COVER PAGE

Minitouch Endometrial Ablation System Treatment for Menorrhagia: An Evaluation of Safety & Effectiveness (EASE Clinical Trial)

Protocol Version Number: 5.0

Title	Minitouch **E**ndometrial **A**blation **S**ystem Treatment for Menorrhagia: An **E**valuation of Safety & Effectiveness
Short Title	EASE Clinical Trial
IDE No.	G180282
ClinicalTrials.gov Identifier	NCT04267562
Protocol No. & Revision	TD18036 v5.0
Version Date	14Dec2021

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Minitouch Endometrial Ablation System Treatment for Menorrhagia: An Evaluation of Safety & Effectiveness (EASE Clinical Trial)

Protocol Version Number: 5.0

National Principal Investigator: [redacted]

National Co-Principal Investigator: [redacted]

Site Principal Investigators and Investigation Sites: Refer to https://ClinicalTrials.gov (NCT04267562)
Details to be provided in the Clinical Investigation Report

Sponsor: MicroCube, LLC
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VERSION HISTORY

Version	Version Date	Summary of Significant Changes (as appropriate, refer to Summary of Changes Table for a detailed listing)
1.0	16Apr2019	[redacted]
2.0	19Nov2019	[redacted]
3.0	01May2020	[redacted]
4.0	31Aug2020	[redacted]
5.0	14Dec2021	[redacted]

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1 SPONSOR APPROVAL SIGNATURE PAGE

Compliance Statement

This protocol is for the conduct of a clinical study that complies with requirements of Protection of Human Patients (Informed Consent) (21 CFR Part 50), Financial Disclosure by Clinical Investigators (21 CFR Part 54), Institutional Review Boards (21 CFR Part 56), Investigational Device Exemptions (21 CFR Part 812), the Declaration of Helsinki, the privacy requirements of the Health Information Portability and Accountability Act (HIPAA) (45 CFR Part 160 and Subparts A and E of Part 164), and Clinical Trials Registration and Results Information Submission (42 CFR Part 11), ICH Good Clinical Practice and ISO 14155 Clinical investigation of medical devices for human subjects — Good clinical practice. The most stringent requirements, guidelines or regulations must always be followed. The conduct of the trial will be approved by the appropriate Institutional Review Board (IRB)/Research Ethics Committee (REC) of the respective investigational site and by the applicable regulatory authorities (e.g., FDA).

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2 INVESTIGATOR SIGNATURE PAGE

- I have read and understood the contents of this protocol: Minitouch Endometrial Ablation System Treatment for Menorrhagia: An Evaluation of Safety & Effectiveness (EASE Clinical Trial).
- I agree that it contains all necessary details for carrying out the study as described and I will conduct this study as outlined herein, including all requirements regarding confidentiality.
- I will make a reasonable effort to complete the study within the time discussed.
- I will provide copies of the protocol and access to all information furnished by the Sponsor to study personnel under my supervision. I will discuss this material with them to ensure that they are fully informed about the investigational device and the study.
- I understand that the study may be terminated, or enrollment suspended, at any time by the Sponsor, with or without cause, or by me if it becomes necessary to protect the best interests of the study subjects.
- I agree to conduct this study in full accordance with this protocol, all applicable regulations, including the Protection of Human Patients (Informed Consent) (21 CFR Part 50), Financial Disclosure by Clinical Investigators (21 CFR Part 54), Institutional Review Boards (21 CFR Part 56), Investigational Device Exemptions (21 CFR Part 812), the Declaration of Helsinki, the privacy requirements of the Health Information Portability and Accountability Act (HIPAA) (45 CFR Part 160 and Subparts A and E of Part 164), ICH Good Clinical Practice and ISO 14155. I will follow the most stringent requirements, guidelines and regulations.
- I understand and agree to abide by the obligations set forth in the Investigator Agreement.
- I agree to participate in the Sponsor's training program prior to site initiation and I will ensure that the investigational device is only used by authorized users.

The Site Principal Investigator may delegate one or more of the above functions to an associate or Sub-Investigator. However, the Site Principal Investigator retains overall responsibility for proper conduct of the study, including obtaining and documenting patient informed consent, compliance with the protocol and the collection of all required data.

Site Principal Investigator's Printed Name

Site Principal Investigator's Signature Date Site Name

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3 SPONSOR CONTACT

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Consult the EASE Clinical Trial Contact Information List for inquiries and further information about the study or for reporting serious adverse events and other emergencies.

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4 ABBREVIATIONS & TERMS

Table 4-1: List of Abbreviations & Terms

AE	Adverse Event
BMI	Body Mass Index
CBC	Complete Blood Count
CEC	Clinical Events Committee
CFR	Code of Federal Regulations
CI	Confidence Interval
CIN	Cervical Intraepithelial Neoplasia
CIP	Clinical Investigation Plan (Protocol)
CRF/eCRF	Case Report Form/Electronic Case Report Form
Discharge	Discharge (in the context of the Minitouch procedure): the point at which the subject leaves the site or institution after undergoing the Minitouch procedure
EA	Endometrial Ablation
EASE	Minitouch Endometrial Ablation System Treatment for Menorrhagia: An Evaluation of Safety & Effectiveness Clinical Trial
EC	Ethics Committee
EDC	Electronic Data Capture
Enrolled	*Consented*-enrolled: a consented patient that does not proceed to treatment for any reason (such as screen failure, declines treatment or participation) is categorized as consented-enrolled *Treated*-enrolled: a qualified patient in whom the Minitouch procedure is initiated is categorized as treated-enrolled
FDA	Food and Drug Administration
FSH	Follicle Stimulating Hormone
GCP	Good Clinical Practice
GEA	Global Endometrial Ablation
HIPAA	Health Insurance Portability and Accountability Act of 1996
HMB	Heavy Menstrual Bleeding
ICF	Informed Consent Form
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
IFU	Instructions for Use
IGE	Investigator Global Evaluation
IRB	Institutional Review Board
ITT	Intent to Treat
IUD	Intrauterine Device
IV	Intravenous
NIH	National Institutes of Health
NRS	Numerical Rating Scale
MIQ	Menorrhagia Impact Questionnaire
NSAID	Non-steroidal Anti-inflammatory Drug
OUS	Outside the United States
OPC	Objective Performance Criteria
PBLAC	Pictorial Blood Loss Assessment Chart

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Table 4-1: List of Abbreviations & Terms	
PGE	Patient Global Evaluation
PE	Physical Exam
PI	Principal Investigator
PN	Part Number
PP	Per Protocol
PRN	As needed / when necessary
QOL	Quality of Life
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SIS	Saline Infused Sonohysterography
SOC	Standard of Care
SOP	Standard Operating Procedure
STD	Sexually Transmitted Disease
UADE	Unanticipated Adverse Device Effect
UK	United Kingdom
ISO 14155	Clinical investigation of medical devices for human subjects — Good clinical practice

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5 PROTOCOL SYNOPSIS

Title	Minitouch **E**ndometrial **A**blation **S**ystem Treatment for Menorrhagia: An **E**valuation of Safety & Effectiveness
Short Title	EASE Clinical Trial
IDE No.	G180282
ClinicalTrials.gov Identifier	NCT04267562
Protocol No. & Revision	TD18036 v5.0
Version Date	14Dec2021
Study Device	Minitouch Endometrial Ablation System ("Minitouch System")
Proposed Indications for Use	The Minitouch Endometrial Ablation System is intended for ablation of the endometrial lining of the uterus for the treatment of menorrhagia (heavy menstrual bleeding) due to benign causes in premenopausal women for whom childbearing is complete
Study Design	This is a prospective, multi-center, open-label, single-arm, clinical investigation to evaluate the Minitouch Endometrial Ablation System in premenopausal women with menorrhagia
Study Objective	To evaluate the safety and effectiveness of the Minitouch System
Study Duration	At least 37 months, including an estimated one month of pre-enrollment assessment and 36 months post-treatment follow up
Planned Number of Sites	Approximately 10 sites from the United States only
Planned Enrollment	Up to 126 premenopausal women with menorrhagia
Primary Effectiveness Endpoint	Percent of patients demonstrating reduction of menstrual flow as evidenced by a Pictorial Blood Loss Assessment Chart (PBLAC) score of $\leq$75 at the 12-month post procedure time point
Study Success	To achieve study success, 12-month success rate should exceed the 66% Objective Performance Criterion (OPC) developed by the FDA, outlined in correspondence of Oct 29, 2015[(1)]
Primary Safety Measure	Reported rate of device and procedure-related serious adverse events at 12-months post-procedure as adjudicated by the CEC

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Secondary Outcome Measures	**Secondary effectiveness outcome measures** include the following: **PBLAC:** at 6 and 12 months • Menstrual Status at 6 and 12 months categorized by: o Amenorrhea: PBLAC score 0 o Light Bleeding: PBLAC score 0 ≤ 35.0 o Normal Bleeding: PBLAC score 35.1 to 75.0 o Eumenorrhea: PBLAC score 75.1 to 99.9 o Menorrhagia: PBLAC score ≥100 **Patient Global Evaluation (PGE):** at 6, 12, 24 and 36 months • Patient satisfaction with treatment • Menstrual status • Recommend to friends **Investigator Global Evaluation (IGE):** at 6, 12, 24 and 36 months • Investigator satisfaction with treatment • Menstrual status **Quality of Life Measures:** at 6, 12, 24 and 36 months • Improvement of quality of life as measured by: o Menorrhagia Impact Questionnaire (MIQ) o Dysmenorrhea-related Numerical Rating Scale (NRS) pain score **Procedure:** • Procedure-related Numerical Rating Scale (NRS) pain score • The following parameters will also be collected: o Total procedure time o Total treatment time (total energy delivery time) o Total procedure energy in joules o Anesthesia regimen o Procedure-related pain at pre-procedure (baseline), discharge and 24-hours post-procedure o Need for cervical dilation **Secondary safety outcome measures** include the following: • Any medical surgical intervention to treat abnormal bleeding anytime following the ablation procedure • Incidence of Adverse Events (AEs), Serious Adverse Events (SAEs) and Unanticipated Adverse Device Effects (UADEs) at 24 and 36 months

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Inclusion Criteria	**<u>Qualified participants must meet all of the following inclusion criteria</u>:** 1) Female age 30 to 50 years 2) Excessive menstrual bleeding due to benign causes 3) Uterine sounding depth measurement of 6.0 – 12.0 cm (external os to internal fundus) 4) A minimum uterine cavity length of 4.0 cm (internal os to internal fundus) 5) A minimum PBLAC score of ≥ 150 for 1 menstrual cycle (obtained during screening) and must also have a documented history of excessive menstrual bleeding prior to study enrollment 6) Endometrial biopsy within 12 months prior to treatment procedure with no abnormal pathology 7) Premenopausal at screening as determined by FSH measurement ≤ 40 IU/L when age is ≥ 40 years 8) Patient agrees to use a reliable form of contraception during the study, and to follow these requirements: a. If a hormonal birth control method is used for contraception, the patient must have been on said method for ≥ 3 months prior to the onset of the screening menstrual cycle and agrees to remain on the same hormonal regimen through the initial 12-month post-treatment follow-up (pills, injections, patches, rings, implants) b. Patient also agrees to not use hormonal birth control during the first 12-month post-treatment follow-up period if they were not using hormonal birth control during the 3 months prior to treatment 9) Ability to provide written informed consent 10) Patient is literate and clearly demonstrates understanding on how to use PBLAC after training 11) Patient agrees to the following during the study: a. No initiation of hormonal contraception or any other medical intervention for bleeding b. Attend all follow-up exams through the 36-month follow-up timepoint c. Exclusive use of study-provided sanitary products and submission of completed PBLAC diaries through the 12-month post-treatment follow-up

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Exclusion Criteria	**<u>Qualified participants must NOT meet any of the following exclusion criteria</u>:** 1) Pregnant, or desires to retain fertility 2) Current or documented history of endometrial hyperplasia 3) Active endometritis 4) Clinically significant or suspected adenomyosis indicated by patient complaints, imaging, or clinician's judgment 5) Active infection of the genitals, vagina, cervix, uterus, adnexa, or urinary tract 6) Active pelvic inflammatory disease 7) Currently using an intrauterine device (IUD), including Mirena™ device, and unwilling to remove the IUD 8) Presence of an implantable contraceptive device (e.g., Essure®) protruding into the uterine cavity 9) Active sexually transmitted disease (STD) at the time of ablation 10) Presence of bacteremia, sepsis, or other active systemic infection 11) Currently on anticoagulants 12) Known clotting defects or bleeding disorders 13) Currently on medications that could thin the myometrium, such as long-term steroid use (except inhaler or nasal therapy for asthma or other pulmonary condition) 14) Previous medical/surgical treatments, or has other conditions, that could lead to anatomic/pathologic weakness or thinning of the myometrium (Classical caesarean section and transmural myomectomy are examples of such treatments that may interrupt the integrity of the uterine wall) 15) Any general health, mental health or social situation which, in the opinion of the investigator, could represent an increased risk for the patient, or the ability of the patient to complete study requirements 16) Known/suspected abnormal uterine/pelvic anatomy or condition, such as frozen pelvis 17) Abdominal, pelvic or gynecological malignancy 18) Untreated/unevaluated cervical dysplasia, except cervical intraepithelial neoplasia I (CIN I) 19) Previous endometrial ablation procedure 20) Abnormal or obstructed, or perforated cavity as determined by investigator via standard clinical practices (e.g., hysteroscopy, saline infusion sonohysterography). This includes, but is not limited to: a. Septate or bicornuate uterus, arcuate uterus or other congenital malformation of the uterine cavity b. Pedunculated or submucosal myomas distorting the uterine cavity or not fully resected c. Polyps larger than 1 cm 21) Intramural or subserosal myomas > 3 cm in size, or any myoma that distorts the uterine cavity 22) Any patient who is currently participating or considering participation in any other research of an investigational drug or device
Study Management	MicroCube, LLC or its designee

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Data Management, Safety Review & Clinical Events Committee (CEC) Coordination	Avania 100 Crowley Drive, Suite 216 Marlborough, MA 01752
Sponsor/Manufacturer	MicroCube, LLC 47853 Warm Springs Blvd. Fremont, CA 94539

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6 BACKGROUND

Menorrhagia (heavy menstrual bleeding) can have significant negative effects on the quality of life of women including medical complications, anemia, time lost from work, physical discomfort, lifestyle and psychological disruption, and increased health costs.

