Information Cover Page

Zeltiq Aesthetics Protocol ZA19-002

Electromagnetic Muscle Stimulation for Abdominal and Gluteal Toning

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ELECTROMAGNETIC MUSCLE STIMULATION FOR ABDOMINAL AND GLUTEAL MUSCLE TONING

Investigational Plan

Sponsor	ZELTIQ Aesthetics, an Allergan affiliate 4410 Rosewood Dr. Pleasanton, CA 94588
Protocol Number:	ZA19-002
Protocol Version:	1.0 May 1, 2019
Sponsor Contact:	Lori Brandt Director, Clinical Trial Management [redacted]

INVESTIGATOR SIGNATURE PAGE

For protocol number ZA19-002

I agree to:

- Implement and conduct this study diligently and in strict compliance with this protocol, GCP, and all applicable laws and regulations.

- Maintain all information supplied by the Sponsor, ZELTIQ Aesthetics, an Allergan affiliate, in confidence and, when this information is submitted to an Ethics Committee (EC), 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.

_____	_____	_____
Investigator printed name	Signature	Date

_____	_____	_____
Co- Investigator printed name	Signature	Date

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Protocol Summary

Title	Electromagnetic Muscle Stimulation for Abdominal and Gluteal Muscle Toning
Design	Prospective, multi-center, non-randomized, interventional
Purpose	Evaluate the use of Electromagnetic Muscle Stimulation for body contouring
Enrollment	Up to 200 subjects
Clinical site(s)	Up to 20 investigational sites
Subject Population	Healthy adult men and women aged 22 – 65 who desire abdominal and/or gluteal muscle toning.
Primary Endpoints	Efficacy endpoint: Measurement of subject feeling about body shape, assessed using the Body Satisfaction Scale at the 4-Week follow-up visit. Safety endpoint: The frequency of device-related adverse events (AEs) including device-related serious adverse events (SAEs) will be summarized.
Secondary Endpoint	Secondary endpoint: Subject-graded improvement in the treated area using the Subject Global Aesthetic Scale (SGAIS) at the 4-Week follow-up visit.
Sponsor	ZELTIQ Aesthetics, an Allergan affiliate 4410 Rosewood Dr. Pleasanton, CA 94588

1. Introduction

1.1 Background

Fat reduction and body contouring procedures, which include invasive, minimally-invasive, and non-invasive procedures, have become increasingly popular aesthetic procedures. Patients who are obese and do not have specific fat bulges but require significant fat reduction to achieve aesthetic results are candidates for invasive and minimally-invasive procedures, such as liposuction and laser-assisted liposuction. Although effective at reducing fat, these invasive and minimally-invasive procedures involve significant patient discomfort, expense, downtime, and the risks typically associated with surgical procedures. As a result, patients who do not require significant fat reduction to achieve meaningful aesthetic results typically seek non-invasive fat reduction and body contouring procedures to avoid the pain, expense, downtime, and surgical risks associated with invasive and minimally-invasive procedures.

ZELTIQ Aesthetics has developed and commercialized a technology for cold-assisted lipolysis. The ZELTIQ CoolSculpting technology is based on the sensitivity of fat cells to cold injury in order to selectively eliminate subcutaneous fat tissue without affecting the skin or other surrounding tissues. The technology, cryolipolysis, enables a non-invasive alternative for subcutaneous fat reduction through cellular apoptosis. The ZELTIQ CoolSculpting System is cleared for use in the United States for the indication of cold-assisted lipolysis of various body areas, including the abdomen, flanks, thighs, submental and submandibular areas, back fat, bra fat, and banana roll. It has been clinically proven to reduce fat bulges, allowing patients to achieve noticeable and measurable aesthetic results without the pain, expense, downtime, and risks associated with existing invasive and minimally-invasive procedures.

While the CoolSculpting procedure is successful in reducing subcutaneous fat in the abdomen, ZELTIQ Aesthetics is exploring the concept of combining other non-invasive aesthetic treatment modalities to enhance and/or improve the contouring effects of CoolSculpting.

One treatment of interest is the use of electromagnetic muscle stimulation (EMS) [redacted] Electromagnetic muscle stimulation (EMS), also known as neuromuscular electrical stimulation (NMES) is the elicitation of muscle contraction using

electric impulses. The impulses mimic the action potential that comes from the central nervous system, causing the muscles to contract. [1]

EMS devices are frequently used in physical therapy or rehabilitation settings to strengthen and tone muscles damaged by illness or disease but they may also be used for other purposes. [2] High intensity EMS devices can elicit stronger, more effective muscle contractions believed to increase muscle strength and endurance. EMS has received an increasing amount of attention in the last few years from fitness enthusiasts as various manufacturers promote the technology for muscle strengthening, firming and improvement in muscle tone specifically in the abdomen, buttocks and thighs. [3]

[redacted]

1.2 Device Descriptions

EMS Devices

Electromagnetic (EMS) devices that may be used in this evaluation produce electromagnetic muscle stimulation by a non-contact magnetic field in tissue. Each device under consideration for use in this study has the same indications for use and similar technological characteristics and principles of operation. Figure 1 below depicts a representative EMS device.

