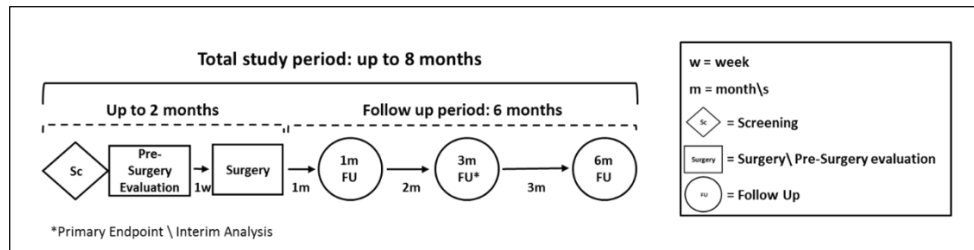
- Improvement in facial aesthetic appearance in subjects that had a procedure of facial fat grafting, as determined by blinded comparison of before and after 2D/3D digital photographs at 1, 3 and 6 months follow up visits compared to baseline (2D or 3D at Assaf Harofeh MC, Israel and 3D at Sanctuary Plastic Surgery, US).
- Reduction in body weight measurement at 1, 3 and 6 months follow up visits compared to baseline.
- Reduction in abdominal fat thickness, among five (5) subjects that had a procedure of abdominal liposuction, as assessed by Magnetic Resonance Imaging (MRI) at 3 months follow up visit compared to baseline. This test will be held at Sanctuary Plastic Surgery, US.
- Increase in facial fat volume, among five (5) subjects that had a procedure of facial fat grafting, as assessed by Magnetic Resonance Imaging (MRI) at 3 months follow up visit compared to baseline. This test will be held at the US site.
- Subject's satisfaction following liposuction procedure, as evaluated by subject's satisfaction questionnaire (based on 5 point Likert scale) at 1, 3 and 6 months follow up visits compared to baseline.
- Subject's satisfaction following facial fat grafting procedure, as evaluated by subject's satisfaction questionnaire (based on 5 point Likert scale) at 1, 3 and 6 months follow up visits.
- Safety endpoints will include adverse events (AE's) and serious adverse events (SAE's) occurring at any time during the trial or follow-ups.
- Fat vitality, as evaluated by cell viability assessment of 10 samples of the harvested fat (optional).

5.2 Study Duration

Duration of subject's participation: Up to 8 months from enrollment to termination.

Study duration for entire study sample: Estimated to be 11 months from the enrollment of the first subject to the termination of the last subject. This is based on an estimate of 3 months for recruitment and up to 8 months subject participation.

Figure 5: Study Design – ALM-Lipo-002



6 Study Population and Subject Selection

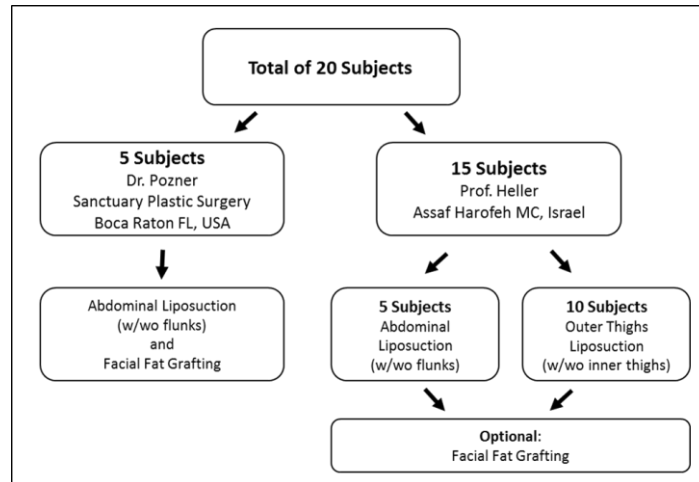
6.1 Source and sample size

Twenty (20) subjects, Ten (10) with excessive fat in the lower abdomen (w/wo flanks) and Ten (10) with excessive fat in the outer thighs (w/wo inner thighs), that are willing to undergo laser assisted liposuction, will be recruited for the study. Five- Twenty (5-20) subjects out of this study group should also be eligible for facial fat grafting.

Five (5) subjects will be recruited at Dr. Pozner's clinic in Sanctuary Plastic Surgery, US and will undergo abdominal liposuction (w/wo flanks) and facial fat grafting. The rest fifteen (15) subjects will be recruited at Prof. Heller's plastic surgery department at Assaf Harofeh Medical Center in Israel and will undergo abdominal liposuction (w/wo flanks) or outer thighs (w/wo inner thighs) liposuction. Facial fat grafting will be optional at the Israeli site. (See Figure 6 for subjects' selection and source).

The subjects will be recruited by the investigator from within the investigator's patient population and if needed from the general population by use of an IRB\Helsinki approved advertisement.