Hysterectomy has traditionally been regarded as the definitive surgical treatment for menorrhagia. However, despite a 100% success rate (complete cessation of menstruation) and high levels of satisfaction, it is a major surgical procedure with significant physical complications and social and economic costs. This led to "first generation" hysteroscopic endometrial ablation devices that utilize a resectoscope and electro-cautery tools to minimally invasively ablate the functional layer of the endometrium, thus preventing abnormal uterine bleeding.

"Second-generation" GEA devices for ablating the lining of the uterus have been introduced in the market with the aim of providing simpler, quicker, safer, and improved outcomes. These procedures involve destroying the endometrium using radiofrequency energy, heated saline (freely circulating in the uterus), heated fluid inside a balloon, cryosurgery, and microwave energy. On October 29, 2015, the Food and Drug Administration (FDA) issued a letter, "Dear Global Endometrial Ablation Manufacturer", that provided guidance to future global endometrial ablation device manufacturers and explained the basis for an objective performance criterion (OPC):

> "Since 1997, the United States Food and Drug Administration (FDA) has approved five non-hysteroscopic global endometrial ablation (GEA) devices based on the results of randomized controlled trials (RCTs) that compared the safety and effectiveness of the GEA device to the same control – hysteroscopic rollerball ablation. Rollerball ablation is an older, well-known surgical technique used to treat heavy menstrual bleeding from benign causes. The study designs that supported the approval of the five GEA devices were very similar. They enrolled between 250 and 350 subjects using either a 1:1 or 2:1 (device: control) randomization scheme and had comparable patient populations. The primary endpoint for all five studies was the reduction in menstrual blood loss measured by the Pictorial Blood Loss Assessment Chart (PBLAC), a validated menstrual blood loss scoring system. One of the inclusion criteria required a baseline PBLAC score of at least 150 or 185, and the individual patient success criteria for effectiveness was defined as a PBLAC score of less than or equal to 75 at one year following the ablation procedure. For all subjects, pretreatment evaluation was performed to confirm the study eligibility criteria were satisfied (e.g., absence of cavity distortions, lesions that might interfere with the GEA therapy). The analysis population consisted of all subjects who presented for their scheduled treatment, having satisfied the study eligibility criteria (intent-to-treat). This analysis population included women who presented for treatment, but did not receive the planned therapy due to reasons such as identification of exclusionary pathology immediately prior to ablation, withdrawal of consent, etc. Patients with missing PBLAC scores at one year following the ablation procedures were considered treatment failures. A study was considered a success if the proportion of successes in the GEA group met a pre-specified non-inferiority margin compared to the proportion of successes in the rollerball ablation control group.
>
> Using a generalized linear mixed model with study as a random effect, the FDA determined that the average success rate across the five GEA devices was 75.6% (65.6%, 83.5%) and 77.2% (66.5%, 85.2%) for the rollerball ablation control. The FDA performed

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additional analyses to evaluate the effect of baseline covariates on the primary endpoint, including age (above and below 40), baseline PBLAC score (at least 150), uterine sound (6 to 12 centimeters), and presence of fibroids (< 3 cm). Using analysis of covariance methods, the FDA found that none of these baseline covariates had a significant impact on the study results. Based on this analysis, the FDA identified an objective performance criterion (OPC) for the minimum success rate for effectiveness. The OPC is 66% based on the lower bound of the 95% confidence interval of the average success rate for the five approved GEA devices."

The Minitouch System is an endometrial ablation device that is similar in principle to the "second generation" endometrial ablation devices. The EASE Clinical Trial is being conducted to assess the safety and efficacy of the Minitouch System.

6.1 Summary of Pre-Clinical and Clinical Testing (Prior Clinical Experience)

Pre-clinical testing for the Minitouch System demonstrates that the system performs as intended. Tests include the following in which the Minitouch System met the required pre-specified acceptance criteria:

- Design and Performance Verification
- Materials Testing (Biological Safety and Biocompatibility)
- Software
- Electrical Safety and EMC
- Usability
- Environmental & Life Cycle Testing
- Packaging/ Transportation Testing
- Sterilization Validation
- Dose Confirmation and Simulation Studies
- Ex-Vivo Human Uteri Ablation

The Minitouch System has been commercially available outside the United States (OUS) since 2011. As a result, there is extensive clinical experience with the device. Specifically:

- To date, there have been over 4000 real-world clinical procedures completed by more than 180 users at over 70 hospitals/centers predominantly located in the UK. Of these, one (1 or 0.025%) incidence of bowel injury occurred during clinical use. This event was attributed to procedural use errors and the patient was not an optimal candidate for the procedure.
- Additionally, there are over 50 publications (abstracts) reporting the OUS clinical experience of the Minitouch System. A safety analysis (review of all adverse events reported) was conducted.
    - A total sampling of 1,040 patients treated with the Minitouch System were included in the safety analysis.
    - A total of 14 events were reported in the literature and are summarized below. The events were consistent with those expected to occur in patients undergoing endometrial ablation.

Event Description/Terminology (as reported in the literature)	Occurrence Rate [n (%)] (where N=1040)
Infection (suspected or confirmed)	5 (0.48%)
Post-procedure pain/cramps	7 (0.67%)
Vasovagal episode	2 (0.19%)

The Minitouch pre-clinical and clinical data are detailed in the Investigator's Brochure.

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7 STUDY OBJECTIVE

7.1 Device and Study Rationale

The Minitouch Endometrial Ablation System is designed with the patient and user in mind to expand women's access to menorrhagia treatments that are safe, effective, and a less invasive alternative to hysterectomy.

To provide a benchmark against which to judge the safety and effectiveness of the investigational system, this study is a prospective, single-arm, non-randomized, multi-center clinical trial of the effectiveness of endometrial ablation with the Minitouch System versus the FDA identified OPC for GEA devices. All procedures will be performed using the Minitouch System manufactured by MicroCube. The goal of the current study is to support reasonable safety and effectiveness of the investigational product compared to currently FDA-approved GEA devices.

7.2 Study Objectives

7.2.1 Primary Objective

The primary objective of this study is to demonstrate the safety and effectiveness of the Minitouch Endometrial Ablation System in treating patients with menorrhagia.

The study will demonstrate the Minitouch System's success rate at 12 months post-procedure exceeds the 66% OPC for minimum success rate of effectiveness developed by the FDA.

The Primary Safety Objective is the reported rate of device or procedure-related SAE at 12 months post-procedure. Serious adverse events are expected to be rare (<1%). [8-13]

The safety endpoint at 24 and 36-months will include all device or procedure-related adverse device effects, SAEs and UADEs defined in **Section 14 Adverse Event Reporting**.

7.2.2 Secondary Objective

Secondary objectives of this study are to evaluate improvement of quality of life, patient and investigator satisfaction, and the need for medical or surgical intervention to treat abnormal bleeding (as determined necessary by the study investigator) in the 12 months following the ablation procedure.

8 DEVICE DESCRIPTION

8.1 System Overview

The Minitouch Endometrial Ablation System (Minitouch System) is a global endometrial ablation (GEA) device intended to treat menorrhagia by ablating the endometrium of the uterus.

The Minitouch System consists of two main components:

Minitouch System Components	Product Number
• Minitouch Hand Piece (Hand Piece)	4501
• Minitouch Generator (Generator)	4001-01

The Generator consists of four (4) main modular components and accessories (Power Cord & Stand Kit):

Generator Components	Product Number
• Central Unit (CU)	4002
• Display	4003

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Generator Components	Product Number
• Inter-connecting Cable (ICC)	4004
• Keypad	4005
• Power Cord NEMA 5-15 (US)	4006
• Stand Kit	
○ Base	4007
○ Swing Arm	4008
○ Dock	4009

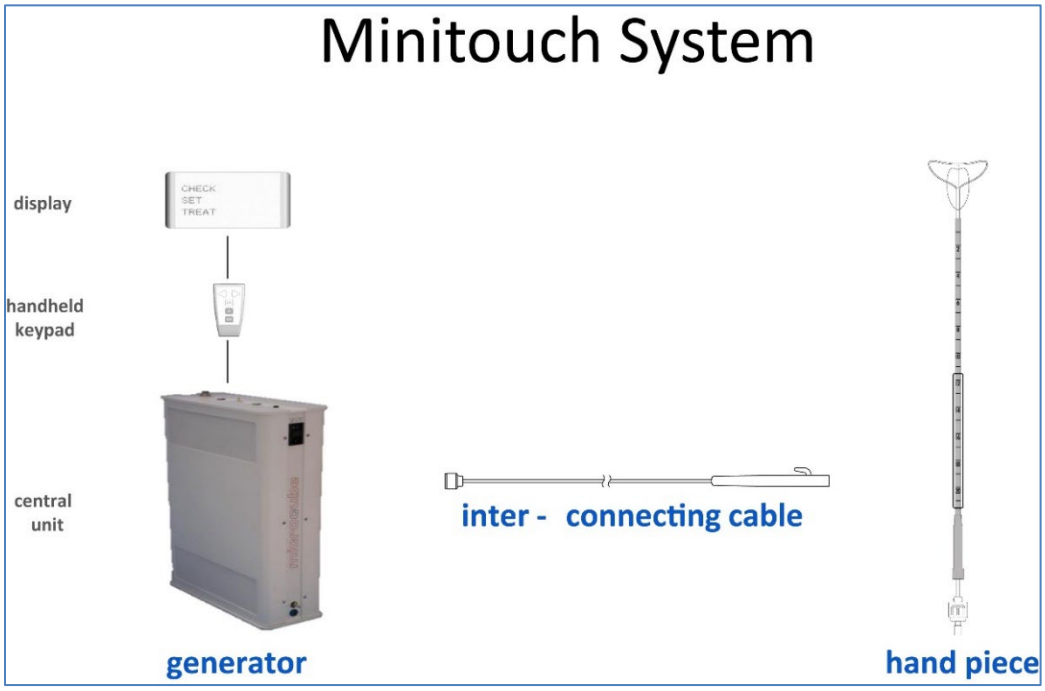

Figure 8-1: Minitouch Endometrial Ablation System

The Hand Piece is a sterile, single-use energy applicator. It is slim, flexible and atraumatic, and designed for transcervical access to the uterine cavity without requiring dilation of the cervix. It is used exclusively with the Generator for delivering microwave energy to the uterine cavity.

The Generator is a non-sterile, reusable, line-powered, modular system intended for generating, delivering and monitoring microwave energy. The Generator is used exclusively with the Minitouch Hand Piece. The Generator software version used in the EASE Clinical Trial is R02-02-02.

The Minitouch System has no gas or fluidic systems or other consumables. Refer to the Instructions for Use for additional details regarding the Minitouch System.

8.2 Principle of Operation

Heavy menstrual bleeding (HMB), also called menorrhagia, can be treated by ablating the endometrial tissue of the uterus. The endometrial lining of the uterus contains most of the endometrial tissue. Additionally, some endometrial tissue may protrude into the myometrium making the endomyometrial

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junction more of a zone rather than a surface. The endometrial layer and the junctional zone together form the Target Tissue for ablation. The Target Tissue is approximately in the shape of a triangular pillow, with the two cornua and the internal os of the uterine cavity forming its three corners. It is thickest in the mid-uterine section, up to 20mm thick, and tapers off towards the edges and corners. Refer to **Figure 8-2** below.

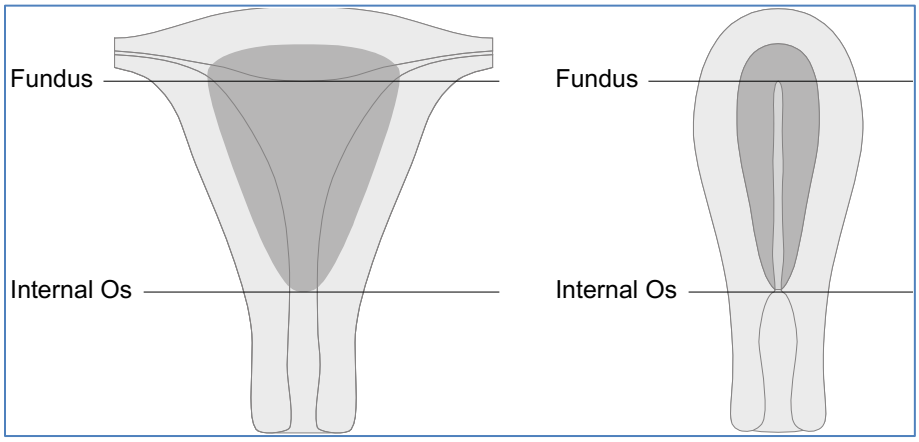

Figure 8-2: Target Tissue Diagram (Left: Mid Coronal View, Right: Mid Sagittal View)

The goal of the procedure is to safely ablate all of the Target Tissue in order to ensure that no endometrial tissue remains viable after the procedure.

8.3 Proposed Indications for Use (IFU)

The Minitouch Endometrial Ablation System is intended for ablation of the endometrial lining of the uterus for the treatment of menorrhagia (heavy menstrual bleeding) due to benign causes in premenopausal women for whom childbearing is complete.

8.4 Device Instructions

A comprehensive Instructions for Use (IFU) for the Minitouch Endometrial Ablation System, including warnings and precautions, has been created. Please refer to the most current version for complete details on preparation and procedural use of the device.

9 STUDY ENDPOINTS

9.1 Primary Effectiveness Endpoint

The primary effectiveness endpoint is a reduction in menstrual blood loss as assessed by the Pictorial Blood Loss Assessment Chart (PBLAC) data, a validated, patient self-reported menstrual diary scoring system. All patients must have a baseline PBLAC score of ≥150 with a documented history of excessive menstrual bleeding to document a clinical diagnosis of menorrhagia.

