STUDY NAME: TREATMENT WITH THE EVOKE SYSTEM FOR FACIAL AND SUBMENTAL LAXITY

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IDENTIFIERS: NCT04719013

PROTICOL ID: DO609886A

Study Name: **Treatment with the Evoke System for Facial and Submental Laxity**

Protocol No.:

Revision No.: 1

Sponsor: **InMode Ltd.**

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1. Protocol Synopsis

Study Title	Treatment with the Evoke System for Facial and Submental Laxity
Protocol No	DO609886A
Sponsor	InMode Ltd.
Investigational Product	Evoke (K191855)
Study Design	Prospective, open label clinical study.
Study Sites	#1-, #2-, #3-, #4-, #5-
Patient Population and Sample Size	Subjects aged 35-75, healthy adults with visible signs of aging, seeking skin laxity treatments. Approximately 15 subjects will be enrolled per site Treatment areas include face, under chin (submental)
Study Duration	Study duration for each subject is approximately 10 months (including screening, three treatments once in 2 weeks and 3 follow-up visits at 1m (except site #3), 3 months and 6 months post last treatment. Overall study duration will be approximately 14 months, depending on the subject recruitment rate.
Study Objectives	The aim of the study is to evaluate the efficacy, patient comfort, and patient satisfaction after Evoke treatment for face and submental area
Primary Objective	1. Evaluate improvement in skin appearance comparing pre and at 1 month (except site #3), 3 months and 6 months post last treatment photographs (as assessed by blinded investigators) 2. Evaluate Improvement in skin appearance using 3D Photographic analysis at 1month (except site #3), 3 months and 6 months follow up visits and compared to the baseline.
Secondary Objectives	1. Evaluate Investigator assessment of the skin appearance improvement comparing pre and post treatment using 0 - 4 -points Likert scale at 1month (except site #3), 3 months and 6 months follow up visits. 2. Evaluate Subject assessment of improvement and satisfaction using 0 - 4 -points Likert scale at 1month (except site #3), 3 months and 6 months follow up visits.

	3. Optional: Evaluate histological changes to treatment area skin taken at 3M FU versus baseline. (except site #3)
Efficacy Endpoints	1. Improvement in skin appearance comparing pre and at 1 month (except site #3), 3 months and 6 months post last treatment photographs (as assessed by blinded investigators): • Success is defined by correct identification of the pre and post treatment photos of patients completed the treatment at 1 month (except site #3), 3 months and 6 months post treatment. • At least 2 out of 3 blinded evaluators should agree on the assessment. 2. 3D Photographic analysis will be conducted at 1 month (except site #3),, 3 months and 6 months follow up visits and compared to the baseline. 3. Investigator assessment of the skin appearance improvement comparing pre and post treatment using 0 - 4 -points Likert scale at 1 month (except site #3), 3 months and 6 months follow up visits: • 4 = Significantly marked improvement; 3 = Marked improvement; 2 = Moderate improvement; 1 = Slight improvement; 0 = No difference 4. Improvement assessment will be performed independently by the subject himself 4 points Likert scale questionnaire (Global Aesthetic Improvement Scale), as follows: • 4 = Significantly marked improvement; 3 = Marked improvement; 2 = Moderate improvement; 1 = Slight improvement; 0 = No difference. 5. Subject assessment of satisfaction will be filled out by subjects using a 5-points Likert scale, as follows: • +2 = Very satisfied; +1 = Satisfied; 0 = Indifferent; -1 = Disappointed; -2 = Very disappointed. 6. Optional: Positive changes in histologic evaluation: up to 5 subjects will undergo biopsies of the treated area for histology at baseline and at 3M follow-up visit. Histological sections will be stained using elastin, H&E and other collagen specific stains. (except site #3)
Safety Endpoint	• Observation, assessment and recording of adverse events. • Discomfort Level assessment - subject will be asked to rate discomfort during the procedure. Discomfort will be assessed based on the Numerical Scale Response (NSR). The subject will be presented a scale and asked to make a mark along the scale. The subject will be asked to rate discomfort from 0 to 10, with 0 equaling no discomfort and 10 equaling the worst possible discomfort. A number is obtained by measuring up to the point the subject has indicated. (**Appendix 3** – Discomfort Assessment) • Evaluations will be done immediately after treatments and at all follow-up visit. The frequency, severity and causality of all adverse events will be recorded.