Figure 6: Subjects selection and source – ALM-Lipo-002



For fat vitality assessment (optional), ten (10) samples of the harvested fat, from 10 subjects at Assaf Harofeh MC will be collected.

6.2 Eligibility

Each subject will be evaluated by the Investigator to assess his/her suitability for entry into this study according to the following inclusion/exclusion criteria:

6.2.1 Inclusion Criteria

Subjects must meet all of the following inclusion criteria to be entered into the study:

- Subjects with excessive fat in the lower abdomen w/wo flanks, or subjects with excessive fat in the outer thighs w/wo inner thighs that are willing to undergo laser assisted liposuction.
- Estimated fat harvesting of 1-3 liters.
- Subjects (5-20) eligible for facial fat grafting of at least 5 cc for each cheek.
- Between 18 and 70 years of age.
- Provided written Informed Consent.

6.2.2 Exclusion Criteria

Any of the following will exclude the subject from the study:

- Body Mass Index (BMI) >35.
- Sever skin laxity.

- Positive pregnancy test.
- Current smoker.
- Presence of known malignancy.
- Active infection in the treatment area.
- History of autoimmune disorder (e.g., Systemic Lupus Erythematosus [SLE]).
- History of connective, metabolic or atrophic skin disease.
- History of keloid scarring.
- Chronic use (>7 consecutive days) of anticoagulants (such as aspirin) or NSAIDs within 15 days prior to enrollment.
- Subjects with immune system diseases.
- Subject unable to follow post treatment instructions.
- Any other reason that in the opinion of the investigator, prevents the subject from participating in the study or compromise the subject safety.

6.3 Subject Withdrawal and Replacement

The participating subjects may withdraw their consent to participate in the study at any time during the study without prejudice as written in the informed consent form. The reason should be clearly stated in the subjects' medical records. Only the data, collected up to the point of consent withdrawal, will be analysed by the Sponsor.

The investigator may withdraw a subject if, in his clinical judgment, it is in the best interest of the subject or if the subject cannot comply with the protocol or if the subject is unable to adhere to appointments. In the event that a subject drops out of the study or is withdrawn from the study, before the primary end point (3 months FU visit), the Termination CRF form should be completed and the subject should be replaced by the investigator, with the sponsor's approval.

The sites will be required to complete treatment and follow-ups for 20 subjects and therefore should enroll 10% more subjects to account for any subject dropouts or subjects that will be lost to follow-up during the course of at least 6 months. Reasonable effort should be made to contact any subject lost to follow up during the course of the study in order to complete assessments and retrieve any outstanding data. The records of subjects who terminate prior to completing the study will be retained and the reason for termination will be documented. The sponsor must be notified of all withdrawals. Subject that have a complete data for the primary endpoint

FU (3 months follow-up after the surgery) is considered as a subject that completed the study.

7 Study Procedures

See table 1 for a summary of the study procedures.

7.1 Screening visit

7.1.1 Subject Enrollment

If the subject has met the preliminary study criteria the PI, and/or his designee, will;

- Obtain an informed consent from the subject, clearly stating that the subject is willing to undergo the screening procedure and indicating subject understanding of the requirements and risks involved with study participation and other applicable treatment options. The informed consent will also include photo release consent, stating that the subject is allowing the sponsor (Alma Ltd.) to use the photos taken during the study for educational and marketing purposes (subject identity will be masked to the best possible extent in these pictures).
- Collect demographic characteristics and general information (DoB, Ethnicity, BMI, previous smoking habits and physical activity).
- Review the subject's medical history and concomitant medications use.
- Screen the subject for eligibility to participate in the clinical study using the Inclusion and Exclusion criteria.
- Confirm negative results of pregnancy urine test.
- Perform physical examination and vital signs assessment.
- Document the designated treatment area (lower abdomen w/wo flanks or outer thighs w/wo inner thighs)
- Document if the subject is eligible for facial fat grafting.

If the subject has met the eligibility criteria, he/ she will be recruited to the study.

7.1.2 Subject Identification

At enrollment, each subject will receive a unique identifying number that will be composed of a consecutive number and subject initials. This unique identifier will be used throughout the entire study and will be entered in the subject's CRF for each visit.

7.1.3 Scheduling surgery visit and referral to pre-surgery examinations

Subjects recruited to the study will be scheduled for a surgery up to 2 months after enrollment and for pre-surgery evaluation visit one week prior to the surgery.

- Subjects will be instructed to perform the following optional examinations, per local institution regulation, prior to the pre-surgery evaluation visit;
 - Blood tests including; CBC (complete blood count), chemistry screening and blood clotting test (coagulation tests).
 - Staph MRSA screen test – nasal swab test. If positive, the subject will receive treatment for 5 days prior to the surgery.
 - E.K.G (for subjects > 40 years old).
 - Chest X-ray (for subjects > 50 years old or with relevant background diseases).