An individual patient will be considered a success if the PBLAC score is ≤ 75 at 12 months post-procedure without incidence of additional interventions or treatments for bleeding prior to the 12-month follow-up

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visit. To achieve study success, the lower bound of the 95% CI of 12-month success rate should exceed the 66% Objective Performance Criterion (OPC) developed by the FDA.[1]

9.2 Primary Safety Endpoint

The primary safety endpoint is the incidence of device- or procedure-related serious adverse events at 12-months post-procedure. The overall rate and severity of all the reported adverse events will also be documented. Procedure-related serious adverse events are expected to be rare (<1%).[8-13]

9.3 Secondary Outcome Measures

Secondary effectiveness and safety outcome measures will be assessed at the timepoints described below.

The secondary safety outcome measure at 24 and 36 months will include all device or procedure-related adverse device effects, SAEs and unanticipated adverse device effects (UADE) are defined in **Section 14 Adverse Event Reporting**.

Any medical surgical intervention to treat abnormal bleeding following the ablation procedure is considered a treatment failure. If menstrual status is assessed as "High/Heavy" by the investigator at the 24 or 36-month follow-up, the patient will be considered a treatment failure.

Secondary effectiveness outcome measures will include the following:

PBLAC: at 6 and 12 months

- 

Patient Global Evaluation (PGE): at 6, 12, 24 and 36 months

- Patient satisfaction with treatment
- Menstrual status
- Recommend to friends

Investigator Global Evaluation (IGE): at 6, 12, 24 and 36 months

- Investigator satisfaction with treatment
- Menstrual status

Quality of Life Measures: at 6, 12, 24 and 36 months

- Improvement of quality of life as measured by:
    - Menorrhagia Impact Questionnaire (MIQ)
    - Dysmenorrhea-related Numerical Rating Scale (NRS) pain score

Procedure:

- Endometrial ablation procedure-related Numerical Rating Scale (NRS) pain score
- The following parameters will also be collected:
    - Total procedure time
    - Total treatment time (total energy delivery time)

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- Total procedure energy in joules
- Anesthesia regimen
- Procedure-related pain at pre-procedure (baseline), discharge and 24-hours post-procedure
- Need for cervical dilation

10 STUDY DESIGN

This study is a prospective, multi-center, open-label, single-arm, clinical investigation to evaluate the Minitouch Endometrial Ablation System in up to 126 premenopausal women with menorrhagia. The treatment procedure may be performed in an office setting or ambulatory / outpatient surgery centers/operating room (OR).

Candidates will be identified via review of existing patient records and, if necessary, as a result of IRB-approved recruitment advertisements (see **Figure 10-1: Study Execution Diagram**). Study staff will confirm general eligibility and identify already existing SOC (standard of care) testing which may be applied to the trial.

Study staff will obtain written informed consent as outlined in **Section 11.5 Informed Consent**.

Screening may require more than one visit. The first visit requires documentation of written informed consent and it is recommended that the visit include patient training on the method of collecting PBLAC diary data, a validated patient self-reported menstrual diary scoring system. [2]

A subsequent visit may occur after approximately one month, and after completion of the PBLAC diary. The subject will return the completed PBLAC diary and the site personnel will confirm menorrhagia with a PBLAC a score of ≥150. Then the patient will continue screening for additional eligibility assessments as outlined in **Figure 10-1: Study Execution Diagram** and **Section 12.3 Screening Visits.**

Patient enrollment occurs on the day of the treatment following confirmation of eligibility. Once confirmed, then the patient may undergo the Minitouch procedure. One day after procedure, the study staff will contact the patient to assess the patient's procedure-related pelvic pain level utilizing the NRS (0-10 scale). Every effort should be made to ensure the 24-hour contact is conducted even if the window falls on a weekend. The follow-up visits will occur at 2 weeks, 3 months, 6 months and 12 months, 24 months, and 36 months post-procedure. Total study duration for a Patient is approximately 37 months, including one month of pre-enrollment assessment, and 36 months post-treatment follow up.

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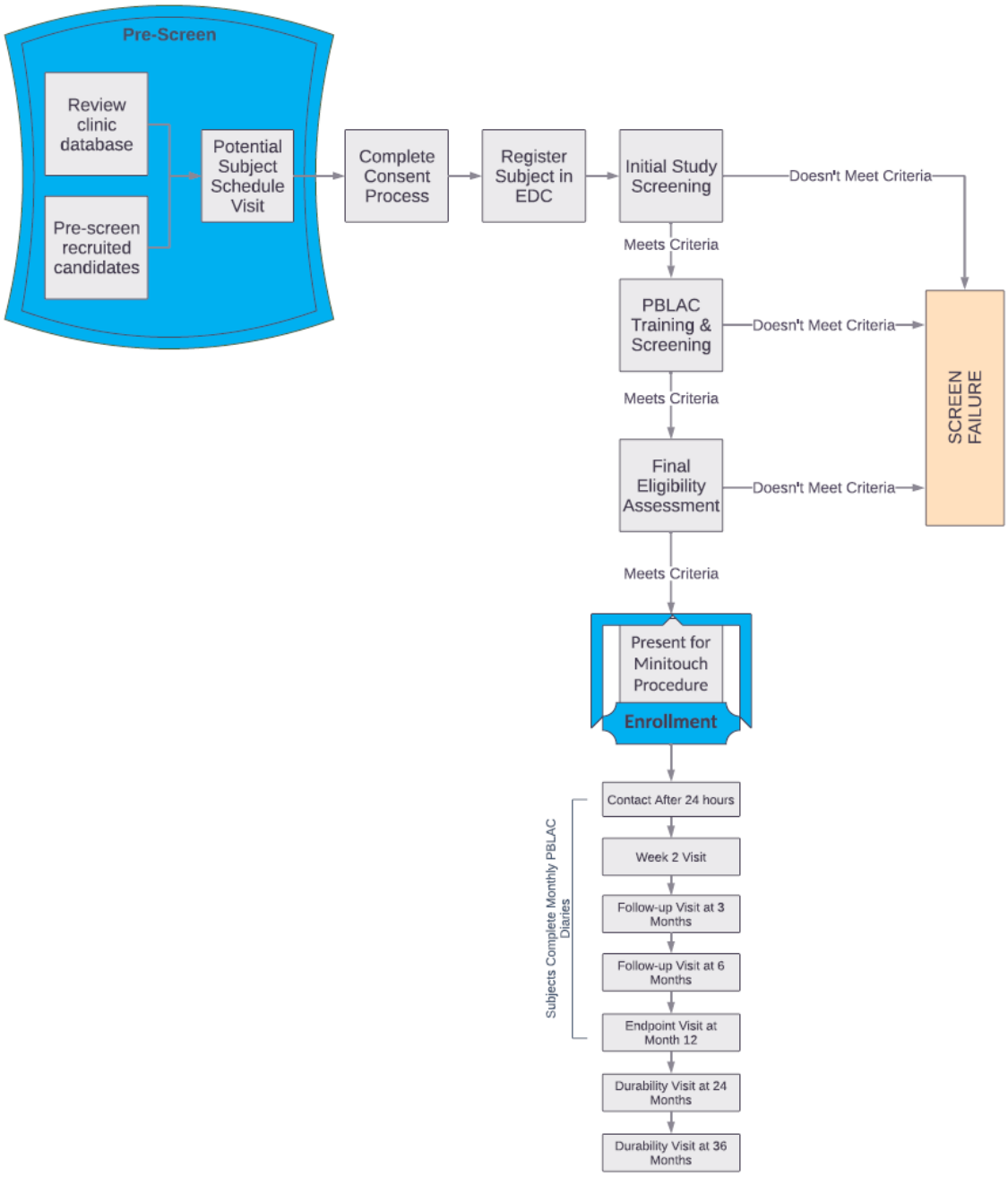

NOTE: Final eligibility must be confirmed by the investigator prior to procedure initiation.

Figure 10-1: Study Execution Diagram

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11 PATIENT ENROLLMENT AND SELECTION

11.1 Study Population

The target patient population is adult females age 30 - 50 years old that meet the eligibility criteria as outlined in **Section 11.3 Patient Selection Criteria**. All patients must sign the study-specific informed consent form and meet all inclusion criteria and have no exclusion criteria.

11.2 Prescreening

The investigators may prescreen prospective candidates prior to consent by reviewing current medical files to assess eligibility according to the selection criteria. Applicable testing or information obtained in standard of care medical visits or obtained via recruitment services may be utilized for the study if the test was completed within the validity windows.

No prospective protocol-specific testing or medication changes shall occur until the informed consent form (ICF) is signed by the patient and the delegated clinical site personnel.

11.3 Patient Selection Criteria

Patients who meet the inclusion criteria and do not fulfill any of the exclusion criteria will be eligible for participation in this study.

11.3.1 Inclusion Criteria

Patients eligible for inclusion in this study must fulfill the following criteria:

1) Female patient age 30 to 50 years
2) Excessive menstrual bleeding due to benign causes
3) Uterine sounding depth measurement of 6.0 – 12.0cm (external os to internal fundus)
4) A minimum uterine cavity length of 4.0cm (internal os to internal fundus)
5) A minimum PBLAC score of ≥ 150 for 1 menstrual cycle (obtained during screening) and must also have a documented history of excessive menstrual bleeding prior to study enrollment
6) Endometrial biopsy within 12 months prior to treatment procedure with no abnormal pathology
7) Premenopausal at screening as determined by FSH measurement ≤ 40 IU/L when age is ≥ 40 years
8) Patient agrees to use a reliable form of contraception during the study, and follows these requirements:
    a. If a hormonal birth control method is used for contraception, the patient must have been on said method for ≥ 3 months prior to the onset of the screening menstrual cycle and agrees to remain on the same hormonal regimen through the initial 12-month follow-up (pills, injections, patches, rings, implants)
    b. Patient also agrees to not use hormonal birth control during the first 12-month post-treatment follow-up period if they were not using hormonal birth control during the 3 months prior to treatment
9) Ability to provide written informed consent
10) Patient is literate and clearly demonstrates understanding on how to use PBLAC after training
11) Patient agrees to the following during the study:
    a. No initiation of hormonal contraception or any other medical intervention for bleeding
    b. Attend all follow-up exams and submission of completed PBLAC diaries through the 36-month follow-up timepoint

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c. Exclusive use of study-provided sanitary products and submission of completed PBLAC diaries through the 12-month post-treatment follow-up

11.3.2 Exclusion Criteria

Patients will be excluded from this study if they meet any of the following criteria:

Patient Conditions:

1) Pregnant, or desires to retain fertility
2) Current or documented history of endometrial hyperplasia
3) Active endometritis
4) Clinically significant or suspected adenomyosis indicated by patient complaints, imaging or clinician's judgment
5) Active infection of the genitals, vagina, cervix, uterus, adnexa or urinary tract
6) Active pelvic inflammatory disease
7) Currently using an intrauterine device (IUD), including Mirena™ device, and unwilling to remove the IUD
8) Presence of an implantable contraceptive device (e.g., Essure®) protruding into the uterine cavity
9) Active sexually transmitted disease (STD) at the time of ablation
10) Presence of bacteremia, sepsis, or other active systemic infection
11) Currently on anticoagulants
12) Known clotting defects or bleeding disorders
13) Currently on medications that could thin the myometrial muscle, such as long-term steroid use (except inhaler or nasal therapy for asthma or other pulmonary conditions)
14) Previous medical/surgical treatments, or has other conditions, that could lead to anatomic/pathologic weakness or thinning of the myometrium (Classical caesarean section and transmural myomectomy are examples of such treatments that may interrupt the integrity of the uterine wall)
15) Any general health, mental health or social situation which, in the opinion of the investigator, could represent an increased risk for the patient, or the ability of the patient to complete study requirements.

Patient Anatomy:

16) Known/suspected abnormal uterine/pelvic anatomy or condition, such as frozen pelvis
17) Abdominal, pelvic or gynecological malignancy
18) Untreated/unevaluated cervical dysplasia, except cervical intraepithelial neoplasia I (CIN I)
19) Previous endometrial ablation procedure
20) Abnormal or obstructed, or perforated cavity as determined by investigator via standard clinical practices (e.g., hysteroscopy, saline infusion sonohysterography). This includes, but is not limited to:
    a. Septate or bicornuate uterus, arcuate uterus or other congenital malformation of the uterine cavity
    b. Pedunculated or submucosal myomas distorting the uterine cavity or not fully resected
    c. Polyps larger than 1 cm
21) Intramural or subserosal myomas > 3 cm in size, or any myoma that distorts the uterine cavity

General Exclusions

22) Any patient who is currently participating or considering participation in any other research of an investigational drug or device

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11.4 Rescreening

At the discretion of the investigator, a patient who previously failed screening may be rescreened. All screening tests, including those conducted prior to rescreening, must still occur within the validity windows.

11.5 Informed Consent

IMPORTANT: The Code of Federal Regulations requires that the consent form signed by the Patient must be dated at the time consent is given. Also, medical records must contain documentation that informed consent was obtained prior to participation in a study. (21 CFR Parts 50 and 812)

The Investigator may determine whether potential Patients are interested in participating in an investigation, but shall not request the written informed consent of any Patient to participate, and shall not allow any Patient to participate before obtaining Institutional Review Board (IRB) approval and prior to receiving documentation of FDA approval from the Sponsor. The consent process shall begin before care is altered beyond the scope of a routine comprehensive examination for the purpose of participating in this study.

All Patients in this research study should be completely informed about the purpose, duration, and pertinent details of the study. If the informed consent is amended by the Sponsor during the study, the investigator is responsible for ensuring the IRB reviews and approves the amended form. The informed consent must be obtained using a written form that has been approved by the IRB and includes all *Basic Elements of Informed Consent* and pertinent *Additional Elements* (21 CFR Part 50.25). The informed consent discussion and process with the potential study subject shall be documented in progress/clinic notes or other source documentation. In the event a potential participant is unable to be seen in person, alternative methods of consenting (via telemedicine, including, but not limited to phone call, video or virtual office/remote visit, electronic signature or any combination of these methods) is allowed provided the consenting process is thoroughly documented in the study records and the signed consent form is maintained in the study records.