Statement of Compliance

This study will be conducted in accordance with the Code of Federal Regulations on the Protection of Human Subjects (45 CFR Part 46), any other applicable US government research regulations, and institutional research policies and procedures. The Principal Investigator will assure that no deviation from, or changes to the protocol will take place without prior agreement from the sponsor and documented approval from the Institutional Review Board (IRB), except where necessary to eliminate an immediate hazard(s) to the trial participants.

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2. Introduction & Study Rationale

The human skin aging process is characterized by thinning dermis, atrophy of the extracellular matrix, and reduced collagen synthesis. Overwhelming epidemiologic and laboratory evidence indicates that sun exposure and other sources of UV radiation play a major role in causing the undesirable skin changes of fine and coarse wrinkles, roughness, laxity, mottled pigmentation, actinic lentigines, actinic keratoses, leathery texture/coarseness, scaling/xerosis, shallowness, and telangiectasia[1].

Although facelift surgical procedure remains an extremely effective and popular method to reduce static rhytids, there has been a dramatic paradigm shift toward non-surgical skin tightening and rejuvenation techniques, as patients seek to achieve skin tightening with no or minimal downtime procedures.

Non-ablative energy treatments for skin laxity and rhytides have grown rapidly in the last 10 years. Mid-infrared lasers were initially studied for potential efficacy in skin tightening, but the results were modest and, additionally, the devices could often not be used on darker skin types due to risk of discoloration and scarring following absorption of energy by the chromophore melanin[2].

Radiofrequency (RF) devices have been reported to achieve modest clinical efficacy in skin tightening without many of the limitations of other energy devices, and may therefore represent an ideal treatment option for non-invasive skin tightening[3-5].

However, most RF treatments are administrated by the operator hence, this treatment is time consuming and causes operator fatigue reducing the most effective outcome of the treatment. Evoke device allowing hands free procedure that eliminates operator dependency factor.

The Evoke device is a non-invasive system based on radiofrequency (RF) energies. The Evoke provides a non-invasive approach to achieve a desired aesthetic effect (skin tightening and wrinkle reduction). The system is designed to enable an automatic, hands-free, full facial treatment that is based on a predefined user protocol. In addition, the system incorporates a skin-temperature control into the protocol, enabling accurate, stable and safer treatment.

This prospective study is intended to evaluate the efficacy and safety of Evoke system using radio frequency for wrinkles reduction and skin tightening. Aging is associated with a decrease in collagen turnover due to a decrease in fibroblasts and elastin. The degradation and disorganization of elastin fibers contribute to skin laxity and wrinkles. We may be able to see improvement in histology.

3. Definitions, Acronyms and Abbreviations

RF -	Radiofrequency
AE -	Adverse Events
SAEs -	Serious Adverse Events
UADEs -	Unanticipated Adverse Device Effects

4. Device Description

The Evoke Platform employs Radio-frequency (RF) technology for various aesthetic applications.

The Evoke System with the Cheek and Chin Applicators is a hands-free medical aesthetic device using RF energy for the treatment of selected medical conditions such as relief of minor muscle aches and pain, relief of muscle spasm, temporary improvement of local blood circulation.

RF energy does not cause any thermal damage to the treated skin. The System provides individual adjustment of RF power to achieve maximum efficiency, safety and comfort for each patient. The System provides enhanced safety while minimizing possible side effects by constantly monitoring RF parameters.

The System incorporates the following safety features. All personnel operating the System should be familiar with these features.

- System has unique password to avoid device operation by non-authorized personnel.
- An audible tone indicates energy activation.
- Special audible tone will be activated in case of bad coupling of one of the applicators.
- During activation, the system performs a self-test of the hardware.
- Hardware is tested every 1 msec. to ensure proper operation of electrical circuits.
- Skin surface temperature is monitored during the treatment. RF energy delivery is terminated when skin temperature accidentally reaches the Cut-Off level.
- System starts at a low setting.

5. Study Objectives

The aim of the study is to evaluate the efficacy, patient comfort and patient satisfaction after Evoke treatment.