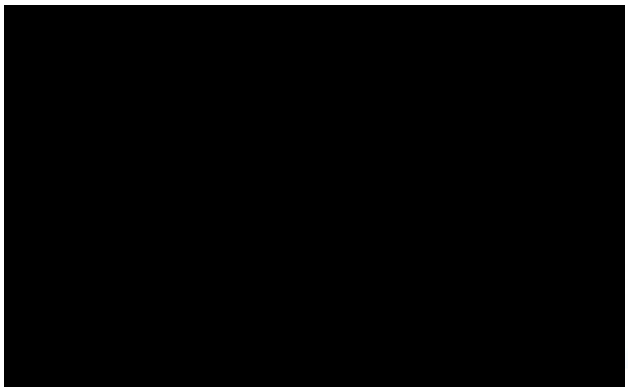

Figure 1. Representative EMS Device

This study will evaluate the feasibility of EMS treatments for improvement in abdominal and buttock contouring. [redacted] One or more EMS devices may be used in this evaluation.

The EMS devices considered for use in the proposed evaluation have the following indications:

- Improvement of abdominal tone, strengthening of the abdominal muscles, development of firmer abdomen.
- Strengthening, toning and firming of buttocks

EMS devices utilized in this study will be operated in accordance with the manufacturer's Instructions for Use.

The materials used for patient-contacting surfaces are all common materials with a history of use in medical and/or skin-contact consumer applications or have been tested for biocompatibility.

1.3 Regulatory Status

The EMS devices that may be used in the proposed evaluation are non-significant risk devices. [redacted]

2. Study Protocol

2.1 Design

Prospective, multi-center, non-randomized, interventional study

2.2 Study Duration

Enrollment and follow-up are expected to take up to four (4) months for each subject.

2.3 Physician Participants

Study Investigators must be practicing medical physicians with experience in the use of the CoolSculpting System.

2.4 Site Requirements

Site Investigators should have at least one study coordinator with experience in conducting aesthetic research and with sufficient time to perform study activities.

2.5 Subject Recruitment

Patients who seek abdominal and/or gluteal muscle firming and toning will be recruited for this study.

2.6 Sample Size

A maximum of 200 subjects will be included in the study.

2.7 Subject Eligibility

To be eligible to participate, subjects must meet all of the inclusion criteria and none of the exclusion criteria listed in **Table 1**.

Table 1. Eligibility criteria.

Inclusion Criteria
a) Male or female ≥ 22 years and ≤65 years of age.
b) Subject has not had weight change exceeding 5% of body weight in the preceding month.
c) Subject agrees to maintain body weight within 5% during the study by not making any changes in diet or exercise routine.
d) Subject has a BMI ≤ 30 as determined at screening.

e) Subject agrees to have photographs taken of the treatment area(s) during the scheduled time periods.
f) Subject agrees to refrain from any new abdominal and/or gluteal muscle training exercises of the treatment area during the course of the study.
g) Subject agrees to avoid sun tanning during the course of the study.
h) Subject has read and signed the study written informed consent form.

Exclusion Criteria

a) Subject has had a recent surgical procedure(s) in the area of intended treatment and muscle contractions may disrupt the healing process.
b) Subject has had an invasive fat reduction procedure (e.g., liposuction, mesotherapy) in the area of intended treatment.
c) Subject needs to administer or has a known history of subcutaneous injections into the area of intended treatment (e.g., heparin, insulin) within the past month.
d) Subject has not had an intrauterine contraceptive device inserted or removed within the past month.
e) Subject has a bleeding disorder
f) Subject is taking or has taken diet pills or supplements within the past month.
g) Subject has a metal implant or active implanted device such as a cardiac pacemaker, cochlear implant, intrathecal pump, hearing aids, defibrillator, or drug delivery system.
h) Subject agrees not to change muscle exercise routine in the treatment area (abdominal and/or gluteal) while participating in the study
i) Subject has pulmonary insufficiency.
j) Subject has a cardiac disorder.
k) Subject has a malignant tumor.
l) Subject has been diagnosed with a seizure disorder such as epilepsy.
m) Subject currently has a fever.
n) Subject is diagnosed with Grave's disease.
o) Subject is pregnant or intending to become pregnant during the study period (in the next 9 months).
p) Subject is lactating or has been lactating in the past 6 months.
q) Subject is unable or unwilling to comply with the study requirements.
r) Subject is currently enrolled in a clinical study of any other investigational drug or device.
s) Any other condition or laboratory value that would, in the professional opinion of the Investigator, potentially affect the subject's response or the integrity of the data or would pose an unacceptable risk to the subject.