All examinations should be performed up to 2 months prior to the surgery.

- At Sanctuary Plastic Surgery, US site subjects will be referred to perform Magnetic Resonance Imaging (MRI) for abdominal fat thickness assessment and facial fat volume assessment.

7.2 Pre-Surgery evaluation visit

At the pre-surgery evaluation visit the study investigator, and/or his designee will perform pre-surgery evaluations, provide instructions to the subjects and perform baseline assessments.

7.2.1 Pre-surgery evaluations

The study investigator, and/or his designee will;

- Review examinations results (detailed in section 7.1.3) and evaluate subject's suitability to the surgery.
- Perform physical examination.
- Evaluate any change in Inclusion/ Exclusion Criteria.

In addition, the subject will meet with an anaesthesiologist, who will give his approval to the surgery (optional, per local institutional regulation).

7.2.1 Pre surgery instructions

Subjects will be recommended to bring to the surgery; abdominal garment (for abdominal liposuction) and wear it for at least 2 weeks after the surgery or thigh garment (for thigh liposuction) and wear it for at least 1 month after the surgery.

7.2.2 Baseline assessments

The study investigator, and/or his designee will;

- Monitor subject adverse events.
- Assess the changes in medication intake since last visit.
- Measure subject's body weight.
- Photograph the subject, only treated area, without the face, while the subject is standing with hanging arms. At Assaf Harofeh site, when using a 2D camera, photograph the subject at frontal, back, 45 and 90 degrees positions, according to a standardized photography instructions (refer to section 8.4).
- For subjects that intended to undergo facial fat grafting procedure, photograph the subject's face at frontal, 45 and 90 degrees positions, when using 2D camera (refer to section 8.4).
- At Sanctuary Plastic Surgery site confirm and document results from the MRI, i.e. abdominal fat thickness and facial fat volume.

The pictures taken in this study may be used by the Sponsor (Alma Lasers Ltd.) in the future for educational and marketing purposes. Subjects' identity will be masked to the best possible extent in these pictures.

7.3 Surgery visit

7.3.1 Reevaluation

Prior to the surgery, the study investigator, and/or his designee will;

- Evaluate any change in Inclusion/ Exclusion Criteria.
- Confirm negative results of pregnancy urine test.
- Assess the changes in medication intake since last visit.
- Monitor subject adverse events.
- Perform physical examination and vital signs.

7.3.2 Surgery Procedure

Perioperative antibiotic will be administered, per surgeon's discretion.

During the surgery, the study investigator, and/or his designee will perform laser assisted liposuction using the LipoLife™ system, including:

1. Instilment of tumescent containing local anesthesia to the treated area (abdomen w/wo flanks or outer thighs (w/wo inner thighs), using the LipoFlow peristaltic mode.
2. Harvest of adipose tissue (1-3 liters) from the treated are, using the Lipoflow suction mode and LipoDiode CW mode.

The LipoLife™ system is designed to be operated only by licensed medical practitioners properly trained in its handling and use. Personnel operating the device must read the operator's manual.

For facial fat grafting procedure (if relevant) the procedure will also include;

3. Injection of the harvested adipose tissue into the face, at least 5 cc per cheek, using the standard fat grafting equipment i.e. syringe, blunt cannula etc.

For fat vitality assessment (optional), ten (10) samples of the harvested fat, from 10 subjects at Assaf Harofeh MC, will be transported to the laboratory, within 4 hours. Cell viability assessment will be performed using trypan blue exclusion assay.

7.3.3 Post-surgery instruction

The subject will usually be discharged from the hospital at the same day or a day after the surgery, according to local institutional regulation, with recommendations to rest for two weeks, wash the surgical area with water and soap, and wear the abdominal/ thigh garment on a daily basis. In addition, a 1 month follow-up meeting will be scheduled.

7.4 Follow-Up visits

Follow up visits will be carried out 1 month \pm 7 days (1m FU), 3 months \pm 7 days (3m FU) and 6 months \pm 7 days (6m FU) after the surgery.

During these visits the following procedures will be performed by the investigator, and/or his designee:

- Assessment of changes in medication intake since last visit.
- Physical examination and vital signs.

- Assessment of adverse events according to subject's report and physical examination.
- Obtaining subjects' satisfaction, following liposuction procedure, according to subject's satisfaction questionnaire (see section 8.3).
- Body weight measurement.
- Subjects' liposuction area photography, according to standardized photography instructions (see section 8.4).
- For subjects that had fat grafting procedure:
 - Facial photography, according to standardized photography instructions (see section 8.4).
 - Obtaining subjects' satisfaction, following facial fat grafting procedure, according to subject's satisfaction questionnaire (see section 8.3).
- At Sanctuary Plastic Surgery site, at 1m FU visit subject will be referred to perform MRI for abdominal fat thickness assessment and facial fat volume assessment, 2-3 weeks prior to the 3m FU visit. At 3m FU visit, the investigator, and/or his designee will confirm and document the results from the MRI assessments.