The Investigator must keep the original signed copies of all consent forms in the Patient's medical records and provide a copy to each Patient. If new information becomes available during the course of the study, the information will be provided to new and existing patients, and if relevant, request existing patients to confirm their continued participation in the study by signing an amended informed consent or consent addendum.

11.6 Patient Privacy

The investigator agrees to comply with all applicable federal, state, and local laws and regulations relating to the privacy of patients' health information, including, but not limited to, the Standards for Individually Identifiable Health Information, 45CFR Parts 160 and 164 and in accordance with the Health Insurance Portability and Accountability Act of 1996 (HIPAA), which states all patients should be informed of potential uses and disclosures of their medical information for research purposes, and their rights to access information about them by covered entities. Each Investigator will follow the procedures for securing HIPAA compliance as directed by their respective IRB or Privacy Board, and to obtain written authorization to use and disclose patient information for all clinical research and research involving questioning of the patient's or patients' physician(s). Per individual site procedures, this authorization may be included as part of the patient informed consent form.

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11.7 Strategies for Recruitment and Retention

Patients will be recruited through a variety of media. Patients may be actively recruited through IRB-approved web-based advertising, television, radio, and newspaper ads. Patients will be financially compensated for their study participation. The amount of compensation and schedule of payments will be documented in the ICF.

11.7.1 Special Population

This study will not focus on any particular subset of patients based on ethnicity or race. Further, no patient will be excluded from the study on the basis of racial or ethnic origin. The racial and ethnic composition of the study is expected to represent the demographics of the typical population seeking relief menorrhagia in the geographical area around the investigational sites. The age of the patients will typically be in the 30 – 50 year old range, the most common ages for menorrhagia.

No patients from the vulnerable population shall be enrolled in the trial. Specifically, elderly patients will not be included because these women are likely post-menopausal; and pediatric patients will not be included in this study because they do not meet the minimum age criteria and because it would be improper to have them undergo a procedure that would limit their potential fertility on a permanent basis.

11.7.2 Control of Bias Section

Upon receipt of IRB/ethics approval, patients with menorrhagia will be considered for the study until the site reaches its enrollment goal. Careful documentation will be kept tracking potential patients' eligibility and consent acceptance or rejection. To maintain a balanced population in the study, no single investigational site will be permitted to enroll more than 35% of the entire study population.

Non-response bias will be prevented by offering reasonable expense reimbursement and incentives to participate in the study. Every effort should be made to send appointment reminders to facilitate completion of study visits within study windows.

11.8 Patient Discontinuation and Replacement

Patients are free to terminate their participation (with or without reason) in the study at any time. Likewise, a patient may be terminated from the study by the investigator or the Sponsor, MicroCube, at any time if either investigator or Sponsor determines that it is not in the patient's best interest to continue participation. Enrolled patients that are terminated because of lack of compliance to protocol will not be replaced and will be considered lost to follow-up. If a patient is terminated prior to the 12-month follow up visit, this patient will be considered a treatment failure.

11.8.1 Reasons for Termination

Every patient should remain in the study until completion of the 36-month follow-up period. Whenever possible, an exit visit should be conducted to record reason(s) for withdrawal, retrieve study materials (PBLAC diaries) and complete relevant visit assessments such: AEs, concomitant medications, patient's menstrual status, NRS for dysmenorrhea-related pain and MIQ. Conceivable reasons for early patient discontinuation may include, but are not limited to, the following:

- **Patient Withdrawal (voluntarily terminates consent):** Patient participation in this clinical study is voluntary. The patient may choose to discontinue participation (refuse all subsequent testing) at any time without loss of benefits or penalty.

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- **Discontinuation:** Patient participation may be discontinued by the patient or investigator because of a treatment modality change, organ transplant, transfer, death or prolonged hospitalization. The Sponsor may also decide to discontinue the testing of the study device.
- **Investigator-initiated Termination:** The Investigator may terminate the patient's participation without regard to the patient's consent if the Investigator believes it is medically necessary. In addition, the following circumstances may require early termination:
    - Patient is unable or unwilling to cooperate with study staff;
    - Emergence of clinically relevant serious adverse events, laboratory abnormalities or other medical condition or situation occurs such that continued participation would not be in the best interest of the patient;
    - Pregnancy
    - Death
- **Exclusion Criterion Discovered After Enrollment:** A small number of patients may be enrolled despite meeting an exclusion criterion. This will be documented by the study personnel on the eCRF and will be considered a protocol deviation (PD), not termination.
- **Lost-to-Follow-up:** This category accounts for patients whose status is unclear because they fail to appear for study assessments/visits without stating intention to terminate consent. The data from this patient is still eligible for the intent-to-treat dataset. Site personnel should make all reasonable efforts to locate and communicate with the patient, at each contact time point, including:

A minimum of three (3) telephone calls to contact the patient should be attempted. Each attempt should be recorded in the patient's medical record, including date, time, and initials of site personnel attempting the contact.

If telephone calls are unsuccessful, a certified letter (with mailing receipt and electronic confirmation of delivery) should be sent to the patient.

If the above-mentioned attempts at communicating with the patient are unsuccessful, the patient will be considered lost-to-follow-up.

NOTE: If the patient is contacted, the patient is no longer considered lost-to-follow-up and study visits will resume at the next applicable time point.

In all cases, the reason(s) for withdrawal, if given, must be recorded on the appropriate eCRF and in the patient's medical record. If more than one reason is cited for withdrawal, study personnel must identify the most significant reason and record this reason on the eCRF. Investigators must also report all patient withdrawals to their IRB as defined by their institutions' procedures. Patients who withdraw or are withdrawn from the study or are lost to follow-up will not be replaced.

11.9 Point of Enrollment

A consented patient will be registered into the study EDC (eCRFs) and a unique subject identification number at the time of registration will be issued via the EDC. All data will be entered in the study EDC. If a patient later declines to participate, or is excluded from enrollment, the investigator will note the reason for non-participation in the study EDC.

A patient is considered enrolled when the following milestones have occurred: (1) the ICF is signed, (2) all applicable screening has been successfully completed, and (3) all study inclusion criteria and no exclusion criteria are met. Since the final selection criteria are re-assessed prior to procedure initiation on the date

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of treatment (e.g.: pregnancy test, current medications, active infections) the patient may not be enrolled until that date. Specifically, final eligibility must be confirmed by the investigator prior to initiating the Minitouch procedure.

For additional clarity, a consented patient that does not proceed to treatment for any reason (such as screen failure, declines treatment or participation), is categorized as consented-enrolled. A qualified patient in whom the Minitouch procedure is initiated is categorized as treated-enrolled.

11.10 Completion of the Clinical Investigation

The completion of the clinical investigation shall be the last visit of the last subject and when follow-up is complete for the clinical investigation, whether the clinical investigation concluded according to the protocol or was terminated prematurely.

12 STUDY VISIT INSTRUCTIONS

12.1 Schedule of Events

This section describes the timing for required testing and procedures during screening and in follow-up. All references to a study visit throughout the protocol are inclusive of visits conducted in person or via telemedicine visit (phone call, video, virtual office/remote), both of which are acceptable for purposes of trial conduct. The overall schedule of events is shown below. Results from these assessments will be captured in the patient's medical record or on source documents, and eCRFs. All study visit windows will be calculated based on the day of procedure (Day 0) and one month will be calculated as 30 calendar days, one week as 7 calendar days. **Section 13 STUDY PROCEDURES / EVALUATIONS** details the processes.

The study primary safety/efficacy endpoint assessment is conducted at the 12-month follow-up visit.

12.2 Validity Windows for Baseline Testing

All Baseline activities, including prescreening and rescreening testing must be conducted within the validity window. Review testing dates prior to procedure to ensure that all required activities have been conducted within window as outlined in **Table 12-1** below.

For example, the assessment of the patient's medical and surgical history must have occurred no more than 6 months prior to the date of treatment. If that assessment is outside of that validity window, then reassess the subject's medical and surgical history prior to the procedure.

Table 12-1: Validity Windows

Screening Activity	Validity Window (where 6 months = 180 calendar days; and 12 months = 365 calendar days)
Demographics	6 Months
Medical and surgical history	6 Months
Documented history of excessive menstrual bleeding	6 Months
Physical examination	6 Months
Pap-Smear	12 Months
Transvaginal ultrasound	6 Months
Endometrial biopsy	12 Months
Sonohysterography / hysteroscopy	6 Months
Complete Blood Count	6 Months
Serum FSH	6 Months
Urine Pregnancy Test	6 Months

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Table 12-1: Validity Windows	
Screening Activity	**Validity Window** (where 6 months = 180 calendar days; and 12 months = 365 calendar days)
Urine Dipstick Pregnancy Test (Day of Procedure)	24 Hours
STD Tests	6 Months
PBLAC	6 Months*
Menorrhagia Impact Questionnaire	6 Months
Dysmenorrhea-related pain	6 Months

* If the qualifying PBLAC diary was completed more than 3 months prior to the date of planned treatment, the investigator must verbally confirm with the subject that she continues to experience heavy menstrual bleeding, i.e., there has not been a clinically significant change in her menstrual status. It will be left to the investigator's judgment whether another monthly PBLAC diary is warranted to reconfirm eligibility prior to treatment.

12.3 Screening Visits

Before conducting any study-specific procedures, including modifications of medications, obtain written informed consent (See **Section 11.5, Informed Consent**) and register the patient in the EDC to obtain a unique patient identification number.

Site personnel may use their medical judgment to best organize patient eligibility testing in a way that optimizes data collection and minimizes invasive testing. Utilize the guidance in Sections 12.1 Schedule of Events and **Section 12.2 Validity Windows for Baseline Testing**.

The screening process may require more than one visit to accomplish all the screening requirements. Then final eligibility must be confirmed by the investigator prior to procedure initiation.

12.3.1 Suggested Order of Events:

1. Written informed consent
2. Determine if any SOC testing may be used
3. Demographic data
4. Medical and surgical history
5. Concomitant Medications / Treatments
6. Patient PBLAC training and testing
7. PBLAC diary and sanitary supply distribution (pads/etc.)
8. Urine pregnancy test (to rule out pregnancy prior to proceeding with invasive diagnostic testing)
9. Physical examination (to include height, weight and BMI)
10. Pap Smear
11. Endometrial biopsy
12. Ultrasound
13. Sonohysterography or hysteroscopy
14. Hematology/CBC
15. As needed, STD testing
16. Serum FSH
17. Menorrhagia Impact Questionnaire (MIQ)
18. Dysmenorrhea-related pain
19. If eligible, schedule procedure

12.3.2 Pictorial Blood Loss Assessment Chart

PBLAC data collection is the most important assessment in this study. It is the endpoint efficacy measure, it may be the most difficult criterion to meet with the requirement of a score of ≥150, and its

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administration may require more than one visit. Details on administrating PBLAC are provided in S**ection 13.11 PBLAC Diaries**.

12.3.3 Screen Failures

Candidates who sign an informed consent form and fail to meet the inclusion and/or exclusion `criteria or who terminate from the study prior to treatment initiation are defined as screen failures. Screen failures are excluded from participation in the study. In some cases, subjects may be rescreened (See **11.4 Rescreening**). If needed, obtain guidance from the Sponsor clinical staff to determine if a screen failed subject may be rescreened.

12.4 Procedure (Day 0) – Enrollment / Discharge

12.4.1 Procedure Visit Strategy

On the day of procedure, first complete the reassessment of the selection criteria. This will include urine pregnancy testing, vital signs, medication review, assessment for the presence of infection or STD. If the urine pregnancy test is positive, then the patient is a screen failure.

Ensure that all existing tests remain within the validity windows.

Once the final eligibility is confirmed, the patient is enrolled and may proceed to treatment.

Prior to administration of procedure meds, have the subject complete the pelvic pain NRS prior to the procedure as a baseline. Then the pelvic pain NRS will be assessed again at discharge and as part of the SOC 24-hour follow-up phone contact.

Perform the procedure using the anesthesia of choice (as appropriate) and in accordance with the IFU.

After the procedure, assess the patient for AEs, SAEs and UADEs, confirm/verify the patient's understanding of the PBLAC diary completion instructions (retrain if necessary) and issue PBLAC diary and sanitary supplies.

Schedule the SOC 24-hour follow-up phone contact and Week 2 post-treatment follow-up visit prior to discharging the subject.

12.4.2 Suggested Order of Events

1. Review eligibility criteria
2. Vital signs
3. Baseline pelvic pain NRS
4. Urine pregnancy test
5. Anesthesia
6. Minitouch treatment
7. Post-procedure pelvic pain NRS – at discharge
8. Assess adverse events
9. Confirm Patient's understanding of PBLAC completion, re-train if necessary (prior to discharge)
10. PBLAC diary distribution and sanitary supplies (prior to discharge)
11. Schedule the SOC 24-hour follow-up contact and Week 2 post-treatment follow-up visit

12.5 Standard of Care Contact After 24 hours

Per standard of care procedures, the patient is to be contacted at the standard of care 24 hour (18-48 hours) post-procedure. The following will be assessed:

1. Procedure-related Pelvic Pain NRS

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2. Concomitant Medications/treatments
3. Assessment of adverse events

12.6 Week 2 Visit (± 7 days)

Ensure that the visit is conducted within the visit windows. The patient will not be expected to provide a PBLAC diary. If a patient cannot attend a visit within window, then collect as much information as possible within window via phone, letter or email.

12.7 Follow-up Visits Conducted 3 and 6 Months (± 2 weeks) After Treatment

At these study visits, the patient will bring in her monthly PBLAC diaries. Review all of the diaries during the visit to ensure that the diaries are being completed correctly. Retrain the patient if necessary.

Ensure that the visit is conducted within the visit windows. If a patient cannot attend a visit within window, then collect as much information as possible within window via phone, letter or email.

12.8 Endpoint Visit at Month 12 (± 4 weeks)

This is the endpoint visit. Ensure that the visit is conducted within window and if a patient cannot attend a visit within window, then collect as much information as possible within window via phone, letter or email. Specifically, try to obtain the 12 Month PBLAC diary within window for all patients.