2.8 Informed Consent

Study candidates shall receive an explanation of the study objectives, possible risks and benefits of the study, and be given adequate time to read the information included in the informed consent document. Candidates will be given an opportunity to ask questions about any of the information contained in the informed consent. Candidates must verbally acknowledge understanding of the informed consent and sign the consent form accordingly. This form must have prior approval of the Institutional Review Board (IRB).

2.9 Screening Procedures

Once informed consent is obtained, interested subjects will undergo screening.

Screening Visit; Required; Day -60 to Day 0

After the informed consent is signed, subjects will be screened to determine if all eligibility criteria are met. The Investigator or designee shall complete a brief medical history and examine the subject to confirm eligibility for the study.

1. Obtain height and weight.
2. Calculate BMI.
3. Assess for any medical conditions that would lead to exclusion of a subject from the study.
4. [redacted]
5. Document medication use, Fitzpatrick Skin Type, and ethnicity.
6. All female subjects of childbearing potential will be asked to take a pregnancy test (urine) prior to being treated. If the subject is pregnant, she will be excluded from participation.

Female subjects of childbearing potential will be advised to avoid becoming pregnant during the study by using a medically accepted form of contraception if they are sexually active. If the subject becomes pregnant during the study, she will not be treated subsequently with the study device or be required to have follow-up photographs taken or any other efficacy assessment performed.

All subjects will be asked to maintain their weight by not making any major changes to their diet or exercise regimen during the study. Subjects who do not maintain their weight within 5% will continue in the study. However, if the weight change is more than 5% after the final treatment, the subjects' data will be excluded from the per-protocol data analysis.

Subjects that do not meet all eligibility criteria will be excluded from further participation in the study.

2.10 Enrollment

Study candidates who sign the informed consent form, meet eligibility criteria, and undergo initiation of study treatment are considered enrolled. Study treatment initiation is defined as the initiation of treatment with a study device after the placement of the applicator on the intended treatment area on the scheduled treatment day.

2.11 Photo Visit; Required, day -30 to 0

All subjects will have their photos taken within 30 days prior to first study treatment.

a) Obtain weight.
b) [redacted]
c) Obtain baseline 2-Dimensional photographs of the treatment area using standardized setup and settings.

2.12 Study Treatment

[redacted]

[redacted] The abdomen and/or buttocks may be treated. [redacted]

Treatment Visit 1

Prior to EMS Treatment

a) Review and confirm subject meets all of the inclusion criteria and none of the exclusion criteria, then proceed with the study treatment.

b) Repeat pregnancy test for female subjects of childbearing potential (urine). Exclude subject from participation if the results are positive.
c) Obtain weight (Note: weight measurement is only required prior to first EMS treatment).
d) Subject completes Body Satisfaction Scale for abdomen and or Body Satisfaction Scale for buttocks as appropriate. Note: Completion of these scales is required prior to first EMS treatment).

EMS Treatment Steps

e) Apply EMS device per manufacturer's Instructions for Use.
f) Support the EMS device with pillows or straps as needed.
g) Initiate treatment using recommended program for toning and firming the targeted treatment area supplied by manufacturer.
h) Record the highest percent (%) energy utilized for the EMS treatment.

[redacted]

Treatment Visits 2 and 3

The required study activities are the same for both Treatment Visits 2 and 3:

Prior to EMS Treatment

a) Review and confirm subject meets all of the inclusion criteria and none of the exclusion criteria.
b) Repeat pregnancy test for female subjects of childbearing potential (urine). Exclude subject from participation if the results are positive.

EMS Treatment Steps

c) Apply EMS device per manufacturer's Instructions for Use.
d) Support the EMS device with pillows or straps as needed.
e) Initiate treatment using recommended program for toning and firming the targeted treatment area supplied by manufacturer.
f) Record the highest percent (%) energy utilized for the EMS treatment.

g) [redacted]

Treatment Visit 4

Prior to EMS Treatment

a) Review and confirm subject meets all of the inclusion criteria and none of the exclusion criteria, then proceed with the study treatment.
b) Repeat pregnancy test for female subjects of childbearing potential (urine). Exclude subject from participation if the results are positive.

EMS Treatment Steps

c) Apply EMS device per manufacturer's Instructions for Use.
d) Support the EMS device with pillows or straps as needed.
e) Initiate treatment using recommended program for toning and firming the targeted treatment area supplied by manufacturer.
f) Record the highest percent (%) energy utilized for the EMS treatment.
g) [redacted]

Post-EMS Treatment # 4

h) Subject completes Body Satisfaction Scale(s) (for abdomen and/or buttocks, as appropriate)
i) [redacted]
j) Optional - Obtain 2-Dimensional photographs of the treatment area using standardized setup and settings.

The need for post-treatment care is not expected following the EMS treatments performed in this study. Subjects will be encouraged to call the study site if they experience any unusual effects (e.g., severe discomfort etc.), which may be related to the study.