Primary Objective:

1. Evaluate improvement in skin appearance comparing pre and at 1 month (except site #3), 3 months and 6 months post last treatment photographs (as assessed by blinded investigators)
2. Evaluate Improvement in skin appearance using 3D Photographic analysis at 1 month (except site #3), 3 months and 6 months follow up visits and compared to the baseline.

Secondary Objective:

1. Evaluate Investigator assessment of the skin appearance improvement comparing pre and post treatment using 0 - 4 -points Likert scale at 1 month (except site #3), 3 months and 6 months follow up visits.

2. Evaluate Subject assessment of improvement and satisfaction using 0 - 4 -points Likert scale at 1 month (except site #3), 3 months and 6 months follow up visits.
3. Optional: Evaluate histological changes to treatment area skin taken at 3M FU versus baseline. (except site #3)

6. Study Endpoints

6.1 Efficacy Endpoints

1. Improvement in in skin laxity comparing pre and at 1 month (except site #3), 3 months and 6 months post last treatment photographs (as assessed by blinded investigators):
- Success is defined by correct identification of the pre and post treatment photos of patients completed the treatment at 1 month (except site #3), 3 months and 6 months post treatment.
- At least 2 out of 3 blinded evaluators should agree on the assessment.
2. 3D Photographic analysis will be conducted at 1 month (except site #3), 3 months and 6 months follow up visits and compared to the baseline.
3. Investigator assessment of the skin appearance improvement comparing pre and post treatment using 0 - 4 -points Likert scale at 3 months and 6 months follow up visits:
- 4 = Significantly marked improvement; 3 = Marked improvement; 2 = Moderate improvement; 1 = Slight improvement; 0 = No difference
4. Improvement assessment will be performed independently by the subject himself 4 points Likert scale questionnaire (Global Aesthetic Improvement Scale), as follows:
- 4 = Significantly marked improvement; 3 = Marked improvement; 2 = Moderate improvement; 1 = Slight improvement; 0 = No difference.
5. Subject assessment of satisfaction will be filled out by subjects using a 5-points Likert scale, as follows:
- +2 = Very satisfied; +1 = Satisfied; 0 = Indifferent; -1 = Disappointed; -2 = Very disappointed.
6. Optional: Positive changes in histologic evaluation: up to 5 subjects will undergo biopsies of the treated area for histology at baseline and at 3M follow-up visit. Histological sections will be stained using elastin, H&E and other collagen specific stains.

6.2 Safety Endpoint

- Observation, assessment and recording of adverse events.
- Discomfort Level assessment - subject will be asked to rate discomfort during the procedure. Discomfort will be assessed based on the Numerical Scale Response (NSR). The subject will be presented a scale and asked to make a mark along the scale. The subject will be asked to rate discomfort from 0 to 10, with 0 equaling no discomfort and 10 equaling the worst possible discomfort. A number is obtained by measuring up to the point the subject has indicated. (**Appendix 3** – Discomfort Assessment)
- Evaluations will be done immediately after treatments and at all follow-up visit. The frequency, severity and causality of all adverse events will be recorded.

- Number, severity and type of any adverse event recorded throughout the course of the study.

7. Study Population

7.1 General Considerations

The study will recruit approximately 15 subjects per site, between the ages of 35-75, healthy adults with visible signs of aging, seeking skin laxity treatments.

Treatment areas include face, under chin

Eligible subjects will be screened. Investigators will screen subjects based on the inclusion/exclusion criteria described below after a written informed consent is signed.

7.2 Subject Withdrawal and Replacement

Subjects enrolled in the study can discontinue their participation at any time for any reason without prejudice or reduction in the quality of their medical care. The investigators or sponsor can terminate a subject's participation in this study to protect the subject's health or if the subject fails to follow directions resulting in noncompliance to study procedures. Subjects who withdraw or are terminated from the study may be replaced to ensure approximately 15 subjects (per site) have completed the study. Subjects who fail to complete the treatment will be replaced and will not be evaluable.

7.3 Subject Identification

A unique subject identification code will be assigned when an individual subject is qualified for enrolment.

Subject identification details will be coded using subject's initials, subject case number and site number. Subject initials will be composed of the first letter of given name and first letter of last name (for example, AS for Adam Smith) and a three-digit sequential number. The investigator will complete subject identification on a confidential site log, which will be used for the purposes of traceability.