12.9 Durability Visits Conducted 24 and 36 Months (± 8 weeks) After Treatment

The 24 and 36-month visit may be conducted via phone, letter, email or in person as described in Section 12.1.

The 36-month visit is the final study visit. Complete both the 36-Month Visit and the Study Completion eCRFs.

12.10 Pre-Endpoint Termination Visit

If a patient terminates from the study prior to the 12-month endpoint visit, collect as much as possible of the testing below.

1. Serious Adverse Event collection
2. Concomitant Medications / Treatments
3. PBLAC diary collection
4. Menorrhagia Impact Questionnaire (MIQ)
5. Dysmenorrhea-related pain (NRS)
6. Patient Global Evaluation
7. Investigator Global Evaluation
8. Assessment of Adverse Events / Serious Adverse Events

12.11 Unscheduled Visits

Collect source documentation from unscheduled visits as required to support the assessment of AEs, SAEs and UADEs. Record these events in the appropriate upcoming eCRF visit module.

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13 STUDY PROCEDURES / EVALUATIONS

13.1 Prescreening

Since this is standard of care information, varying information may be available. Therefore, review existing testing to see if any may fit within the validity windows.

The following clinical information to review for eligibility in prescreening is a suggestion only. Look for:

- Female patient age 30 to 50 years, inclusive
- Excessive menstrual bleeding due to benign causes
- Ability to provide written informed consent

Eliminate candidates with any of the following (not an inclusive list):

- Pregnant
- Known/suspected uterine cancer or pre-malignant conditions of the endometrium
- Clinically significant or suspected adenomyosis
- Known clotting defects, bleeding disorders or conditions that would affect menstrual bleeding or menses in general
- Currently on medications that could thin the myometrial muscle, such as long-term steroid use (inhaler or nasal therapy for asthma or other pulmonary conditions are allowed)
- Currently on anticoagulants
- Previous medical/surgical treatments, or has other conditions, that could lead to anatomic/pathologic weakness or thinning of the myometrium (Classical caesarean section and transmural myomectomy are examples of such treatments that may interrupt the integrity of the uterine wall)
- Any general health condition which, in the opinion of the investigator, could represent an increased risk for the patient or limit the ability of the patient to complete study requirements.

13.2 Demographic Data and Medical History

Demographics are to be collected on all patients during screening, including age (based on day of consent), sex, race, and ethnicity. Height in centimeters (cm), body weight (kg, in indoor clothing but without shoes) and BMI will also be measured. BMI shall be calculated as kg/m2. The site should use the NIH website BMI calculator https://www.nhlbi.nih.gov/health/educational/lose_wt/BMI/bmi-m.htm. Alternatively, BMI can be calculated in EDC so long as height (cm) and weight (kg) are entered accordingly. Relevant specific medical history and current medical conditions will be captured.

Collect relevant medical diagnoses, specific medical history, surgical history and current medical conditions. In order to qualify, patients must have documented history or diagnosis of HMB, and therefore, source documents from non-participating institutions may need to be requested. History may also include failed or contraindication to medical therapy, subject-reported historical use of sanitary products consistent with HMB, menstrual cycles that interfere with normal daily activities (e.g., work, social/leisure) due to prolonged duration or heavy menstrual flow, date of subject's first perception of or when treatment was first sought for HMB, or assigned diagnosis code(s) consistent with HMB.

Other eligibility criteria potentially identified from medical history (not an inclusive list):

- Untreated/unevaluated cervical dysplasia, except cervical intraepithelial neoplasia I (CIN I)
- Previous endometrial ablation procedure
- Known/suspected abnormal uterine/pelvic anatomy or condition, such as frozen pelvis

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- Previous medical/surgical treatments, or has other conditions, that could lead to anatomic/pathologic weakness or thinning of the myometrium (Classical caesarean section and transmural myomectomy are examples of such treatments that may interrupt the integrity of the uterine wall)
- Known clotting defects or bleeding disorders
- Abdominal pelvic or gynecological malignancy

13.3 Physical Examination / Gynecological Exam

A physical exam will be performed according to the Schedule of Events (at Screening/Baseline), as well as when judged necessary by the investigator or designee. Physical exam will be conducted per SOC (pelvic exam) and will include a Pap smear (at baseline only). During the screening physical exam, consider the following criterion to detect clinically significant findings which are exclusionary:

> *Any general health condition which, in the opinion of the investigator, could represent an increased risk for the patient or affect the effectiveness of GEA treatment, or limit the ability of the patient to fully participate in the study*.

13.4 Endometrial Biopsy, Ultrasound, Sonohysterography, Hysteroscopy

Screening and gynecologic evaluations will be performed by a qualified and trained investigator and include endometrial biopsy, transvaginal ultrasound, sonohysterography or hysteroscopy to verify eligibility and prior to conducting the treatment procedure. Screening ultrasounds will be interpreted by experienced investigators using inclusion and exclusion criteria.

Record the reference uterine sounding depth measurement. Once these tests are completed, the patient must not undergo any other gynecological procedures prior to the Minitouch procedure.

13.5 Vital Signs

Vital signs including systolic blood pressure, diastolic blood pressure, temperature, respiratory rate, and pulse rate will be measured according to the Schedule of Events after at least 5 minutes at rest in the sitting or supine position.

13.6 Concomitant Medications

The use of concomitant medications is reviewed with the patient according to the Schedule of Events. Any changes in medication from the time of consent to the end of study should be recorded in the Concomitant Medications eCRF.

13.6.1 Screening and Follow-up

During screening, all medications should be captured, thereafter, any medication changes through the end of study should be recorded in the Concomitant Medications eCRF.

> Note that any intermittent (“PRN”) use of medication, or any new prescribed medication in follow-up may indicate the occurrence of, or a change to an ongoing Adverse Event.

13.6.2 Contraception

The patient must be on a reliable method of contraception for the duration of the study. Special attention should be paid to medication review of hormonal contraception since the patient must have been on said method for ≥ 3 months prior to the onset of the screening menstrual cycle used for PBLAC diary completion and must remain on the same hormonal regimen through the 12-month follow-up visit.

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Also, a subject may not begin hormonal contraception during the follow-up period if she were not on one at the time of screening.

13.7 Adverse Events

Serious adverse events (SAEs) and adverse events (AEs) are collected from the time of enrollment (on the day of the Minitouch procedure). Information on the collection and reporting of AEs and SAEs can be found in **Section 14 ADVERSE EVENT REPORTING.**

13.8 Complete Blood Count (CBC) and Serum FSH

Complete Blood Count (CBC) and Serum Follicle Stimulating Hormone (FSH) test results may be obtained from the patient medical records if the test was performed 6 months or fewer from the procedure date.

Conduct additional testing as needed to confirm eligibility criteria.

Premenopausal status is to be confirmed by FSH measurement ≤ 40 IU/L when the patient is ≥ 40 years old.

13.9 Urine Pregnancy Test

Patients will have urine pregnancy test at screening and urine dipstick pregnancy test at the Procedure Visit prior to treatment. Patients with a positive urine pregnancy test result must not be provided investigational treatment. If a patient becomes amenorrheic after the procedure, it will be left to the investigator's judgment whether to consider a pregnancy test to rule out a possible pregnancy for the cause of amenorrhea.

13.10 Menorrhagia Impact Questionnaire (MIQ)

Patients will be asked to assess their quality of life and impact of heavy menstrual bleeding (HMB) using a validated patient-reported outcome measurement. This questionnaire measures effects of HMB on limitations in social/leisure activities, physical activities, and ability to work.

The questionnaire will be completed during baseline and at each follow-up visit.

13.11 PBLAC Diaries

Patients will self-report their menstrual blood loss as measured by validated Pictorial Blood Loss Assessment Chart (PBLAC). The 12-month follow-up PBLAC score will comprise the primary endpoint data for this study.

13.11.1 PBLAC Training

During the site initiation visit (SIV) or as needed, the Sponsor or designee will train the authorized study staff to administer the PBLAC education to patients. The study staff will train candidates regarding proper PBLAC completion and assess the patient's understanding.

Conduct PBLAC training early in the screening process, preferably at the first screening visit. The subject will be provided with study materials including the PBLAC diary(ies), instructions and sanitary products. At the subsequent visit, score the PBLAC diary before resuming screening to be assured that the patient has completed it correctly and has a score of ≥ 150. Once the patient passes the PBLAC assessment, complete any remaining screening testing.

See **Section 11.4 Rescreening** for details regarding repeating PBLAC training or repeating PBLAC diary administration.

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13.11.2 Administering PBLAC Diaries

During Screening

If a patient has undergone a procedure (e.g., polyp removal, fibroid removal, IUD removal, etc) that could affect menstrual bleeding, the screening PBLAC may be administered after 30 days from the date of that procedure.

If a patient discontinued taking oral hormonal contraception, the screening PBLAC may be administered after a washout interval of at least 90 days from the last dose of the hormonal contraception.

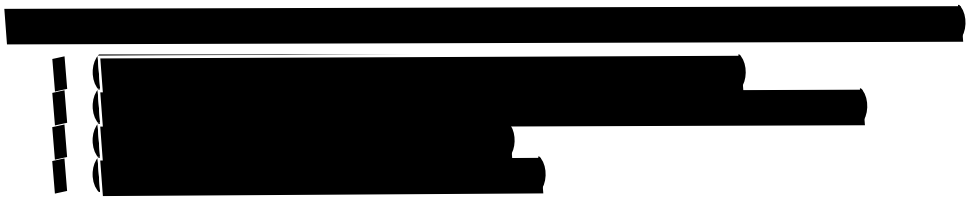
If a patient is currently on hormonal medication for heavy menstrual bleeding, the patient must discontinue the medication. The screening PBLAC may be administered after a washout interval of at least 90 days from the last dose of the hormonal medication.

During Follow-Up

PBLAC diaries will be distributed and collected through the 12-month follow-up (365 days or 1-year anniversary); accordingly, 13 PBLAC diaries are expected to be collected during the study follow-up. In between visits, participants should return their diaries (in person or by mail) every month upon completion. Electronic scans or photos of diaries are permitted to be submitted monthly, however, the original diaries must still be submitted to the site and retained in the study records as source documents.

At a minimum, the PBLAC diary will be reviewed with the patient at each follow-up visit, and any needed additional sanitary products provided. Confirmation of understanding and/or retraining patients on PBLAC diary completion throughout follow-up is encouraged.

13.11.3 Sanitary Products



The Sponsor will provide the sanitary product inventory for study staff to distribute to each patient. Patients are required to exclusively use the sanitary products provided at screening through the 12-month follow-up visit. Every effort should be made to ensure that all patients comply with this requirement.

13.12 Numerical Rating Scale (NRS)

13.12.1 NRS for Dysmenorrhea-related Pain

Patients will be asked to assess their dysmenorrhea-related pain using an 11-point scale with 0 on one end, representing no pain, and 10 on the other, representing the worst pain ever experienced.

13.12.2 NRS for Procedure-related Pelvic Pain

Patients will be asked to assess their pain level (pelvic pain) experienced at discharge and at the 24-hour contact on a 11-point scale with 0 on one end, representing no pain, and 10 on the other, representing the worst pain ever experienced.

13.13 Patient Global Evaluation

Each patient will be asked to report their satisfaction with the study treatment using a 5-point categorical scale: Very Satisfied, Satisfied, Not Sure, Dissatisfied, Very Dissatisfied.

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This will be assessed at all follow-up visits up, starting at the 3-month follow-up.

13.14 Investigator Global Evaluation

The investigator or designee will report their satisfaction with the patients' study treatment using a 5-point categorical scale: Very Satisfied, Satisfied, Not Sure, Dissatisfied, Very Dissatisfied.

13.15 Device-related Issues or Device Deficiency/Malfunction

A device-related issue or device deficiency/malfunction is a failure of the device to meet its performance specifications or otherwise perform as intended.

During device set-up, treatment administration and post-treatment, site personnel and/or the PI will be requested to inspect and identify any defective parts. The study Investigator (or designee) will keep documentation, notify the Sponsor and comply with Sponsor procedures for returned goods.

13.16 Minitouch Procedure

The Investigator is to confirm patient eligibility prior to initiating the procedure. The Minitouch procedure is to be performed after the PI and any other delegated investigator have undergone the necessary training. The PI/sub-investigators will perform the procedure in accordance with the IFU and this protocol. See **Section 12.4 Procedure (Day 0) – Enrollment / Discharge,** for guidance on the sequence of events for this visit.

13.16.1 Investigational Devices

Refer to **Section 18.3 Investigational Devices** for details.

13.16.2 Support

The research coordinator should be present during the procedures to ensure that the study data are collected. A Sponsor-designated technical support person may be present for the clinical procedure as support for the investigator.

13.16.3 Procedure Medications

The use and type of anesthesia is up to the discretion of the investigator and anesthesiologist. This may include, but is not limited to, general, local (e.g., paracervical block) and/or IV sedation. Pre-procedure prophylactic administration of over-the-counter NSAIDs and/or analgesics should also be considered for pain management.

Eligible patients will receive a single treatment, meaning the procedure is completed one time in one clinical setting. Single treatment includes four scenarios:

a. Analgesic Regimen (No Sedation or Anesthesia)
b. Sedation Regimen
c. Single Anesthesia Regimen[1]
d. Multiple Anesthesia Regimen

[1] Patient completes treatment with one anesthesia regimen. Intermittent pauses in between energy delivery will be allowed to manage patient pain and to allow for U-value to increase if it drops to less than 40 during procedure.

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Record all medications provided prior to, during and after the procedure. Determine if all prescribed pre- and post-procedure medications were taken. Inquire about the use of non-prescribed pain medication.

Medications will be documented in the EDC (Concomitant Medication eCRF).