2.13 Follow-up Procedures

Subjects who receive study treatment are required to complete all follow-up visits and assessments (4-Week and 12-Week).

2.13.1Four-Week Post-Final Treatment Visit; 4 Weeks ± 1 week;

The following activities will be performed at the 4-week visit:

a) Obtain weight.
b) Assess for adverse events.
[redacted]
d) Obtain standard 2D imaging of treatment areas
e) Subject Completes SGAIS questionnaire
f) Subject completes Body Satisfaction Scale for abdomen and/or Body Satisfaction Scale for buttocks as appropriate.

[redacted]

2.13.2 Twelve-Week Post Final Treatment Visit; 12 Weeks ± 2 weeks

The following activities will be performed at the 12-Week visit:

a) Obtain weight.
b) Assess for adverse events.
[redacted]
d) Optional - Obtain standard 2D imaging of treatment areas
e) Subject Completes SGAIS questionnaire
f) Subject completes Body Satisfaction Scale for abdomen and/or Body Satisfaction Scale for buttocks as appropriate.

[redacted]

2.13.3 Optional Follow-Up Evaluations (up to 4 within study period)

The full evaluation is not required at optional follow-up visits; the extent of the assessment will be at the discretion of the Investigator.

Table 2 summarizes the study schedule and events at each visit.

Table 2. Schedule of Visits

	Screening (< 1hr)	Photo Visit (<1hr)	EMS Treatment #1 (<4hrs)	EMS Treatment #2 (<4hrs)	EMS Treatment #3 (<4hrs)	EMS Treatment #4 (<4hrs)	4-Wk Follow-Up (< 1 hr)	12-Wk Follow-Up (< 1 hr)	Optional Follow-Up**
Time Frame	Day -60 to 0	Day -30 to 1	Week 1 (Day0)	Week 1	Week 2	Week 2	Week 4 (± 1 weeks)	Week 12 (± 2 weeks)	Open
Informed Consent*	X								
Eligibility Criteria	X		X	X	X	X			
Medical History	X								
Height & BMI	X								
Weight	X	X	X				X	X	
3D Photos and/or tape measurements		X				X#	X	X#	
2D Photos		X				X#	X	X#	
EMS			X	X	X	X			
[redacted]			X	X	X	X	X	X	
AE Assessment			X	X	X	X	X	X	
BSQ*** per body area			X			X	X	X	
[redacted]							X	X	
Subject GAIS							X	X	

* Informed Consent to be signed by subject prior to the collection of any data or initiation of any study procedures.
** Investigator discretion as to timing and extent of follow-up assessment for optional visits.
*** BSQ (Body Satisfaction Questionnaire)
# Optional

2.14 Assessments

Study-related assessments are described below.

2.14.1 Global Aesthetic Improvement Scale (GAIS-Subject)

At 4-Weeks post-final treatment, subjects will be asked to rate the improvement observed in the treated area(s) using the Global Aesthetic Improvement Scale:

- 3 = Very much improved
- 2 = Much improved
- 1 = Improved
- 0 = No change
- -1 = Worse
- -2 = Much worse
- -3 = Very much worse

2.14.2 Body Satisfaction Questionnaire – Abdomen

At 4-Weeks post-final treatment, the subjects' feeling about the shape and appearance of their abdomen will be assessed using the Body Satisfaction Questionnaire. The scale measures body image using a set of ten dichotomous items used to describe aspects of shape and appearance. The items are rated on a five-point semantic differential scale.

2.14.3 Body Satisfaction Questionnaire – Buttocks

At 4-Weeks post-final treatment, the subjects' feeling about the appearance of their buttocks will be assessed using the Body Satisfaction Questionnaire. The scale measures body image using a set of ten dichotomous items used to describe aspects of shape and appearance. The items are rated on a five-point semantic differential scale.

2.14.4 Photography

Three-Dimensional (3-D) photography will be used in this evaluation and may be performed using a commercially available photography system, such as the Quantificare LifeViz Body or similar device.

In addition, standardized photos of the treatment areas will be obtained at pre-treatment and 4-week visits, using standardized setup, lighting, and camera settings

to ensure consistency. All standard photographs will be captured at fixed angles and posture. Using a series of pre-determined markings on the floor, the photographer will position the camera at the pre-determined reference points to ensure that the reproduction ratio and focal distance are maintained throughout the image series during the study. A subject Foot Positioning Guide (FPG) will be used to standardize images of each body angle. During follow-up visits, the photographer will re-align subjects on the FPG by referencing baseline images.

[redacted]

2.14.7 Photograph Review

Independent physician(s) experienced in body contouring treatment may review study photographs to evaluate the outcome of treatment.

2.15 Endpoints

[redacted]

2.15.1 Primary Endpoints

The primary endpoints of the study will be defined as follows:

- Efficacy endpoint: Measurement of subject feeling about body shape, assessed using the Body Satisfaction Questionnaire at the 4-Week follow-up visit.