An example is provided below:

AS 101

In any case, other identification details (i.e. full names, phone numbers, etc,) will not be filled in any way in the CRF. The identification log will be kept in the study file only.

7.4 Inclusion Criteria

- Signed informed consent to participate in the study.
- Female and male subjects, ≥ 35 and ≤ 75 years of age at the time of enrolment

- If female, not pregnant, lactating and must be either post-menopausal, surgically sterilized, or using a medically acceptable form of birth control at least 3 months prior to enrolment (i.e., oral contraceptives, contraceptive implant, barrier methods with spermicide or abstinence).
- In addition, negative urine pregnancy test as tested before each treatment and at the last visit for women with childbearing potential (e.g. not menopause).
- General good health confirmed by medical history and skin examination of the treated area.
- Willing to have photographs and images taken of the treated areas to be used de-identified in evaluations, publications and presentations.
- The patients should be willing to comply with the study procedure and schedule, including the follow up visit, and will refrain from using any other aesthetic treatment methods for the last 6 months and during the entire study period.

7.5 Exclusion criteria

- Pacemaker or internal defibrillator, or any other active electrical implant anywhere in the body.
- Permanent implant in the treated area such as metal plates and screws, silicone implants or an injected chemical substance, unless deep enough in the periostal plane.
- Current or history of skin cancer, or current condition of any other type of cancer, or premalignant moles.
- Severe concurrent conditions, such as cardiac disorders, epilepsy, uncontrolled hypertension, and liver or kidney diseases.
- Pregnancy and nursing.
- Impaired immune system due to immunosuppressive diseases such as AIDS and HIV, or use of immunosuppressive medications.
- Patients with history of diseases stimulated by heat, such as recurrent Herpes Simplex in the treatment area, may be treated only following a prophylactic regimen.
- Poorly controlled endocrine disorders, such as diabetes or thyroid dysfunction.
- Any active condition in the treatment area, such as sores, psoriasis, eczema, and rash.
- History of skin disorders, keloids, abnormal wound healing, as well as very dry and fragile skin.
- History of bleeding coagulopathies or use of anticoagulants in the last 10 days.
- Any surgery in treated area within 3 months prior to treatment.
- Six months delay is required if other recent treatments like light, CO2 laser or RF were performed on the same area.
- Use of Isotretinoin (Accutane®) within 6 months prior to treatment.
- Simultaneously participating in another investigator drug or device study or has completed the follow-up phase for the primary endpoint of any previous study less than 1 year prior to the first evaluation in this study.
- As per the practitioner's discretion, refrain from treating any condition that might make it unsafe for the patient

8. Study Procedures

The Time and Events Schedule is provided in Appendix 1.0.

8.1 Screening and Baseline (Visit 1)

Screening visit will be performed in order to determine subject eligibility and to collect all required demographic and baseline clinical information. Study procedures and available treatment options, including the RF technology will be described in detail to the subject. Subject will be assured that the decision regarding participation in the study is strictly voluntary and that they are free to change their mind at any stage.

The subject will review the informed consent form and the study will be explained to the subject including all risks, potential benefits, procedures, visit requirements, and other alternative treatment options. If the subject qualifies and wishes to participate, he/she will complete the ICF with a signature and date. The original will be retained with subject's records and a copy will be provided to the subject. Subjects will then be screened for study eligibility according to inclusion and exclusion criteria.

The following Demographic and Baseline Measurements will be performed:

- Demographic data including gender, age, race, skin type (Fitzpatrick scale).
- ICF - Prior to any study procedures, informed consent will be obtained. When the subject fully understands the possible benefits and risks of the study, the subject will be asked to sign and date the informed consent form (ICF). The subject will be given a copy of the signed ICF.
- Subject ID - subjects will be assigned a study subject ID number.
- Medical History - A medical history will be obtained to determine if the subject meets the study criteria, including a list of all prescribed and over the counter medications taken within the previous 6 months will be recorded.
- Pregnancy Screen - Subjects who are capable of becoming pregnant will undergo a urine pregnancy test. This will be repeated prior to all treatments, and at the end of the study (last FU visit, 6-month FU).
- If the Screening and Treatment procedures are not conducted on the same day, the urine pregnancy test will be repeated on the first treatment day.
- Photography – Baseline photographs will be obtained using a consistent camera and subject placement settings with a digital imaging system.
- 3D Photography – Baseline 3D pictures will be obtained using 3D system. PI will ensure the same camera is used throughout the study.
- Up to 5 study participants be selected for baseline biopsy
- Scheduling: Subjects will be scheduled to return for the baseline and first treatments visit within 3 weeks following the screening visit