14 ADVERSE EVENT REPORTING

14.1 Adverse Event Definitions

14.1.1 Adverse Event (AE):

An adverse event (AE) is any untoward medical occurrence in a study patient which does not necessarily have a causal relationship with the medical device. This includes any unfavorable and unintended sign (including an abnormal, clinically significant laboratory finding), symptom, or disease temporally associated with the use of a medical device, whether or not related to the medical device. It also includes any pre-existing condition that increases in intensity or severity or any new events after the patient had the procedure. (Also refer to Sections 14.1.5 and 14.1.6 for additional information.)

14.1.2 Serious Adverse Events (SAEs)

A serious adverse event is any untoward medical occurrence that results in one of the following:

- Led to death
- Led to serious deterioration in the health of the subject, that either resulted in
    - A life-threatening illness or injury, or
    - A permanent impairment of a body structure or a body function, or
    - In-patient hospitalization or prolongation, or
    - Medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function,
- Led to fetal distress, fetal death, congenital abnormality or birth defect
- Note: Planned hospitalization for a pre-existing condition or a procedure required by the protocol, without serious deterioration in health, is not considered a serious adverse event.

14.1.3 Anticipated Adverse Device Effects Associated with Endometrial Ablation

With all endometrial ablation procedures, serious injury or death can occur. The following adverse effects could occur or have been reported in other EA studies and may occur when the Minitouch System is used. The listing includes potential risks/effects associated with administration of anesthesia.

Table 14-1: Anticipated Adverse Device Effects of Endometrial Ablation
More Commonly Reported Device/Procedural and/or Post-Procedural Complications (occurs in 20 or more patients out of 100)

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- Cramping or pelvic pain
- Nausea and vomiting
- Vaginal bleeding or spotting
- Vaginal discharge and/or unpleasant vaginal smell or burning or other abnormal sensation

Other Common Possible Adverse Device Effects (occurs in 20 or less patients out of 100)

- Abdominal pain or bloating
- Adhesions
- Backache
- Cervical stenosis
- Chills
- Constipation
- Diarrhea
- Fever
- Headache
- Hematometra (collection of blood in the uterus)
- Lightheadedness or fainting
- Menometrorrhagia (abnormally heavy, prolonged and irregular uterine bleeding)
- Post-ablation tubal sterilization syndrome (PATSS)
- Skin rash and/or itching burning sensation
- Weakness, fatigue, sleepiness, lack of concentration, dizziness

Rare Adverse Device Effects (occurs in 5 or less patients out of 100)

- Agitation
- Air embolism (blood vessel blockage caused by an air bubble)
- Cardiac complications
- Cervical or vaginal laceration or tear
- Complications leading to serious injury or death
- Difficulty with defecation or micturition
- Dyspareunia (painful intercourse)
- Dysuria (painful urination)
- Endometritis or Endomyometritis (inflammation of the uterine tissue)
- Hemorrhage (excessive bleeding)
- Hydrosalpinx (blocked fallopian tubes filled with fluid)
- Infection or sepsis
- Pelvic inflammatory disease (PID)
- Pregnancy-related complications
- Tissue injury (thermal, mechanical or electrical)
- Uterine necrosis (uterine tissue death due to lack of blood supply)

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- Uterine perforation (hole in the uterus)
- Vulvar pruritis (itchiness of the vulva)

14.1.4 Unanticipated Adverse Device Effects (UADEs)

Any serious adverse effect on health or safety, 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 application; or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of patients per 21 CFR 812.3 and ISO 14155.

14.1.5 Not Adverse Events

- **Pre-existing Conditions:** Any condition that is recorded in medical records and diagnosed prior to the Minitouch procedure, is considered a pre-existing condition. This condition is not considered an adverse event unless there is a clinically significant worsening of that condition in terms of nature, severity, or degree of incidence. For example, if a patient experiences HMB prior to procedure [e.g., PBLAC score = 300] and continues to experience HMB post-procedure [e.g., PBLAC score = 150 or ≤ 300], this is a pre-existing condition and should not be reported as an adverse event in the study).
- **Device Deficiencies or Malfunctions**: An undesirable device technical event is not an adverse event. However, if a device deficiency or malfunction leads to a medically undesirable situation or an adverse device effect, then that event must be reported on an Adverse Event Form.
- **Lack of Effectiveness:** Lack of improvement of symptoms is not considered an adverse event.

14.1.6 Adverse Events that do not require reporting to Sponsor

For purposes of the trial, events that are typically expected to occur in and/or are associated with standard of care endometrial ablation therapies are not required to be reported unless they occur with greater severity or intensity than anticipated. Examples of these commonly occurring anticipated post-procedural events include:

- Nausea and vomiting (usually with administration of anesthesia)
- Post-operative pelvic or uterine cramping
- Vaginal discharge (Note: Vaginal discharge usually happens during the first few days following treatment and may last as long as several weeks. It is generally described as bloody during the first few days, a mixture of blood and fluid for another week, then followed by a watery discharge that can be substantial at times. This is an anticipated symptom of the treatment and is not considered an adverse event unless the vaginal discharge suggests infection.)
- Vaginal bleeding/spotting

Note: This listing of events is intended to provide guidance to Investigators for the purpose of adverse event reporting. The investigator should utilize his/her own clinical judgment in evaluating adverse experiences, and may decide that the above events should be reported as adverse events based on site IRB/EC reporting requirements or the subject's clinical condition.

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14.2 Recording Adverse Events

14.2.1 Adverse Event Evaluation and Categorization

All AEs/ADEs will be assessed by the Investigator. Adverse events and Adverse Device Effects will be classified as serious or non-serious. Adverse Events are also qualified by intensity (severity), causality (relatedness), and expectedness.

14.2.2 Intensity (Severity)

- **Mild**: Mild or transient discomfort, without limitation or normal daily activities; no medical intervention or corrective treatment required
- **Moderate**: Mild to moderate limitation of normal daily activities; minimal medical intervention or corrective treatment required
- **Severe**: Marked limitation of normal daily activities; medical intervention and corrective treatment required; possible hospitalization.

Prior to analysis, all adverse events (AEs) will be coded using the Medical Dictionary for Regulatory Activities (MedDRA). Based on these coded terms, treatment emergent AEs will be summarized by treatment period, by severity, relation to procedure and relation to device.

14.2.3 Other Adverse Events

The Investigator will monitor the occurrence of adverse events for each Patient during the course of the study. All AEs will be listed on the adverse event case report forms. All pre-existing medical conditions and baseline signs and symptoms will be recorded on baseline case report forms for medical history and signs and symptoms.

Adverse events will be monitored until they are adequately resolved or explained.

14.2.4 Determination of the Relationship (Causality)

The Investigator, on the basis of his or her clinical judgment, should determine whether there is a reasonable possibility the investigational device or procedure caused or contributed to the event. Guidelines to assess AE/SAE/UADE are provided below:

Unrelated: The adverse event is determined to be solely caused by the underlying disease, disorder or condition of the patient, or attributable solely to other extraneous causes (unrelated to the device, device malfunction, or the procedure).

Possibly related: The adverse event has onset within a clinically relevant temporal relationship to exposure to the device or procedure and is plausibly at least partially caused by or aggravated by the use of the device, device malfunction, or the procedure. It must also meet one of the following criteria: (1) follows a known or easily foreseen pattern of response to device use or procedure and (2) is not fully attributable to the underlying disease, disorder or condition of the patient, or attributable to other extraneous causes.

Probably related: The adverse event has onset within a clinically relevant temporal relationship to exposure to the device or procedure and is more likely than not to be at least partially caused by or aggravated by the use of the device, device malfunction, or the procedure. It must also meet both of the following criteria: (1) follows a known or easily foreseen pattern of response to device use or procedure; and (2) is not fully attributable to the underlying disease, disorder or condition of the

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patient, or attributable to other extraneous causes. In addition, if the adverse effect is reversible upon reoperation or device exchange, and such a procedure is done, the effect disappears or lessens in severity within the expected time interval.

Definitely related: The adverse event is clearly caused by the use of the device, device malfunction, or the procedure. It must meet all the following criteria: (1) has a clear temporal relationship between device exposure and onset of the event; (2) follows a known pattern of response to device use or procedure; and (3) is not reasonably attributable to the underlying disease, disorder or condition of the patient, or attributable to other extraneous causes. In addition, if the adverse effect is reversible upon reoperation or device exchange, and such a procedure is done, the effect disappears or lessens in severity within the expected time interval.

14.3 Reporting Requirements for SAEs or UADEs

It is the responsibility of the Principal Investigator to report SAEs or UADEs to the Sponsor within 24 hours of becoming aware of the SAE or UADE. Notification should occur via completion of the eCRFs. Reporting of the event to applicable regulatory bodies should occur per the established reporting criteria. For UADE reports, investigators are required to submit a report of a UADE to the Sponsor and the reviewing IRB as soon as possible, but in no event later than 10 working days after the investigator first learns of the event (§ 812.150(a)(1)). Sponsors must immediately conduct an evaluation of a UADE and must report the results of the evaluation to FDA, all reviewing IRBs, and participating investigators within 10 working days after the Sponsor first receives notice of the effect (§§ 812.46(b), 812.150(b)(1)).

14.4 Medical Treatment for AEs, SAEs and UADEs

Medical treatment for events occurring during and following the Minitouch treatment will be at the discretion of the investigator.

15 CLINICAL EVENTS COMMITTEE

A Clinical Events Committee (CEC) will be comprised of qualified multi-disciplinary individuals who are not investigators in the trial or a clinician at a trial site and who are independent of the Sponsor. The CEC is responsible for adjudicating the safety aspects of this study based on the charter . The composition, guiding policies, operating procedures and stopping rules (if safety concerns arise during their review of the study data) that govern the CEC will be described in a separate CEC Charter developed by the CEC members.

16 RISKS AND BENEFITS

16.1 Potential Risks

The potential risks and benefits of participation in this study are identified in the ICF and are to be explained to the patient prior to participating in the study. The potential risks are also summarized in the IFU. It is not anticipated that there will be any additional risks to the patient with the use of the Minitouch System that are different than those associated with current second generation GEA procedures.

16.1.1 Procedure Risks

Potential adverse events that may be associated with a second-generation GEA procedure include but are not limited to events listed in **Section 14.1.3 Anticipated Adverse Device Effects Associated with Endometrial Ablation**. With all endometrial ablation procedures, serious injury or death can occur.

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16.2 Risk Management Procedures

For several decades, endometrial ablation has been available as a treatment for HMB and subsequently, the potential risks associated with the therapy are well-known. While no new risks have been identified regarding the Minitouch System for the proposed indications for use, the following measures have been or will be taken to mitigate risk for all patients participating in the EASE Clinical Trial:

- Well-defined clinical protocol to enroll appropriate patients in the study. Specifically, eligibility criteria have been selected that exclude patients who are at higher risk for experiencing an anticipated adverse event in order to reduce the risks to patients who participate in this study.
- Close monitoring of patients will take place during the investigational procedure and throughout the study, and adverse events will be recorded in the patients' charts and on eCRFs.
- Engineering testing has been performed on the Minitouch System to help mitigate risks to the patients due to product failure.
- Investigators in this study will be selected based on their experience and competency to perform endometrial ablation and perform the research.
- Investigational device training will be conducted at each initiated study center and appropriate training records will be maintained.
- Ongoing monitoring of study data and results, including the use of an independent oversight committee: Clinical Events Committee.
- As appropriate, Sponsor or designee will be onsite to support Minitouch procedures performed under the EASE Clinical Trial protocol.

16.3 Potential Benefits

The patient may experience clinically significant relief from their menorrhagia or dysmenorrhea symptoms. There are no guaranteed additional benefits from participation in this study. Information gained from the conduct of this study may be of no benefit to others with the same medical condition.

17 STATISTICAL METHODS AND CONSIDERATIONS

The Statistical Analysis Plan (SAP) for the study will describe the data sets to be analyzed, the methods of analysis, and the specific analyses to be conducted in support of the study's primary and secondary endpoints. Those key elements are outlined below.

17.1 Analysis Cohorts

Statistical analysis will use definitions listed below.

17.1.1 Intent-to-Treat (ITT) Cohort

All patients who are enrolled in the study (enrollment defined as patients who met all study eligibility criteria and in whom the procedure is initiated) are included in the Intent-to-Treat (ITT) cohort.

The ITT cohort will be used for the following analyses (as defined in Section 9.1 & 9.2):

- Primary safety and effectiveness analyses at 12-month follow-up visits.
- Safety & effectiveness analyses at 24, and 36-month follow-up visits.

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17.1.2 Per Protocol (PP) Cohort

This cohort consists of all ITT Patients who are considered treatable patients, completed ablation therapy and attended 12-month follow-up visit.

The PP cohort will be used for the following analyses:

- Safety and efficacy outcome measures at 12, 24, and 36-month follow-up visits
- Secondary Analyses to assess amenorrhea rates, improvement of quality of life, evaluate patient and user (investigator) satisfaction.
- Subgroup Analyses
- Exploratory Analyses

17.2 Analysis of Primary Efficacy Endpoint at 12-month

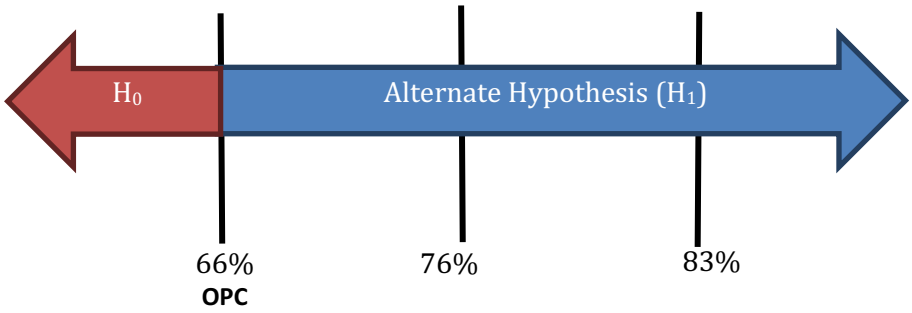
The primary efficacy endpoint is binary (success/failure). Success is defined as PBLAC score of $\leq$75 at the 12-month follow-up assessment without incidence of additional interventions or treatments for bleeding prior to the 12-month follow-up visit. The proposed study's primary hypothesis is:

Null Hypothesis (H_0) = $p_{minitouch} \leq$ OPC

Alternate Hypothesis (H_1) = $p_{minitouch}$ > OPC

where $p_{minitouch}$ is the Minitouch Endometrial Ablation System success rate and OPC is 66% which is the FDA identified objective performance criterion (OPC) for global endometrial ablation (GEA) devices.