- Safety endpoint: The frequency of device-related adverse events (AEs) including device-related serious adverse events (SAEs) will be summarized.

2.15.2 Secondary Endpoints

- Subject-graded improvement in the treated area using the Subject Global Aesthetic Scale (SGAIS) at the 4-Week follow-up visit.

2.16 Statistical Analysis Plan

2.16.1 Statistical Methods: Overall Plan

Data will be summarized based on the nature of the data. Dichotomous (e.g., gender, independent photographic review) and ordinal (e.g., Fitzpatrick Skin type) data will be tabulated by category. The mean, standard deviation, maximum and minimum will be tabulated for continuous data (e.g., age). The significance level will be two-sided 0.05 for all statistical tests.

2.16.2 Analysis Population

Analysis Populations are defined as following:

Per-protocol Population (PP):
The Per-protocol Population will consist of all treated subjects followed for 4 Weeks and with weight change of no more than five percent (5%) of total body weight at the time the 4-Week images are taken compared to the weight taken at the first treatment visit. Since significant weight change may affect the effectiveness of the treatment, the primary efficacy analysis will be performed based on this study population. Subjects who do not complete treatment will not be included in the efficacy analyses.

As-Treated Population (AT):
This population consists of all treated subjects regardless of weight change etc.

2.16.3 Endpoint Analysis

Primary Endpoints:

The secondary endpoint of the study will measure subject feeling about body shape, assessed using the Body Satisfaction Questionnaire at the 4-Week follow-up visit. The scale measures body image using a set of ten dichotomous items used to describe aspects of shape and appearance. The items are rated on a five-point semantic differential scale. Mean scores will be tabulated. Differences and percentage change from baseline at the 4-week follow-up visit will be determined.

The primary safety endpoint will be the frequency of device-related adverse events (AEs) including device-related serious adverse events (SAEs). The number and percentage of subjects experiencing each AE will be descriptively summarized. Adverse events and SAEs will be presented as summary tables showing the frequency and type of events.

Secondary Endpoint:

The secondary efficacy endpoint will be the subject rating of improvement of the treatment area based on the SGAIS score 4 weeks after the fourth (final) EMS treatment. Subjects who have reported 'Very much improved,' 'Much Improved,' and 'Improved' will be categorized as 'Improved.' The counts and percentage of subjects who noted improvement will be summarized and the 95% confidence interval will be calculated. .

2.17 Protocol Adherence

The study Investigators are responsible for performing the study in compliance with the protocol. Non-adherence to the protocol is to be classified as a protocol violation or protocol deviation as defined below.

Protocol Violation

Non-adherence to the protocol that may result in significant additional risk to the subject (e.g., enrollment of a subject who does not meet the study criteria). Or, non-adherence to Good Clinical Practices (GCP) that may impact patient safety (e.g., failure to obtain proper consent prior to performing study procedures). Violations should be reported to the study Sponsor within 5 working days and reported to the IRB per IRB guidelines.

Protocol Deviation

Non-adherence to study procedures which does not result in additional risk to the subject (e.g., subject missed visit). Protocol deviations are not required to be reported to the IRB; however, they must be recorded on the study case report forms and may be reported and reviewed in conjunction with the progress report as part of the annual review process.

2.18 Adverse Events

Adverse events (AEs) will be assessed continuously throughout the study. An adverse event is defined as any untoward medical occurrence in a participant, regardless of whether the event is related to the device.

All AEs and device deficiencies will be recorded on the corresponding CRF for the subject.

Adverse Device Effect (AE)

Any sign, symptom, or disease in a study participant that occurs during the course of a clinical trial that is determined by the Investigator to have a causal relationship or possible causal relationship with the device under investigation.

Device Deficiencies

A device deficiency is defined in accordance with ISO 14155 as inadequacy of a medical device including issues 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 investigational site will document the event using the CRF. Device deficiencies will be documented throughout the study and appropriately managed and reported to regulatory authorities and IRBs as required by Federal regulations.

Serious Adverse Event (SAE)

Any untoward medical occurrence in a participant, regardless of whether the event is related to the device that:

a. results in death;

b. results in a life-threatening illness or injury;

The term life threatening in the definition of serious refers to an event in which the participant was at risk of death at the time of the event. It does not refer to an event, which hypothetically might have caused death, if it were more severe.

c. results in a permanent impairment of a body structure or body function;

- Impairment of body function means a substantial disruption of a person's ability to conduct normal life functions.
- This definition is not intended to include experiences of relatively minor medical significance such as uncomplicated headache, nausea, vomiting, diarrhea, influenza, and accidental trauma (e.g., sprained ankle) which may interfere with or prevent everyday life functions but do not constitute a substantial impairment.

d. requires in-patient hospitalization or prolongation of existing hospitalization;

- In general, hospitalization signifies that the participant has been detained (usually involving at least an overnight stay) at the hospital or emergency ward for observation and/or treatment that would not have been appropriate in the physician's

office or outpatient setting. Complications that occur during hospitalization are AEs. If a complication prolongs hospitalization or fulfills any other serious criteria, the event is serious. When in doubt as to whether hospitalization occurred or was necessary, the AE should be considered serious. Hospitalization for elective treatment of a pre-existing condition that did not worsen from baseline is not considered an AE.

e. results in medical or surgical intervention to prevent impairment to body structure or function;
f. results in fetal distress, fetal death, or a congenital abnormality/birth defect.