7.5 Termination visit

The termination visit occurs in parallel with the last follow up visit (6m FU visit). During this visit the coordinator/investigator will fill the termination CRF.

7.6 Summary of study procedures

Schedule of times and events, including required study visits, procedures and assessments to be performed at each visit can be found at the table below (Table 1).

Table 1: Study Procedures- ALM-Lipo-001

FU=follow up; m= month; W=week; d=days

	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6
	Screening	Pre-Surgery evaluation	Surgery	1m FU	3m FU Primary endpoint	6m FU
Weeks	Up to -2m	-1w	0	4W ±7d	12W ±7d	24W ±7d
Informed consent	X					
Demographic assessment	X					
General information (previous smoking habits and physical activity)	X					
Medical History	X					
Concomitant Medications	X					
Concomitant Medications change		X	X	X	X	X
Physical examination	X	X	X	X	X	X
Vital signs	X		X	X	X	X
Pregnancy test	X		X			
Inclusion/Exclusion Criteria assessment	X					
Inclusion/ Exclusion Criteria evaluation for change		X	X			
Pre/ Post-surgery instructions to the subjects		X	X			
Review pre-surgery examinations (optional) e.g.; Blood test, Staph NRSA screen test, E.K.G and chest X-Ray		X				
Consultation with an anesthesiologist (optional)		X				

	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6
	Screening	Pre-Surgery evaluation	Surgery	1m FU	3m FU Primary endpoint	6m FU
Weeks	Up to -2m	-1w	0	4W ±7d	12W ±7d	24W ±7d
Liposuction procedure- Subject's satisfaction questionnaire (5 point Likert scale)				X	X	X
Facial fat grafting procedure - Subject's satisfaction questionnaire (5 point Likert scale)*				X	X	X
Body weight measurement		X		X	X	X
Subject photography**	Liposuction area (when using 2D camera at Assaf Harofeh MC : Frontal, back, 45 and 90 degrees positions)	X		X	X	X
	Face* (when using 2D camera at Assaf Harofeh MC: Frontal, 45 and 90 degrees positions)	X		X	X	X
Blinded evaluations				X	X	X
MRI results *** (abdominal fat thickness and facial fat volume)		X			X	
AE assessment		X	X	X	X	X
Termination CRF						X

* For subject that will have/had facial fat grafting procedure.

** 3D camera at Sanctuary Plastic Surgery, US and 2D or 3D camera at Assaf Harofeh MC, Israel

*** At Sanctuary Plastic Surgery, US

8 Evaluations

8.1 Collecting demographic information, medical history and concomitant medications

At the screening visit, information regarding medical history, concomitant medications and demographic information; i.e. age, ethnicity, BMI (calculated from height and weight measurements), previous smoking habits and physical activity (type and times/week) will be collected.

According to this information eligibility to participate in the study will be evaluated. Change in concomitant medications will re-evaluated at all study's visits.

8.2 Physical examination

Physical examination will be performed at screening visit, in order to evaluate eligibility to participate in the clinical study and eligibility to the surgery.

In addition physical examination of the surgery site will be evaluated at all studies' visits and will be used, inter alia, to assess AEs.

8.3 Subject's satisfaction questionnaire

Following laser assisted liposuction, subjects will be requested to scale their satisfaction from the treatment according to Subject's Satisfaction Questionnaire, based on 5 point Likert scale, as detailed in Table 2.

Subjects that underwent facial fat grafting procedure will be requested to fill in additional form, while referring to their satisfaction from the facial fat grafting procedure.

Table 2: Subject's Satisfaction Questionnaire- ALM-Lipo-002

Subject's Satisfaction Questionnaire	
Procedure: Lower abdomen (w/wo flanks) / Outer thighs (w/wo inner thighs) / Facial fat grafting <i>(Please circle the relevant procedure)</i>	
Subject Improvement and Satisfaction	
1. <i>Please rate your satisfaction from the treatment results</i>	
Subjects Improvement: 1- No Improvement 2- Mild Improvement 3- Moderate Improvement 4- Good Improvement 5- Excellent Improvement	Subjects Satisfaction: 1- Very dissatisfied 2- Dissatisfied 3- Somewhat satisfied 4- Satisfied 5- Very satisfied
Satisfaction from skin reaction (tightening)	
2. <i>Please rate your satisfaction from the skin reaction (tightening) after the surgery</i>	
1- Very dissatisfied 2- Dissatisfied 3- Somewhat satisfied 4- Satisfied 5- Very satisfied	
Subject Personal Experience	
3. <i>Will you recommend the treatment to your family/friends?</i>	
1- Extremely unlikely 2- Very unlikely 3- Somewhat unlikely 4- Very likely 5- Extremely likely	

8.4 Blinded digital photography evaluations

Standardized photography instructions

- **At Sanctuary Plastic Surgery Boca Raton FL,US**

3D digital photographs will be taken using Canfield Scientific, Inc. camera, including;

- Lower abdomen w/wo flanks, without the face, for liposuction procedure evaluation
- Subject's face for facial fat grafting procedure evaluation.