The exact binomial test will be conducted to compare the investigational device success rate to OPC minimum success rate for effectiveness. To achieve study success the measured success rate should exceed the 66% OPC.



ITT with imputation will be utilized to test the primary hypothesis, such that all missing data are failures for the primary endpoint. The following imputation techniques will be conducted for sensitivity analysis:

- Multiple Imputation (MI) using fully conditional specification (FCS) method, in which logistic regression is used to predict whether the missing value is likely to be a success or failure. The number of imputations will depend on the fraction of missing information.
- Tipping point, in which the numbers of successes or failures amongst missing data necessary to meet the primary endpoint hypothesis are determined.

Fisher-Freeman-Halton test will be conducted to compare the success rates between investigational sites. Results will also be stratified and compared across relevant baseline characteristics including demographics.

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17.2.1 Study Power

Utilizing a minimum effectiveness rate of 66% (OPC), an expected success rate of approximately 78% for Minitouch, and a one-sided alpha of 0.025, the study sample size required to obtain at least 80% power is 114 Patients. Assuming a dropout rate of approximately 10% at 12 months, the required enrolled sample size is determined to be 126 Patients.

The 78% investigational device success rate is derived from other GEA studies recently conducted and published. For sample size calculation, Minerva utilized an expected success rate of 78% (Laberge et al. J Minim Invasive Gynecol 2015;7:1169-77) and Aegea utilized an expected success rate of 76% (Levie MD, Chudnoff SG. J Minim Invasive Gynecol 2018; S1553-4650).

Multiple scenarios were used to calculate the sample size. Statistical Analysis Software (SAS) POWER procedure Z test for binomial proportion was utilized with the following fixed scenario elements: normal approximation method, 66% null proportion, 0.025 one-sided alpha, 80% nominal power, and null variance estimate.

17.3 Predictive Analysis 12, 24, and 36-month Efficacy Outcome

Univariate analyses will be conducted using analysis of covariance (ANCOVA) to evaluate the effect of demographics, gynecologic history, procedure-related characteristics and diagnosis of COVID-19 or COVID-19 vaccination status on PBLAC score post procedure, while controlling for baseline PBLAC scores.

17.4 Analysis of Primary Safety Endpoint at 12-month

The primary safety endpoint is the rate of device or procedure-related serious adverse events. It will be evaluated 12 months post-procedure.

17.5 Analysis of All Safety Outcome

All safety events reported in the study will be tabulated. The study's safety analysis focuses on specific device- or procedure-related safety events listed in Section 13. Intra-operative and post-operative serious adverse event (SAE) and overall rates of AEs (number and percentage with 95% confidence interval) will be reported.

The need for medical or surgical intervention to treat abnormal bleeding following the ablation procedure will also be reported.

17.6 Analysis of Secondary Endpoints

No hypothesis will be tested with regards to secondary endpoints. Secondary endpoints will be reported using descriptive statistics along with sample size. Measures of central tendency (mean, median, and mode) and of variation (range and standard deviation) for continuous variables. Measures of frequency (count and proportions) for categorical variables.

17.7 Subgroup Analyses

The following subgroup analyses will be performed for both treatment success (reduction of menstrual blood loss) and amenorrhea rates for the following timepoints during study follow-up: 12, 24, and 36-months post procedure.

- Age (<40 years vs. >40 years)
- Active bleeding at the time of the operative visit (Yes vs. No)

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- Transverse or low segment C-section (Yes vs. No)
- Anesthesia regimen (None vs. Sedation vs. Local Anesthesia vs. General Anesthesia vs. Multiple)
- Use environment (Office vs. Non-office)
- Uterine sound depth (6-9.0cm vs. 9.1-12cm and 6-8.0cm vs. 8.1-10cm vs. 10.1-12cm)
- Presence of anemia at Baseline defined as hemoglobin < 12 g/dL (Yes vs. No)
- Presence of fibroids at Baseline (Yes vs. No)
- Presence of ovarian cysts at Baseline (Yes vs. No)
- Presence of any intrauterine pathology at baseline (Yes vs. No)
- Contraceptive use (hormonal method vs. non-hormonal method)
- COVID-19 Status (diagnosed with COVID-19 vs. did not have COVID-19)
- COVID-19 Vaccination Status (vaccinated vs. not vaccinated)

The study is not powered for these subgroups, and therefore, there will be no hypothesis testing for the primary endpoints within these groups. These analyses will be done using the PP population.

17.8 Exploratory Analyses

The following exploratory analyses will be performed:

- Mean percent change in PBLAC score from Baseline per PGE Patient Satisfaction Category Question 1 (Very Satisfied, Satisfied, Not Sure, Dissatisfied, Very Dissatisfied)
- Average change in quantity of sanitary products used
- Relation between Baseline PBLAC score and treatment success or failure
- Change in pain medication use for dysmenorrhea from baseline to 12 months

Additional exploratory analyses may be performed.

18 STUDY RECORD MANAGEMENT

For the study duration the investigator will maintain complete and accurate documentation, including but not limited to, medical records, study progress records, source worksheets, laboratory reports, eCRFs, signed and dated informed consent forms, all relevant correspondence (e.g., with the IRB, Sponsor personnel/representatives, and other regulatory agencies), the protocol, and documentation for each deviation from the protocol, records of receipt, use, or disposition of each device, record of the exposure to the investigational device, adverse event records, information regarding patient discontinuation or completion of the study, any other supporting data, and any other records that FDA requires to be maintained by regulation or by specific requirement.

18.1 Source Documentation

Regulations require that an investigator maintain information in the patient's medical records which can corroborate data collected on study eCRFs. In order to comply with these regulatory requirements, at a minimum, the following information should be recorded in the patient's study records:

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- Medical history and physical condition of the patient prior to participation in the study sufficient to verify inclusion/exclusion criteria.
- Dated and signed study progress or clinic notes on the day of entry into the study referencing the protocol number, site, unique patient ID number assigned, and a statement that informed consent was obtained.
- Dated and signed notes from each patient's visit.
- All collected AE, SAE, UADEs and their resolution, including supporting documents such as discharge summaries and diagnostic test results.
- Patient medical condition upon completion of or withdrawal from the study.

Data recorded in the patient's medical records will be reviewed for verification of agreement with critical data on the eCRFs as specified in the monitoring plan. The investigator/study personnel will allow the Sponsor (or designee) and appropriate regulatory authorities access to these records. If a non-study physician, at a non-study institution, sees a study patient regarding a study requirement or an AE, SAE or UADE, then a copy of the medical record will be copied and placed in the patient's study records and made available for review.

18.2 Data Collection and Electronic Case Report Form Completion

All study data will be collected and recorded by authorized study personnel on the required electronic Case Report Forms (eCRFs). Identifiable patient information will not be recorded in the eCRFs. Patients will be assigned unique study identification numbers. Only study site personnel directly involved with study and Sponsor, monitors or designee(s) will have access to the documentation that links the study identification numbers to identifying patient information.

The eCRFs will capture information relevant to the patients' clinical presentation, medical history, laboratory values, and results of clinical and/or gynecological testing. Follow-up clinical data will include laboratory assessments, current medications, physician office visits, hospitalizations, and/or adverse events that have occurred since study enrollment or from the prior visit.

The site PI will be required to sign and date the completed eCRFs on the appropriate page(s) to verify that he/she has reviewed the recorded data, and assures its accuracy and completeness.

18.3 Investigational Devices

18.3.1 Labeling

The Sponsor will label all investigational devices in accordance with FDA regulations per 21CFR 812.5.

18.3.2 Ordering, Receiving and Storing Investigational Device

The Sponsor will ship Investigational devices to a clinical site once the requirements for site activation and authorization to enroll are met.

Components of the investigational device system will be shipped to each investigational site with a packing slip. The packing slips will be verified to ensure that they reflect the correct shipping quantities and will be signed and dated by the study personnel upon receipt of the devices. A copy of the signed packing slip should be provided to the Sponsor or designee.

Investigational devices shall be stored in a secure area. The PI or an authorized designee will be responsible for maintaining control of and verifying each device's disposition.

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18.3.3 Investigational Device Accountability

The Investigator shall maintain adequate records of the receipt, use, and disposition of the Investigational Device.

Investigational devices will only be used with this clinical investigation. The principal investigator or an authorized designee shall keep device accountability log tracking documenting the receipt, use, return and disposal of the investigational devices, which shall include:

a) the date of receipt and the signature of the individual who received the product(s),

b) identification of each investigational device (batch number/serial number or unique code),

c) the expiry date, if applicable,

d) the date or dates of use,

e) unique patient identification number,

f) date when the investigational device was returned (for any reason), and

g) the date of return of unused, expired or malfunctioning investigational devices, if applicable.

This log must be maintained at each investigational site and must be filed in the regulatory binder. At the end of enrollment, Sponsor or designee shall ensure that documentation of the final reconciliation of all devices is signed or initialed by the PI or authorized designee.

18.3.4 Device Disposal or Return

Devices are to be disposed utilizing the study site's specific biohazard procedures unless return is required or requested by the Sponsor.

Devices that did not work as expected (device deficiency or malfunction) or are involved with an adverse event during treatment may be returned. If a Sponsor representative is present, work with them to complete the device return. If not, then, please contact the Sponsor clinical staff as soon as possible to discuss the return of products. The Sponsor will provide instructions for biohazard device return. Return of these devices will be captured on the device accountability log.

A Sponsor representative or designee will collect all unused devices remaining at the end of the enrollment period.

18.4 Data Management and Processing

Overall data management will be the responsibility of the study Sponsor or designee. All data will be managed in a 21 CFR Part 11-compliant database. Data edit checks will be performed and the study sites will be queried as needed to ensure completeness and accuracy of study data.

All above-mentioned tasks will be performed according to the Data Management Plan and Sponsor or CRO SOPs. Audits may be performed for quality assurance of procedures and data handling.

19 TRAINING

19.1 Site Training

The investigator should have adequate resources and time to conduct the study properly and should have adequate number of qualified and trained staff to assist with conduct of the study. The investigator shall delegate tasks and responsibilities only to other investigational site personnel qualified by education, training and experience to perform delegated tasks. The investigator shall have direct oversight of all

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delegation activities and shall document delegation of responsibilities. The investigator is responsible for ensuring all delegated staff has been properly trained on the protocol and their assigned study responsibilities. A delegation log identifying all delegated duties and the individual to whom they have been delegated will be maintained at the investigational site and approved by the site principal investigator.

19.2 Device Training

Investigators responsible for treating subjects with the Minitouch will receive sufficient training to ensure competence in the execution of all aspects of the procedure. Training may include hands-on experience with demonstration videos and didactic presentations. Training will also include extensive review of the Instructions for Use (IFU). Training for first use will be conducted before the first cases, and subsequent cases preceded by refresher training as necessary.

20 MONITORING

20.1 Site Monitoring Procedures

All study monitoring activities will be managed and performed by the Sponsor or designee monitors. eCRFs will be source-document verified according to the monitoring plan. The extent, nature, and frequency of on-site visits will be based on considerations such as study objectives and/or endpoints, study design and complexity, and enrollment rate. These tasks will be performed according to relevant SOPs and the study monitoring plan. The monitoring plan will describe in detail who will conduct the monitoring and at what frequency, and distribution of monitoring reports. It will focus on preventing or mitigating non-compliance and risks to critical data and processes.

At regular intervals during the study, the Sponsor study monitors will contact the study sites via onsite and/or remote visits, telephone calls, emails and letters in order to review the study progress and eCRF completion and to address any concerns or questions regarding study conduct. The number of monitoring visits and their duration will be conducted according to the monitoring plan. By verifying compliance, these activities will ensure:

- The study is conducted in accordance with the study protocol, relevant Good Clinical Practice (GCP) and International Conference on Harmonization (ICH) guidelines, as well as in conjunction with 21 CFR Part 812, 50, 54, 56 and ISO 14155; Protection of Human Patients (Informed Consent) (21 CFR Part 50), Financial Disclosure by Clinical Investigators (21 CFR Part 54), Institutional Review Boards (21 CFR Part 56), Investigational Device Exemptions (21 CFR Part 812), the Declaration of Helsinki, the privacy requirements of the Health Information Portability and Accountability Act (HIPAA);
- Adequate protection of the rights and safety of the informed patients involved in the study by thoroughly providing accurate and complete data; and
- Quality and integrity of the data.

The frequency and scope of periodic site visits will be determined according to the monitoring plan, but at a minimum, shall occur at least once per year. Monitoring activities may include: review of the informed consent process and research authorization confirmation, regulatory document review, overall investigational plan adherence, GCP/ICH compliance, facility assessment, study staff assessment and additional study related functions that contribute to the safety of study Patients and the integrity of study data.

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Investigators must provide adequate time and resources to the study and will be available to the study monitor and/or designee via telephone, and in person during site visits. The Investigator will also provide the study monitor with a suitable working environment for review of study-related documents.

20.2 Compliance

20.2.1 Site Compliance

The study at the investigational site may be subject to an audit by the Sponsor or its designees for quality assurance purposes, as well as inspection by appropriate regulatory authorities.

In the event that an Investigator is contacted by a Regulatory Agency in relation to this study, the Investigator shall notify the study Sponsor immediately. The Investigator shall permit authorized representatives from appropriate regulatory authorities, at reasonable times and in a reasonable manner, to:

- Enter and inspect any establishment where the device is held or records relating to the investigational device are kept, inspect and copy records relating to the investigational device use.
- Inspect and copy records that identify Patients upon notice that the Regulatory Agency has reason to suspect that adequate informed consent was not obtained, or that reports required to be submitted by the Investigator to the Sponsor or IRB have not been submitted or are incomplete, inaccurate, false, or misleading.