8.2 Treatment (visits 1-3)

The Evoke treatment may occur on the same day of screening and baseline visit (or within 3 weeks following screening).

Enrolled subjects will undergo up to 3 successive bi-weekly (every 2 weeks) treatments (Tx.1, Tx.2 and Tx.3). Additional three (3) visits in the clinic will occur to follow-up the skin appearance changes and wrinkles reduction at visits 4,5 and 6 (4 weeks (except site #3) 12 weeks and 24 weeks following last treatment).

Treatment area: Treatment area will include face and under chin

Urine Pregnancy Test will be performed prior to each procedure.

Treatment procedure:

- Remove any jewellery in the treatment area
- Clean the Evoke Applicator with 70% alcohol. Detach electrodes from the mask frame (Cheek Applicator) using magnetic connection if needed.
- Test the Patient Call Button prior to each session. This will pause the treatment.
- Long and dense hairs may affect the treatment and should be shaved according to physician's discretion.
- Clean and dry the skin surface prior to applying the Applicators. Ensure there are no creams, lotions or sweat residue on the area to be treated.
- Treatment is performed in an upright sitting position. Ensure patient is comfortably seated.
- Make sure that the Applicator for the treatment corresponds to the device interface.
- Apply 2-4mm clear ultrasound gel (not oil) to the treatment area.
- Apply the Evoke Applicator (Chin or Cheeks) on top of the treatment area and adjust according to patient comfort.
- For Cheek Applicator:
    - Position the applicator-stabilizer (black metal hoop) on the back of the neck. Adjust the applicator according to patient anatomy. For a wider face, pull the stabilizer all the way out. For a narrow face, bring the stabilizer all the way in. Ensure that patient is seated upright when positioning the applicator on the head. Do not allow the patient to lean their head backward as the applicator will shift forward out of position. Patient head must remain upright throughout the entire treatment.
    - Secure the Applicator with 2 additional adjustable straps. One strap is positioned on the back of the head, and one across the top or the head.
- For Chin Applicator:
    - Place the Applicator on the under-chin area. Ensure that the electrodes are positioned on the soft tissue, not on bony areas. The position of the applicator should not be angled or tilted.
    - Secure the Applicator with the adjustable strap on the top of the head. Use additional silicone strap to secure the Applicator on the chin to prevent it from sliding to the neck.
    - There should be a complete coupling between all Applicator electrodes and the skin during the treatment session.
    - Adjust or reposition the Applicator if one or more electrodes do not have complete contact with the skin. In the event that the proper coupling between the electrodes and the skin cannot be achieved, due to patient anatomy or surface irregularities (such as

moles, scars, etc.), disable the specific electrode. Treatments can still be conducted if one or more of the electrodes are disabled.

- Provide patient with Patient Call Button and educate on proper use.
- Start with lower energy levels and gradually increase according to patient's comfort level. Set treatment time to desired treatment duration and press the Start button.
- Treatments can be paused by pressing the Pause button in the upper left corner of the screen.
- In case the Applicator needs to be readjusted or repositioned, pause the treatment, readjust the Applicator and restart the treatment. DO NOT readjust the Applicator when treatment is activated.
- The procedure should NOT feel hot or intolerable to the patient. If the patient complains of discomfort, immediately pause the treatment and inspect the area. Treatment can be continued with one or more of units disabled. Reduce RF power if required.
- Consequent cyclic electrodes activation during the procedure will be reflected on the screen.
- The treatment attendant should not leave the room after starting the treatment as it is important for the clinician to ensure that all Applicators reach the desired cut-off temperature and that the RF energy is maintained at the cut-off level. This should take approximately 2-5 minutes.
- During the procedure check Applicators position occasionally, as they can be shifted from the original placement.