- ***At Assaf Harofeh Medical Center, Israel***

2D and/or 3D digital photographs will be taken at Assaf Harofeh Medical Center. When using 2D camera (Nikon D7100), the camera will be placed at a distance of 2 meters from the subject. Only treated area will be photographed (i.e. lower abdomen w/wo flanks or thighs), without the face, at frontal, back, 45 degrees (left and right) and 90 degrees (left and right) positions, with arms resting on the side. In addition, for subjects that underwent facial fat grafting procedure, subject's face will be photographed at frontal, 45 and 90 degrees positions. Each position will be photograph 3 times.

Photographs will be taken at baseline and at 1, 3 and 6 months FU visits. The photographs will be downloaded to a computer under subject's identification number folder, and will be compiled into a PowerPoint presentation for panel evaluation.

Before and after photographs - Blinded evaluation

Panel of 3 physicians, blinded to the study design will evaluate the aesthetic outcomes of the treated area. The physicians will be presented with two photographs (baseline and 1/3/6 months after the surgery) and will be requested to assess which photograph represent the "before" (baseline) and which one the "after" (1/3/6 months after the surgery). In addition they will be requested to scale the improvement according to Global Aesthetic Improvement Scale (GAIS), as detailed in table 3.

Table 3: Global Aesthetic Improvement Scale (GAIS)- ALM-Lipo-002

Scale	Level of Improvement	
1	Very much improved	Optimal cosmetic results.
2	Much improved	Marked improvement in appearance, but not completely optimal.
3	Improved	Improvement in the appearance, better than initial condition, but re-treatment is advised.
4	No change	The appearance substantially remains the same compared to initial condition.
5	Worse	The appearance has worsened compared to the initial condition.

8.5 Fat vitality assessment

Fat vitality assessment will be optional.

Ten (10) samples of the harvested fat, from 10 subjects at Assaf Harofeh MC, will be transported to the laboratory, within 4 hours.

Cell viability assessment will be performed using trypan blue exclusion assay.

9 Adverse Events (AE) and Serious Adverse Events (SAE)

The investigator is responsible for the detection and documentation of events meeting the criteria and definition of an adverse event (AE) or a serious adverse event (SAE) as provided in this protocol. During the study, when there is a safety evaluation, the investigator or site staff will be responsible for detecting AEs and SAEs, as detailed in this section of the protocol. All adverse events reported between consent and final follow-up will be recorded in the case report form (CRF).

9.1 Definition of an Adverse Event (AE)

Any untoward medical occurrence in a participant or clinical investigation participant, temporarily associated with the use of a medicinal product, whether or not considered related to the medicinal product.

An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. For marketed medicinal products, this also includes failure to produce benefits (i.e. lack of efficacy), abuse or misuse.

9.2 Anticipated Outcome Related Adverse Events

Anticipated related AE for liposuction procedure may include; local pain, hematoma, contour deformities, infection, local fibrosis of scars or systemic side effects such as electrolyte disorders.

Anticipated related AE for facial fat grafting procedure may include; infection, ecchymosis, fat necrosis or injury of adjacent tissue.

Any anticipated AE that occurs at any time during or after the use of the study device must be reported by the Investigator to Alma Lasers Ltd. If the anticipated AE, in the

opinion of Alma Lasers or the Investigator, is likely to affect the safety of the subjects or the conduct of the study, the IRB/ Helsinki/ other ethic committee will be notified of the effect within 10 working days after Alma Lasers first receives notice of it.

9.3 Unanticipated Outcome Related Adverse Events

An unanticipated adverse device effect as defined by the Federal Regulations [21 CFR 812.3(s)] is “any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.” From a practical perspective, an unanticipated adverse device effect means a serious adverse event that is not listed in the device labelling, or the frequency or severity is greater than reported in the device labelling.

9.4 Definition of a Serious Adverse Event (SAE)

A serious adverse event is any untoward medical occurrence that, at any dose:

- a) Results in death
- b) Is life threatening
- c) Requires hospitalization or prolongation of an existing hospitalization.
Hospitalization for elective treatment of a pre-existing condition that did not worsen from baseline is not considered an AE.
- d) Results in disability/incapacity
- e) Is a congenital abnormality / birth defect.
- f) Any event deemed by the investigator as being a significant medical event.