Time Period and Frequency for Collecting AE and SAE Information

All AEs and SAEs from the signing of the ICF until the follow-up visit will be collected at the time points specified in the schedule of activities, and as observed or reported spontaneously by study participants.

Medical occurrences that begin after signing of informed consent and before administration of study treatment will be recorded on the Medical History/Current Medical Conditions section of the CRF not the AE section.

Unanticipated Adverse Device Effect (UADE)

Any serious adverse effect on health and 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, or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of participants.

The Investigator shall be responsible for determination of the causal relationship of all adverse events to the device and/or procedure. The Principal Investigator is responsible for monitoring the safety of the participants enrolled.

Reportable Incidents

Serious adverse events (SAEs) and unanticipated adverse device effects (UADEs) must be recorded and reported to the manufacturer of the study device and to the Sponsor or designee within 24 hours of knowledge of the event.

Sponsor Contact:

Lori Brandt
Director, Clinical Trial Management
ZELTIQ Aesthetics, an Allergan affiliate
4410 Rosewood Dr.
Pleasanton, CA 94588
[redacted]

A full reporting of the event shall be provided within 10 working days of the event. The Sponsor is then responsible for notifying the IRB, as required.

Other adverse events, deemed by the investigator to be non-serious, should be provided to the Sponsor as soon as possible and not later than 1 week after knowledge of the event. This will be forwarded to the Product Surveillance team within 24 hours of receipt by the Sponsor Contact.

Additional information obtained by the Clinical Site regarding any adverse event, both serious and non-serious, will be reported to the Sponsor within 24 hours of awareness.

3. Study Management and Quality Control

3.1 Study Data Collection

Standardized Case Report Forms (CRFs) will be provided to all participating sites. Data will be reviewed by the study monitor and data management to identify inconsistent or missing data and to ensure compliance with the study protocol.

3.2 Confidentiality

All information and data concerning study subjects will be considered confidential, and handled in compliance with all applicable regulations including the requirements of the Health Insurance Portability and Accountability Act (HIPAA) of 1996.

Only authorized site staff, the study Sponsor or the Sponsor's designee, IRB and FDA will have access to these confidential files. All data used in the analysis, reporting and publication of this clinical trial will be maintained without identifiable reference to the subject. Any data that may be published in abstracts, scientific journals, or presented at medical meetings will reference a unique subject code and will not reveal the subject's identity.

3.3 Investigator Responsibilities

General Responsibilities

Investigators are responsible for ensuring the investigation is conducted according to all signed agreements, the Investigational Plan, and applicable FDA regulations. The Investigator must protect the rights, safety, privacy and welfare of the subjects under the Investigator's care. Investigators will assume overall responsibility and accountability for study site staff and for the clinical data obtained during the study. The Investigator assumes all responsibilities per 21 CFR 812 and other applicable regulations, including but not limited to:

IRB approval: The Investigator may not begin the study until the governing institutional review board (IRB) provide written approval of the study protocol and consent form. The Investigator is also responsible for fulfilling any conditions of approval imposed by the IRB.

Informed Consent: The Investigator must ensure that informed consent is obtained from each prospective study subject in accordance with 21 CFR Part 50 and that the study is not commenced until IRB approvals have been obtained.

Device Accountability: The Investigator is responsible for controlling all investigational device(s) stored at their site, including supervision of device use, disposal of the device or returning the device as instructed by the Sponsor.

Financial Disclosure: Investigators shall provide financial disclosure according to federal regulations (21 CFR 54).

Study Coordinator: To assure proper execution of the study protocol, each Investigator must identify a study coordinator for the site who will work with and under the authority of the Investigator to assure that study requirements are fulfilled as appropriate.