- After the face is treated with Cheek Applicator (for approximately 45 min), if subject's anatomy allows the under-chin area will be treated with Chin Applicator for another 30-45 minutes using the same technique as with the Cheek Applicator.
- Typical response to treatment is erythema, slight edema.
- Subject will be asked to rate discomfort during the procedure. Discomfort will be assessed based on the Numerical Scale Response (NSR). The subject will be presented a scale with both words and numbers along a horizontal line and asked to make a mark along the scale. The subject will be asked to rate discomfort separately for cheeks and chin areas from 0 to 10, with 0 equalling no discomfort and 10 equalling the worst possible discomfort. A number is obtained by measuring up to the point the subject has indicated.
- After each treatment, observation, assessment and recording of adverse events will be conducted.

8.3 Follow up visits (Visits 4, 5 and 6)

Follow up visits will be conducted at 4 weeks (1-month FU) (except site #3), 12 weeks (3M FU) and 24 weeks (6M FU) following last treatment.

The 1 month (except site #3), ***3 months and 6 months follow up visits*** will include the following assessments:

- Standardized medical photography
- 3D Photography

- Urine Pregnancy Test (only last 6 months FU visit)
- Investigator assessment of the skin appearance improvement comparing pre and post treatment using 4-point Likert scale
- Subject's Improvement and Satisfaction questionnaires
- Post final treatment biopsy will be performed (up to 5 subjects)
- AE evaluation recording
- Concomitant medication recording

9. Adverse Events Reporting

9.1 Definitions

Adverse Event:

An adverse event (AE) is any adverse change in health or side effect that occurs in a study participant during their participation in the study.

Serious Adverse Event (SAE):

A serious adverse event (SAE) is any adverse event that:

- Led to death
- Led to a serious deterioration in the health of the subject that resulted in a life-threatening illness or injury
- Resulted in a permanent impairment of a body structure or a body function
- Required in-subject hospitalization or prolongation of existing hospitalization
- Resulted in medical or surgical intervention to prevent permanent impairment to body structure or a body function
- Led to fatal distress, a congenital abnormality, birth defect or death

Unanticipated Adverse Event:

An unanticipated adverse event is any serious, device-related adverse event, if that event was not previously identified in the risk analysis and Informed Consent form in nature, severity, or frequency.

AE Severity:

Adverse events are graded according to severity as follows (Table 3):

Mild	Sign or symptom, usually transient, requiring no special treatment and generally not interfering with usual activities.
Moderate	Sign or symptom, which may be ameliorated by simple therapeutic measures; yet, may interfere with usual activity.

Severe	Sign or symptom that are intense or debilitating and that interfere with usual activities. Recovery is usually aided by therapeutic measures.

Relationship to Device:

The relationship of the adverse event to the treatments or procedures is defined as follows (Table 4):

Most Probably Related:	Follows a reasonable temporal sequence from study device delivery/retrieval and cannot be reasonably explained by known characteristics of the subject's clinical data or the surgical procedure applied.
Possibly Related:	Follows a reasonable temporal sequence from study device delivery/retrieval but could have been produced by the subject's clinical state or by the surgical procedures regardless of the study device.
Probably not Related:	Temporal association is such that the study device is not likely to have had any reasonable association with the observed event.
Unrelated	No relationship to study device activation is perceived

9.2 Anticipated Adverse Events in this Clinical Evaluation

Possible Evoke adverse effects include but are not limited by:

- discomfort or pain,
- excessive skin redness (erythema)
- swelling (edema),
- damage to natural skin texture (crust, blister and burn),
- change of pigmentation (hyper- and hypo-pigmentation),
- bruising,
- scarring.

9.3 Precautions to Minimize Complications

A list of warning and precautions is provided in the Operator Manual which is provided to site personnel. Additionally, the exclusion criteria listed in this protocol further reduce the abovementioned risks.