9.5 Recording of AEs and SAEs

When an AE/SAE occurs, it is the responsibility of the investigator to review all documentation (e.g. hospital progress notes, laboratory, and diagnostic reports) relative to the event. The investigator will then record all relevant information regarding an AE/SAE in to the CRF. It is not acceptable for the investigator to send photocopies of the subject’s medical records to Alma Lasers Ltd. in lieu of completion of the appropriate AE/SAE CRF pages. However, there may be instances when copies of medical records for certain cases are requested by Alma Lasers Ltd. In this instance, all subject identifiers will be blinded on the copies of the medical records prior to submission to Alma Lasers Ltd.

For each adverse event, start and stop dates, action taken, outcome, intensity and relationship to study product (causality) must be documented. If an AE changes in frequency or intensity during a study, a new entry of the event must be made in the CRF.

The investigator will attempt to establish a diagnosis of the event based on signs, symptoms, and/or other clinical information. In the absence of a diagnosis, the individual signs/symptoms should be documented. All details of any treatments initiated due to the adverse event should be recorded in the subject's notes and the CRF.

9.6 Prompt Reporting of SAEs to Alma Lasers Ltd.

Once an investigator becomes aware that an SAE has occurred in a study subject, he/she will immediately notify the sponsor by contacting the study monitor via telephone to notify him/her of the event. The SAE form must be completed as thoroughly as possible with all available details of the event, signed by the investigator, and faxed within 24 hours of first becoming aware of the event to the following person:

Ronit Lipson

Alma Lasers Ltd.

14 Halamish Street, POB 3021

Caesarea Industrial Park

Caesarea, Israel 38900

Phone: 972-52-2337768

Fax: +972-4-627-5368

If the investigator does not have all information regarding an SAE, he/she will not wait to receive additional information before notifying the study monitor of the event and completing the form. The form will be updated when additional information is received.

The investigator must also notify the Reviewing IRB/ Helsinki/ other ethic Committee of any SAEs according to the guidelines of the Ethics Committee.

9.7 Evaluating AEs and SAEs

9.7.1 Assessment of Intensity

The investigator will make an assessment of intensity for each AE and SAE reported during the study. The assessment will be based on the investigator's clinical

judgement. The intensity of each AE and SAE recorded in the CRF should be assigned to one of the following categories:

Mild: An event that is easily tolerated by the subject, causing minimal discomfort and not interfering with everyday activities.

Moderate: An event that is sufficiently discomfoting to interfere with normal everyday activities.

Severe: An event which is incapacitating and prevents normal everyday activities.

An AE that is assessed as severe should not be confused with an SAE. Severity is a category utilised for rating the intensity of an event; and both AEs and SAEs can be assessed as severe. An event is defined as “serious” when it meets one of the pre-defined outcomes as described in Section “Definition of an SAE”.

9.7.2 Assessment of Causality

The investigator is obligated to assess the relationship between investigational device and the occurrence of each AE/SAE. The investigator will use clinical judgment to determine the relationship. Alternative causes, such as natural history of the underlying diseases, concomitant therapy, other risk factors, and the temporal relationship of the event to the investigational product will be considered and investigated. The investigator will also consult the IB and/or device information in the determination of his/her assessment.

The causal relationship to the study product assessed by the Investigator (or medically qualified delegate) should be assessed using the following classifications:

Not Related In the Investigator’s opinion, there is not a causal relationship between the study product and the adverse event.

Unlikely The temporal association between the adverse event and study product is such that the study product is not likely to have any reasonable association with the adverse event.

Possible The adverse event could have been caused by the study participant’s clinical state or the study product.

Probable The adverse event follows a reasonable temporal sequence from the time of study product administration, abates upon discontinuation of

the study product and cannot be reasonably explained by the known characteristics of the study participant's clinical state.

Definitely The adverse event follows a reasonable temporal sequence from the time of study product administration or reappears when study product is reintroduced.

10 Statistical Analysis

10.1 General Considerations

When statistical tests are performed, they will be two-sided. The required significance level of findings will be equal to or lower than 5%. Where confidence limits are appropriate, the confidence level will be 95%.

Baseline values are defined as the last valid value prior to the surgery.

All statistical analyses of safety and performance measures will be descriptive in nature. Continuous variables will be summarized by a mean, standard deviation, minimum, median and maximum, and categorical variables by a count and percentage. Confidence intervals will be provided where relevant.

10.2 Disposition of Subject

The numbers of subjects who were enrolled and completed each visit of the study will be provided, as well as the reasons for all enrollment discontinuations, grouped by major reason (e.g., lost to follow-up, adverse event, poor compliance). A list of discontinued subjects, protocol deviations, and subject excluded from the efficacy analysis will be provided as well.

10.3 Safety Analysis

A detailed list of all adverse events will be presented. The adverse event rate and incidence will be compiled with respect to frequency, nature, seriousness of the event, severity of the event, and relationship to the study device. In addition, listings of all safety measures will be produced.