Investigator Records

The Investigator and study staff must maintain accurate, complete, and current records relating to the conduct of the investigation. Records must be retained for a period of two years following (1) the date the investigation was completed or terminated, or (2) the records are no longer required to support a regulatory submission or completion of a product development protocol, whichever is longer. Participating Investigators shall maintain the following:

- All correspondence with the Sponsor, another Investigator, the IRB, or a monitor

- Records of all persons authorized to conduct the study (e.g. Delegation of Duties/Signature Authorization, CV)
- Records of receipt, use or disposition of the devices
- Informed Consent documentation for all enrolled subjects
- Records of each subject's case history, including study-required Case Report Forms and source documentation (e.g. physician notes, lab reports, study worksheets, clinic charts)
- All relevant observations of adverse device effects
- Records of any protocol deviations
- The condition of each subject upon entering and during the course of the investigation and any relevant medical history and results of any diagnostic tests
- Record of each subject's exposure to the devices, including the date and time of use
- Investigational plan with all amendments
- Current IRB approved informed consent and all previously approved versions
- Signed Investigator agreement
- Investigators will be responsible for the accurate and timely completion of CRFs during the trial.

These records must be available and suitable for inspection at any time by Sponsor representatives (monitor) or the reviewing IRB. The Investigator will supply access to study-related medical records, original laboratory data, and other records and data as they relate to the trial. The Investigator will ensure that both he/she and his/her study staff have adequate time and resources to devote to the study, including study enrollment, subject evaluations, study documentation and site monitoring.

Investigator Reports

The Investigator is responsible for preparation and submission of the following reports:

- Report of any unanticipated adverse device effects shall be submitted to the Sponsor within 24 hours and no later than 10 working days after the Investigator first learns of the effect.
- Withdrawal of IRB approval of the Investigator's part in the investigation shall be reported to the Sponsor within 5 working days

- Progress reports on the investigation to the Sponsor, the monitor, and the reviewing IRB annually. Alternatively, the Sponsor may prepare the report.
- Deviations from the investigational plan shall be reported to the Sponsor and the IRB.
- Failure to obtain informed consent prior to use of a device in a subject shall be reported to the Sponsor and IRB within 5 working days after the use occurs.
- A final report shall be submitted to the Sponsor and IRB within 3 months after termination or completion of the investigation, or the Investigator's part of the investigation.

3.4 Sponsor Responsibilities

General Responsibilities:

As the Sponsor, ZELTIQ Aesthetics assumes overall responsibility for the conduct of the study. ZELTIQ Aesthetics assumes all responsibilities per 21 CFR 812 and other applicable regulations, and shall:

IRB approval: Ensure IRB approval for the investigation before shipping the device to any Investigator.

Investigators: Select Investigators qualified by training and experience, and providing them with the information they need to conduct the investigation properly (21 CFR 812.43). Obtain a signed Investigator Agreement (21 CFR 812.43(c)) from each participating Investigator. Study sites will be evaluated to ensure that they have an adequate patient base and can provide sufficient staff and documentation support to conduct the study properly.

Monitoring: Select monitors qualified by training and experience to monitoring the study (21 CFR 812.43), and ensure proper monitoring of the investigation (21 CFR 812.46).

Investigational devices: Provide devices only to qualified Investigators (21 CFR 812.43). No study site may receive shipment of study devices until the following documents are received by the Sponsor:

- Signed Investigator's Letter of Agreement
- Signed Clinical Site Agreement
- Investigator current curriculum vitae

Data Management and analysis: Ensure data collection, verification, analysis, records storage, etc. Sponsor will assist with presentation(s) and/or publication(s).

Training

Study Training: To ensure uniform data collection and protocol compliance, Sponsor personnel will provide an educational session to study site personnel as needed, which will cover the Investigational Plan, techniques for the identification of eligible subjects, data collection and form completion, and the device directions for use. The Investigator and study staff will be trained on the study devices and protocol, applicable regulations and requirements, and expectations of the study, enrollment expectations, subject selection, informed consent, required clinical data and record keeping, etc.

Investigational Device Use: Representatives of the Sponsor will train Investigators in use of the study device prior to study initiation. Sponsor representatives may be present at study procedures.

Site Monitoring

The Sponsor will ensure that qualified clinical monitors are available to monitor and oversee the conduct of the trial and that monitoring is performed in accordance with the Sponsor's approved procedures or third-party procedures approved by the Sponsor.

The clinical monitors will evaluate compliance with the investigational plan, FDA regulations, any specific recommendations made by the site's IRB and the signed Investigator Agreement.

Monitoring Visits

On-site monitoring visits will assess the progress of the clinical study and identify any concerns that result from device performance or review of the Investigator's study records, study management documents, and informed consent documents.

Monitoring will ensure continued protocol compliance, accurate data reporting, and adequate accounting of shipments of study devices. Monitoring visits will occur at minimum once before study close-out.

During monitoring visits, the monitor will compare subject records and other supporting documents with reports at the site to determine that;

- The facilities used by the investigation continue to be acceptable for the purposes of the clinical study

- Informed consent was properly obtained and documented for all enrolled study participants
- The Investigational Plan is being followed, and only eligible subjects are being enrolled into the study
- Deviations to the Investigational Plan have been reported to ZELTIQ and the IRB, as appropriate
- Adverse events are promptly being reported
- Device accountability is being maintained
- Information recorded in the case report forms and study reports are accurate, complete, legible and consistent with source documentation.
- Subjects failing to complete the clinical study and the reason for failure are recorded.
- Missed follow-up visits are noted in the study documentation

Clinical monitors will provide feedback to the site regarding protocol or study compliance.