9.4 Investigator Records

The Investigator will report all Adverse Events which occur with each subject throughout the study and follow-up period and will record them in the CRF Adverse Events Investigation Form. The Investigator will categorize Adverse Events according to:

- Serious or non-serious
- Severity

- Anticipated or unanticipated
- Relationship to device use

9.5 Investigator Reporting of AEs

The Investigator will report all serious adverse events (SAEs) to InMode Ltd by telephone as soon as becoming aware of them. A written follow-up report will be emailed or faxed to InMode Ltd and the reviewing IRB within 24 hours and will include the following information:

1. Nature of AE
2. Statement regarding the degree to which it is considered device related, and rationale.
3. Results of any diagnostic tests that were performed.
4. Description of any treatment implemented.
5. Statement of subject's current clinical status.
6. Investigator's signature and date.

Non-serious adverse events that are unanticipated and may be device related will be reported to the InMode Ltd by telephone within 24 hours. A written follow-up written report will be emailed or faxed to InMode Ltd within 5 working days and will include the following information:

1. Nature of adverse effect.
2. Statement as to why it is considered unanticipated.
3. Statement as to the degree to which it is considered device related, and rationale.
4. Results of any diagnostic tests that were performed.
5. Description of any treatment implemented.
6. Statement of subject's current clinical status.
7. Investigator's signature and date.

All other Adverse Events will be reported in writing to InMode Ltd in writing within 5 working days of the Investigator becoming aware of them.

The Investigator will continue to clinically monitor the AE, with laboratory tests where appropriate, until it is resolved, stabilized or there is a return to baseline.

10. Regulatory Aspects

10.1 Institutional Review Board

The study protocol, informed Consent forms (all versions), and any specific advertising will be submitted to and approved by Sterling Institutional Review Board (IRB), at 6300 Powers Ferry Road Suite 600-351, Atlanta, GA 30339, Toll-Free: (888) 636-1062, Phone: (770) 690-9491, Fax: (770) 690-9492 before the start of the study. The notification of approval will be provided to the sponsor and site.

10.2 Informed Consent

An Informed Consent that includes all the relevant elements currently required by FDA or state regulations will be provided to each prospective study patient at screening and before enrolling into the study. The type and method of study, any potential or possible hazards, and the patient's right to

withdraw from the study at any time will be explained to the patients by the Investigator or designee. Once the Investigator is assured that an individual candidate understands the implications of participating in this study, the patient will be asked to give Consent by signing and dating in the appropriate areas of the Informed Consent form. The Investigator or Designee will also sign and date the form in accordance with ICH E6R2 guidance. A copy of the IRB approved ICF will also be provided to the subject.

10.3 Protocol and Informed Consent Changes

Changes to the protocol or Informed Consent Form will be implemented as amendments to the original document and approved by the IRB. The approvals will be processed in accordance with the established IRB procedures. Any addenda, amendment or revision that substantially alters the study design or increases potential risk to the patient requires the patient's Consent to continue in the study.

10.4 Product Supply and Maintenance

The device will be maintained by the Sponsor, as needed. The device will be used according to the instructions of the Sponsor and manufacturer, InMode. At the end of this study, any materials provided specifically for use in this study may be returned to the Sponsor, as described in the Clinical Trial Agreement and study budget.

10.5 Privacy of Personal Data

The subject's name and personal data will remain confidential and will not be published in any way. All reports and communications relating to study subjects will identify the subject only by his/her subject number and study 3-letter code. The Study staff will complete subject identification in a confidential enrolment log, which will be used for the purposes of traceability and follow-up. This will be treated with strict adherence to professional standards of confidentiality and will be filed under adequate security and restricted accessibility.

10.6 Confidentiality Statement

This document contains confidential information that must not be disclosed to anyone other than the Sponsor, the Investigator Team, regulatory authorities, and members of the Research Ethics Committee.

11. Documentation

11.1 Case Report Forms (CRFs)

Paper case report forms will be used in this trial. All protocol-required information collected during the study must be entered in the appropriate field of the case report form (CRF). The investigator, or designated representative, should complete the appropriate CRF fields as soon as possible after information is collected. The information must match the information that exists as source documents in

the clinic chart, hospital chart, and/or investigator's files. An explanation should be given for all missing data.

It is the investigator's responsibility to assure the accurate completion, review, and approval of all CRFs and the timely completion and submission of all adverse event forms.