10.4 Interim Analysis

An interim report to analyse safety and efficacy will be performed at 3 months Follow-Up.

11 Administrative Procedures

11.1 Investigator Responsibility

Except where the Principal Investigator's signature is specifically required, it is understood that the term 'Investigator' as used in this Protocol and on the CRFs refers to the Principal Investigator or an appropriately qualified member of the staff that the Principal Investigator designates to perform specified duties of the Protocol. The Principal Investigator is ultimately responsible for the conduct of all aspects of the study.

Each Investigator will comply with the local regulations regarding clinical trials and the Investigator responsibilities outlined in the ICH GCP guidelines.

11.2 Ethic committee Approval

The Protocol will be submitted for approval to the Reviewing IRB/ Helsinki/ other ethic committee, and written approval obtained, before study subjects are enrolled. The Investigators will receive all the documentation needed for submitting the present Protocol to the Ethics Committee. A copy of the respective approval letters will be transmitted to the Study Monitor before starting the study. The composition of the Ethics Committee must also be provided to the Study Monitor. If approval is suspended or terminated by the Reviewing Ethics Committee, the Investigator will notify the Study Monitor immediately.

It is the responsibility of the Investigator to report study progress to the Reviewing Ethics Committee as required or at intervals not greater than one year.

The Principal Investigator, or his/her nominee, will be responsible for reporting any serious adverse events to the Ethics Committee as soon as possible, and in accordance with the local guidelines.

11.3 Informed Consent

Before recruitment and enrollment into the study, each prospective candidate will be given a full explanation of the nature and purposes of the study, and a copy of the Informed Consent Form to review. Once the essential study information has been provided, and the Investigator is assured that each potential subject understands the implications of participating in the study, the subjects will be asked to give consent to participate in the study by signing the informed consent form. The consent forms shall

be signed and dated by the appropriate parties. A notation that written informed consent has been obtained will be made on the participant's CRF. The completed consent forms will be retained by the Investigator and a copy of these will be provided by the Investigator to the participant.

11.4 Case Report Forms (CRF)

A Case Report Form (CRF) will be completed for each study subject summarising all clinical screening and study data. Subjects will only be referred to in the CRF by their subject number and initials in order to retain their confidentiality.

The Investigator is responsible for completely and accurately recording study data in the appropriate sections of the CRFs provided by Alma lasers. The CRFs must be signed by the Investigator or by his/her authorized person as designated in the Signature Authorization Log.

The completed original CRF's are to be sent to the Sponsor as soon as practical after completion and review. A copy of each completed CRF is to be retained by the Investigator for a period of time as determined by local regulations.

11.5 Monitoring and Quality Assurance

The task of the Study Monitor is to guarantee the best conduct of the study through frequent contacts by phone and in person with the responsible Investigator, in accordance with the Monitor's Standard Operating Procedures, with the purpose of facilitating the work and fulfilling the objectives of the study. The Monitor is responsible for monitoring adherence to the Protocol and completion of the CRF, and for the relationship between the Investigator and Alma Lasers Ltd.

The organisation, monitoring, supply of study materials and quality assurance of the present clinical study is the responsibility of Alma Lasers Ltd. or its designee.

In order to ensure the accuracy of data, direct access to source documents by the representatives of both the Study Monitor and regulatory authorities is mandatory. Anonymity of the subject will be maintained at all times. Alma Lasers Ltd. reserves the right to terminate the study for refusal of the Investigator/Institution to supply source documentation of work performed in the study.

11.6 Financial Aspects

The conduct of the study is subject to a Financial Agreement between Alma Lasers Ltd. and the Investigator or Institution.

11.7 Device Use/Accountability

Use and storage of LipoLife™ system and accessories will be performed according to the Operation Manual. All received used and unused LipoLife™ system components will be documented on the accountability form.

11.8 Protocol Amendments

Neither the Investigator nor Alma Lasers Ltd. will modify the Protocol without first obtaining the concurrence of the other in writing. Protocol modifications that impact on participant safety or the validity of the study will be approved by the Ethics Committee.

No changes (amendments) to the Protocol may be implemented without prior approval from the Sponsor and the Reviewing Ethics Committee. If a Protocol amendment requires changes to the Informed Consent Form, the revised Informed Consent Form, prepared by the Investigator, must be approved by the Reviewing Ethics Committee.

Once the final Protocol has been issued and signed by the Investigator and the authorised signatories, it shall not be informally altered. Protocol amendments are alterations to a legal document and have the same legal status. Therefore, they must pass through appropriate steps before being implemented. In general, any important change that theoretically increases risk to participants constitutes an amendment. Minor changes are administrative changes and need documentation without approval.