Study Site Closeout

At the close of the study at an investigational site, the monitor will ensure that all case report forms have been monitored and retrieved and that the Investigator's files are accurate and complete. The monitor will ensure that all investigational devices and study supplies are accounted for and provide for appropriate disposition of any remaining supplies. The monitor will review record retention requirements with the Investigator and any remaining Investigator obligations are reviewed and ensure that all applicable requirements are met for the study. The monitor will prepare a report of the site closeout visit.

Final Report

A final report will be prepared at the conclusion of the trial. Copies of the final report will be provided to each Investigator and to the respective IRB.

4. Data Ownership

ZELTIQ Aesthetics, the study Sponsor, retains ownership of all data generated in this study, and controls the use of the data for purposes of regulatory submissions to the US and/or other governments. Investigator(s) and institution(s) (which shall include their employees, agents, and

representatives) may not issue or disseminate any press release or statement, nor initiate any communication of information regarding this study (written or oral) to the communications media or third parties without the prior written consent of the Sponsor.

5. Publication Policy

Participating Investigators and/or Institutions may publish information or data collected or produced as a result of participation in appropriate scientific conference or journals or other professional publications subject to written permission from the Sponsor, provided that drafts of the material are provided to the Sponsor for purposes of review and comment at least sixty (60) days prior to the first submission for publication or public release. Investigators may not publish information regarding site-specific data until a multicenter study report has been published.

6. Risk/Benefit Analysis

The Sponsor has undertaken a comprehensive risk-benefit analysis.

6.1 Benefits

Muscle toning and contouring in the treatment area is anticipated to provide an aesthetic benefit and the EMS device is a non-invasive device that accomplishes the desired effect without anesthesia and with minimal-to-no recovery time. [redacted] Considering the number of body contouring surgical procedures performed for the removal of fat each year (1.3 million procedures worldwide, according to the 2011 International Society of Aesthetic Plastic Surgeons Biennial Global Survey), the use of such a non-invasive procedure has the potential to significantly reduce the incidence of complications and post-surgical limitations associated with those procedures.

6.2 Risks

Although this study presents minimal risks to the subject, there is always the potential for some risk when a medical procedure is performed. Per manufacturers' user manuals, side effects of EMS treatment includes muscular pain, temporary muscle spasm, temporary joint or tendon pain, and local erythema. Scientific literature regarding use of EMS devices for aesthetic purposes to tone and strengthen abdominal and gluteal muscle describe mild muscle soreness, minor discomfort during treatment[4-8].

Anticipated Device Effects of EMS:

- muscular pain in the treatment area
- temporary muscle spasm
- temporary joint or tendon pain
- local erythema and/or skin redness
- muscular contraction adjacent to the treatment area during treatment

Adverse Effects

The following summarizes the potential adverse effects in this study:

Potential Adverse Effect	Description
Severe Erythema	The appearance of erythema (redness) that is rated as severe by the Investigator
Prolonged Erythema	Erythema lasting longer than 2 weeks.
Infection	Infection at the treatment site, diagnosed by a physician and requiring medical intervention.
Discomfort During Procedure	Discomfort during the procedure that is intolerable to the subject and results in discontinuation of the procedure.
Discomfort Post Procedure	Significant discomfort, pain, cramping, tenderness, soreness, muscle spasm following the procedure which results in medical intervention (physician visit and/or prescription pain reliever)
Sensory Alteration Outside Treatment Area	Sensory or motor nerve alteration that does not resolve within twenty minutes following applicator removal.
Nerve injury	Injury to the motor nerves that innervate the legs.
Vasovagal Symptoms	The occurrence of symptoms of anxiety, lightheadedness, dizziness, nausea, sweating, near syncope, or syncope (fainting).
Gynecological symptoms	Menstrual cycle irregularity
Allergic/Irritant Contact Dermatitis	Itchy rashes and skin peeling that may result exposure to wrap/bonnet material or applicator pressure
Hernia	Exacerbation of hernia. Hernia is defined as a protrusion of an organ or the fascia of an organ through the wall of the cavity that normally contains it.
Other	Any other untoward medical event determined by the Investigator to be an adverse event, regardless of the relationship to the device or treatment.

7. Selected References

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3. Jacob CI, Paskova K. Safety and efficacy of a novel high-intensity focused electromagnetic technology device for noninvasive abdominal body shaping. J Cosmet Dermatol. 2018;00:1-5.

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6. American Society for Laser Medicine and Surgery abstract, 2019. Kinney BM, Kent DE. Long-term Follow-up on Patients with HIFEM-Induced Abdominal Tissue Changes: MRI and CT Assisted Quantification of Muscle Growth and Fat Reduction.

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