11.2 Maintenance and Retention of Records

Investigators will maintain all study related documentation for a period of five years following: 1) marketing authorization for device commercialization, or 2) sponsor's withdrawal of submission for approval, or 3) completion of the study, if the investigational device is already approved for commercialization.

All printouts and records of tests and procedures are to be kept in a secure and safe place throughout the study. Once the study is completed, the records will be kept as required by local regulations, but in no case less than the period defined above.

The Investigator will not relocate or dispose of any study documents before obtaining sponsor's written permission.

Documentation should be kept so as to make its retrieval easy should an audit take place.

All study documentation will be kept locked under the Investigator's responsibility.

11.3 Reports

Study reports include a Final Report that will be issued by the Sponsor. Report format will be designed by the Sponsor.

All study reports will be signed by the Principal Investigators approving its contents, analysis, results and conclusions.

AE related reporting requirements are specified above.

12. Monitoring Plan

12.1 General Considerations

Monitoring functions will be performed in compliance with Good Clinical Practices, EN ISO 14155, and as outlined in 21CRF§812.43(d) and 21CRF§812.46. InMode Ltd procedures detail monitoring procedures and monitor responsibilities.

The study will be monitored by the sponsor periodically at the site, per Sponsor discretion.

12.2 On-Site Visits

Periodic on-site monitoring visits are intended to assess the Investigator's adherence to the protocol, maintenance of records and reports, and review of source documents for accuracy, completeness, and legibility, and monitoring of Adverse Events.

During periodic visits the monitor is required to:

- Assess the progress of the study towards meeting study objectives.
- Identify any concerns that stem from observations of device performance and/or review of the subject's CRF, study management documents, and informed Consent documents.
- Monitor AE reporting and investigations.

Reports of on-site visits will be submitted by the monitor and will include, as applicable, resolution of concerns, completion of appropriate follow-up activities, completion of assigned tasks, and corrective actions. Some 'visits' may be performed using a conference call/video conference call and will not be actual physical visits.

12.3 Site Initiation Meeting

A Site Initiation visit will take place prior to initiation of study procedures. All study related documents and procedures will be explained to all staff involved in the study to ensure understanding of the study requirements. Suitability of potential study subjects will also be evaluated prior to their inclusion.

12.4 Adverse Event Reporting and Follow-up

Monitoring of adverse events, their follow up and outcomes will take place at each study visit.

12.5 Site Closure Visit

A Site Closure Visit will be conducted to ensure that all relevant documentation is filed and archived under the Investigator's responsibility according to regulations.

13. Risk/Benefit Analysis

13.1 Expected Risks:

As indicated in section 10.2 possible Evoke handpiece adverse effects include but are not limited by:

- discomfort or pain,
- excessive skin redness (erythema)
- swelling (edema),
- damage to natural skin texture (crust, blister and burn),
- change of pigmentation (hyper- and hypo-pigmentation),
- bruising,
- scarring.

These risks are minimal when compared to other methods of skin tightening that are being utilized (such us surgical facelift).

13.2 Expected Benefits:

The expected benefit of using the Evoke is achieving the desired skin improvement via non invasive technique. It is obvious that the low risk profile of the RF utilizing Evoke device greatly benefits the individual seeking treatment for skin appearance improvement and wrinkles reduction as it significantly minimizes the risks associated with other techniques such as surgery.

13.3 Conclusion:

It can therefore be claimed that the expected benefits associated with the use of the Evoke device outweigh its risks.

14. Data analysis

14.1 Analysis Sets

- Safety Analysis Set

The safety analysis set will include all subjects using Embrace procedures at least a single time.

- Performance Analysis Set

Performance analysis set will consist of all subjects providing at least one post treatment performance measurement.

- Treatment of Missing Values

Only observed data will be used; i.e. missing data will not be imputed.

14.2 Statistical Analysis

Means, and standard deviations for each characteristic will be calculated. Paired sample t-test will be computed to assess changes in before treatment and follow-up scores. Statistical significance will be calculated and two-tail significance level of 0.05 will be used.

15. Data Management Plan

Case Report Forms will be retrieved by Monitors after verification and resolution of monitoring queries. Documents will be delivered to InMode Ltd onsite data management facility where forms will be logged in, and then data will be entered into a prepared Excel file.

Data will be entered using a double entry method and controlled by periodic and random validation check.