It is the responsibility of the Investigator to submit the amendment to the Reviewing Ethics Committee for their approval; written approval should be obtained and a copy provided to the Sponsor. The Sponsor is responsible for determining whether or not the local regulatory authority must be notified of the Protocol change. Completed and signed Protocol amendments will be circulated to all those who were on the circulation list for the original Protocol.

The original signed copy of amendments will be kept in the Study File with the original Protocol. It should be noted that where an amendment to the Protocol substantially alters the study design or the potential risks to the participants, each participant's consent to continue participation should be obtained.

11.9 Protocol Compliance

The instructions and procedures specified in this Protocol require diligent attention to their execution. Should there be questions or consideration of deviation from the Protocol, clarification will be sought from the Study Monitor. Any participant treated in a manner that deviates from the Protocol, or who is admitted into the study but is not qualified according to the Protocol as amended by Alma Lasers Ltd. and the Investigator, may be ineligible for analysis and thereby compromise the study.

Only when an emergency occurs that requires a departure from the Protocol for an individual will there be such a departure. The nature and reasons for the Protocol violation/deviation shall be recorded in the CRF and the investigator should notify the sponsor and Ethics Committee as soon as possible.

11.10 Archives: Retention of Study Records

All source documents, CRFs and trial documentation will be kept by the Investigator for the appropriate retention period as stipulated by local regulations and ICH-GCP.

11.11 Early Termination of the Study

The study may be terminated prematurely by the principal investigator or his/her designee and the sponsor if:

- The number and/or severity of adverse events justify discontinuation of the study
- New data become available which raise concern about the safety of the study device, so that continuation might cause unacceptable risks to subjects.

In addition, Alma Lasers Ltd. reserves the right to discontinue the trial prior to inclusion of the intended number of participants, but intends only to exercise this right for valid scientific or administrative reasons.

After such a decision, the Investigator must contact all participating subjects, and written notification must be sent to the Reviewing Ethics Committee and relevant Regulatory Authorities.

11.12 Reporting Requirements

The investigator must promptly report to Alma lasers any withdrawal of IRB/Helsinki/other ethic committee approval at the site. Additional reporting requirements include:

- Notify Alma Lasers' designee and to the ethic committee a report of any serious adverse device effect, whether anticipated or unanticipated, that occurs during the study as soon as possible, but in no event later than 10 working days after the investigator first learns of the effect. This report is to include a description of the effect, subsequent treatments, clinical outcomes, and outcome diagnoses. If the site personnel are not sure whether an event meets these criteria they should call the clinical monitor.
- Notify Alma Lasers or Alma Lasers' designee and the ethic committee immediately (within 24 hours) if an emergency situation arises in which the subsequent treatment, in the best interests of the subject, requires a deviation from the protocol. This should be followed with written confirmation that describes the emergency action and outcomes, to Alma Lasers and the ethic committee within 5 working days.
- Report to the ethic committee and Alma Lasers, within 5 working days, the use of the study device without signed informed consent from the subject.
- Report adverse events in accordance with 21 CFR 803.
- Submit regular progress reports to the approval committee and Alma Lasers or Alma Lasers' designee, as requested by the investigators or the ethic committee.
- Submitting a final report on the study to the ethic committee and Alma Lasers or Alma Lasers' designee within 3 months after termination or completion of the study.

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13 Appendix

13.1 Appendix A: Subject's satisfaction questionnaire

Subject's Satisfaction Questionnaire	
Procedure: Lower abdomen (w/wo flanks) / Outer thighs (w/wo inner thighs) / Facial fat grafting <i>(Please circle the relevant procedure)</i>	
Subject Improvement and Satisfaction	
1. <i>Please rate your satisfaction from the treatment results</i>	
Subjects Improvement: 1- No Improvement 2- Mild Improvement 3- Moderate Improvement 4- Good Improvement 5- Excellent Improvement	Subjects Satisfaction: 1- Very dissatisfied 2- Dissatisfied 3- Somewhat satisfied 4- Satisfied 5- Very satisfied
Satisfaction from skin reaction (tightening)	
2. <i>Please rate your satisfaction from the skin reaction (tightening) after the surgery</i>	
1- Very dissatisfied 2- Dissatisfied 3- Somewhat satisfied 4- Satisfied 5- Very satisfied	
Subject Personal Experience	
3. <i>Will you recommend the treatment to your family/friends?</i>	
1- Extremely unlikely 2- Very unlikely 3- Somewhat unlikely 4- Very likely 5- Extremely likely	

13.2 Appendix B: Global Aesthetic Improvement Scale (GAIS)

Global Aesthetic Improvement Scale (GAIS)

Scale	Level of Improvement	
1	Very much improved	Optimal cosmetic results.
2	Much improved	Marked improvement in appearance, but not completely optimal.
3	Improved	Improvement in the appearance, better than initial condition, but re-treatment is advised.
4	No change	The appearance substantially remains the same compared to initial condition.
5	Worse	The appearance has worsened compared to the initial condition.