The Investigator must provide the Sponsor with copies of all correspondence that may affect the review of the current clinical investigation (e.g., Form FDA 483, Inspectional Observations, and Warning Letters). The study Sponsor may provide any needed assistance in responding to regulatory audits.

20.2.2 Protocol Deviations

All protocol deviations will be classified as major or minor and documented and discussed in the Clinical Study Report.

A deviation is defined as any departure from clinical study requirements, including those cited within Good Clinical Practice (GCP) guidelines. Protocol deviations that affect the rights, safety, or welfare of human Patients must be reported to the study Sponsor as soon as possible from the occurrence of the deviation.

Major protocol deviations are defined as any protocol deviation that affects the soundness of the data or a Patient's rights. A major protocol deviation is non-compliance with the approved protocol and trial requirements that may impact patient safety, affect the integrity of the data and/or affect the patient's willingness to participate in the study.

Examples may include:

- Failure to meet all entry criteria;
- Non-compliant with device treatment regimen

A **minor** protocol deviation is non-compliance with the approved protocol and a trial requirement that does not impact Patient safety, compromise the integrity of the data and/or affect the Patient's willingness to participate in the study.

Protocol deviations must be reported to the IRB per the Institutional Review Board's reporting requirements. The occurrence of protocol deviations will be monitored by the study Sponsor and

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designee for evaluation of Investigator compliance to the study protocol, GCP guidelines, and regulatory requirements. Protocol deviations will be reviewed and evaluated by the study Sponsor or designee on an ongoing basis in accordance with the Protocol Deviation Management Plan, as applicable.

21 QUALITY CONTROL AND ASSURANCE

MicroCube or designee, a regulatory authority, or an IRB representative may visit the study site at any time during the study or after completion of the study to perform audits or inspections. The purpose of these audits or inspections is to examine systematically and independently all study-related activities and documents to determine whether they were conducted in accordance to the protocol, GCP, and any other applicable regulatory requirements. Investigators should contact the Sponsor immediately if contacted by a regulatory agency about an inspection at their site.

21.1 Selection of Sites and Investigators

Site selection and qualification may be conducted by visits to the site in which the many aspects of the study and investigators obligations are discussed. The Sponsor will ascertain the suitability of the investigator to conduct the study according to applicable guidelines and regulations. The protocol or synopsis, study objectives, efficacy and safety variables and study procedures will be reviewed.

The Sponsor will verify the investigator's understanding of roles and responsibilities via the review of the obligations set forth by the statement of the investigator (investigator agreement). Discussion of previous clinical experience, expertise in therapeutic areas, education and training qualifications (i.e., board certification in Obstetrics & Gynecology or equivalent), facility functions and staff resourcing and capabilities, and adequate pool of potential subjects from which to recruit will be reviewed to determine if the investigator and site are qualified to conduct the study.

21.2 Financial Disclosure

All Investigators must provide the Sponsor with documentation of financial interest related to MicroCube. Investigators must complete and provide Financial Disclosure in compliance with 21CFR 812.43 (c) (5) to the Sponsor during the approval process of the site and maintain this documentation throughout the study and for 1 year following completion of the study.

21.3 Institutional Review Board Protocol and Informed Consent Approvals

A sample ICF will be provided for the study investigator(s) to prepare for use at his/her site prior to participation in the study. The written ICFs should be prepared in the language(s) of the potential patient population. The ICFs that are used should be in accordance with the current guidelines as outlined by the 21CFR Part 50, Good Clinical Practices (GCP) guidelines.

The study Sponsor and reviewing IRB must first approve the language and the content within the Informed Consent form that is to be used by each study site. A copy of the proposed ICF, other written patient information and any proposed advertising material must be submitted to the IRB for written approval. A copy of the written IRB approval of the protocol and Informed Consent form must be received by the study Sponsor before recruitment and enrollment of patients into the study. The written approval must identify the study, protocol version, and the date of approval. The Investigational site must submit to and, where necessary, obtain approval from, the IRB for all subsequent protocol amendments and changes to the ICF prior to implementation.

The Investigator will be responsible for obtaining annual IRB approval and renewal throughout the duration of the study. The Investigator and site personnel must forward copies to the Sponsor of all

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required correspondence with the IRB, including the annual and continuing review reports and IRB continuance of approval. Copies of such correspondence should be filed in the site study files. Additionally, the investigator will provide an IRB membership list or assurance number to the Sponsor annually.

21.4 Protocol Amendments

This protocol will only be altered by written amendments from the study Sponsor. All significant protocol changes must receive written approval from appropriate Sponsor personnel, FDA (as appropriate) and from the IRB prior to implementation at the study site. Upon IRB approval, the protocol amendment(s) will be distributed to all site study personnel and training will be performed as appropriate.

21.5 Confidentiality

All information and data sent to Sponsor, and its authorized representatives, concerning patients or their participation in this study will be considered confidential. All data used in the analysis and reporting of this evaluation will be used in a manner without identifiable reference to the patient.

21.6 Study Administration

21.6.1 Pre-Study Documentation Requirements

Prior to initiation of screening and recruitment activities at any clinical site, the following documents must be provided to the Sponsor:

- A signed and dated Investigator Agreement
- A copy of the IRB approval letter of the protocol, Informed Consent and subject-facing documents/materials (e.g., questionnaires, PBLAC diary, etc.)
- A copy of the IRB approved Informed Consent Form
- Copy(ies) of the current signed and dated Curriculum Vitae of the Investigator (PI) and sub-investigators (Sub-I)
- A signed and dated Financial Disclosure Form
- Approval of contract and budget
- Copy(ies) of the current medical license(s) of the Investigator (PI) and sub-investigators (Sub-I)

21.6.2 General Investigator Responsibilities

In order to ensure that the protocol is conducted in compliance to applicable regulations, each site Investigator must:

- Conduct the study in accordance with the current revision of the regulations and guidelines of FDA (Protection of Human Patients (Informed Consent) (21 CFR Part 50), Financial Disclosure by Clinical Investigators (21 CFR Part 54), Institutional Review Boards (21 CFR Part 56), Investigational Device Exemptions [(21 CFR Part 812), the Declaration of Helsinki, the privacy requirements of the Health Information Portability and Accountability Act (HIPAA)], ICH Good Clinical Practice and ISO 14155.
- Assure that the study is not commenced until IRB approval has been obtained.
- Complete all study related documents promptly.

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- Agree to participate in an appropriate training program prior to first patient enrolled and as required by the Sponsor throughout the conduct of the study.
- Sign and adhere to the Investigator Agreement / Financial Disclosure Form.
- Assure that informed consent is obtained from each patient using the IRB-approved ICF. Informed consent must be obtained before conducting any study-specific tests or procedures (including activities to determine patient eligibility for the study) and without any coercion of or undue influence of patients to participate.
- Ensure adverse events are reported within the guidelines provided in this protocol.
- Provide all required data and agree to source document verification of study data with patient's medical records. Allow study Sponsor staff and its authorized representatives to inspect and copy any documents pertaining to this clinical study.
- Adhere to any institutional clinical care guidelines or protocols.
- Comply with all required elements of this protocol (e.g., perform testing and follow-up as specified, especially during personnel transitions).

21.7 Record Retention

21.7.1 Health Insurance Portability and Accountability Act of 1996

The Investigator agrees to comply with all applicable federal, state, and local laws and regulations relating to the privacy of patients' health information, including, but not limited to, the Standards for Individually Identifiable Health Information, 45 CFR Parts 160 and 164 (the Health Insurance Portability and Accountability Act of 1996 privacy regulation). The Investigator shall ensure that study patients authorize the use and disclosure of protected health information in accordance with the privacy regulations of the Health Insurance Portability and Accountability Act.

The Investigator agrees to maintain all essential study documents and source documentation, in original format, that support the data collected on the study patients in compliance with the ICH/GCP guidelines (the Investigator's File, including signed Informed Consent forms and patient-related materials) in a location that is secure and to which access can be gained if required.

Documents must be retained for at least two years after (1) study completion and FDA or other regulatory marketing approval, or (2) the study has been terminated by the Sponsor. These documents will be retained for a longer period of time by agreement with the Sponsor or in compliance with other site-specific or local regulatory requirements. When these documents no longer need to be maintained, it is the study Sponsor's responsibility to inform the Investigator. The Investigator will take measures to ensure that these essential documents are not accidentally damaged or destroyed. If, for any reason, the Investigator withdraws responsibility for maintaining these essential documents, the Sponsor must be notified prior to any transfer of responsibility. Custody must be transferred to an individual who will assume responsibility. The Sponsor must receive written notification of this custodial change and will then notify FDA.

21.7.2 Criteria for Suspending/Terminating a Study Center

If Sponsor, Investigator, or officials from regulatory agencies discover conditions arising during the study that indicate the study should be halted or that the study site should be closed, this action may be taken after appropriate consultation between Sponsor and Investigator. If the study is prematurely terminated

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or suspended, the Principal Investigator will promptly inform the IRB and provide reason(s) for the termination or suspension. Conditions that may warrant termination of the study include, but are not limited to:

- Discovery of an unexpected, serious, or unacceptable risk to potential subjects or to the Patients already enrolled in the study.
- Submission of knowingly false information from the research facility to Sponsor, study monitor, or regulatory agencies.
- Failure of the Investigator to comply with GCP (e.g., ICH guidelines, regulatory agency guidelines)
- Insufficient adherence to protocol requirements or unacceptable high rate of missing, erroneous, or improperly collected data.
- A decision from Sponsor to suspend or discontinue testing, evaluation or development of the product.
- Failure of the Investigator to enroll patients into the study at an acceptable rate.

Subjects whose participation is prematurely discontinued as a result of trial termination or suspension should be followed in accordance with the standard of care for those that have undergone endometrial ablation.

21.8 Publication Policy

The data and results from the study are the sole property of the Sponsor. The Sponsor retains all rights to publish its data. The clinical investigation will be registered, and the description and results of the clinical investigation will also be made available in a publicly accessible database such as https://ClinicalTrials.gov.

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11. Summary of Safety and Effectiveness Data for Minerva™ Endometrial Ablation System; Premarket Approval Application (PMA) Number: P140013; Date of FDA Notice of Approval: July 27, 2015
12. Summary of Safety and Effectiveness Data for NovaSure Impedance Controlled Endometrial Ablation System; Premarket Approval Application (PMA) Number: P010013; Date of FDA Notice of Approval: September 28, 2001
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23 SCHEDULE OF EVENTS

Table 23-1: Schedule of Events

Assessments[2] / Validity Windows	Screening / Baseline	Procedure/ Discharge	SOC 24-hour contact	Week 2	Month 3	Month 6	Month 12	Months 24 & 36
	Various[3]	Day 0	18-48 hours	± 7 days	± 2 weeks	± 2 weeks	± 4 weeks	± 8 weeks
Informed Consent[4]	X							
Demographics	X							
Medical and surgical history (including documented history of excessive menstrual bleeding)	X							
Physical examination[5]	X							
Pap-Smear[6]	X							
Endometrial biopsy[7]	X							
Transvaginal ultrasound/ Sonohysterography /hysteroscopy[8]	X							
Vital Signs[9]		X						
Complete Blood Count	X							
Serum FSH	X							
Urine Pregnancy[10],[11]	X	X						
Minitouch Procedure		X						
Con. Medications/ Treatments[12]	X	X	X	X	X	X	X	X

[2] If a patient terminates from the study during a visit, site will attempt to complete all assessments, and review Early Termination section requirements for additional testing.

[3] See Section 12.2 for screening validity windows. Reassess dates of all study requirements prior to procedure to ensure that none are out of window.

[4] The informed consent process and signatures must precede any study-specific test or medication change.

[5] PE at Baseline includes pelvic and abdominal exam, height, weight, BMI. Note height, weight, and BMI are required only at screening.

[6] Results from previous pap-smear may be used if done within 12 months of treatment.

[7] Results from the endometrial biopsy may be obtained from a prior biopsy result if done within 12 months of treatment.

[8] At least one gynecological diagnostic test is required. Measure uterine sounding depth, cervix length and cavity length.

[9] Vital signs to include temperature, pulse, respiratory rate and blood pressure after at least 5 minutes at rest in the sitting or supine position.

[10] Pregnancy test must be negative during screening and on day of procedure prior to procedure initiation. Also, if study patient becomes amenorrheic at any time post-procedure, a urine pregnancy test should be administered.

[11] Conduct urine pregnancy tests as needed during follow-up; conduct STD tests as needed.

[12] Special attention should be paid to medication review of contraception since patient must have been on said method for ≥ 3 months prior to enrollment and must remain on the same hormonal regimen through the 12-month follow-up visit.

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Table 23-1: Schedule of Events								
Assessments[2] / Validity Windows	Screening / Baseline	Procedure/ Discharge	SOC 24-hour contact	Week 2	Month 3	Month 6	Month 12	Months 24 & 36
	Various[3]	Day 0	18-48 hours	± 7 days	± 2 weeks	± 2 weeks	± 4 weeks	± 8 weeks
Patient PBLAC Training[13]	X	X						
Screening PBLAC[14]	X							
Distribute PBLAC Diary and Product[15]	X	X		X	X	X		
PBLAC Diary Collection	X				X	X	X	
Final Eligibility Assessment[16]		X						
Menorrhagia Impact Questionnaire	X				X	X	X	X
Dysmenorrhea-related pain	X				X	X	X	X
Procedure-related pelvic pain[17]		X	X					
Patient Global Evaluation (PGE)					X	X	X	X
Investigator Global Evaluation (IGE)					X	X	X	X
AE / SAE / UADE[18]		X	X	X	X	X	X	X

[redacted]

[16] Eligibility criteria will be assessed at baseline and reconfirmed prior to procedure initiation. Only patients who meet all eligibility criteria at that time will be included.

[17] Pelvic pain (utilizing the NRS) will be evaluated BEFORE (prior to administration of procedure meds) and AFTER the procedure at discharge and during the SOC 24-hour telephone contact).

[18] AE / UADE / SAE collection starts after subject is enrolled (on the day of the Minitouch procedure).

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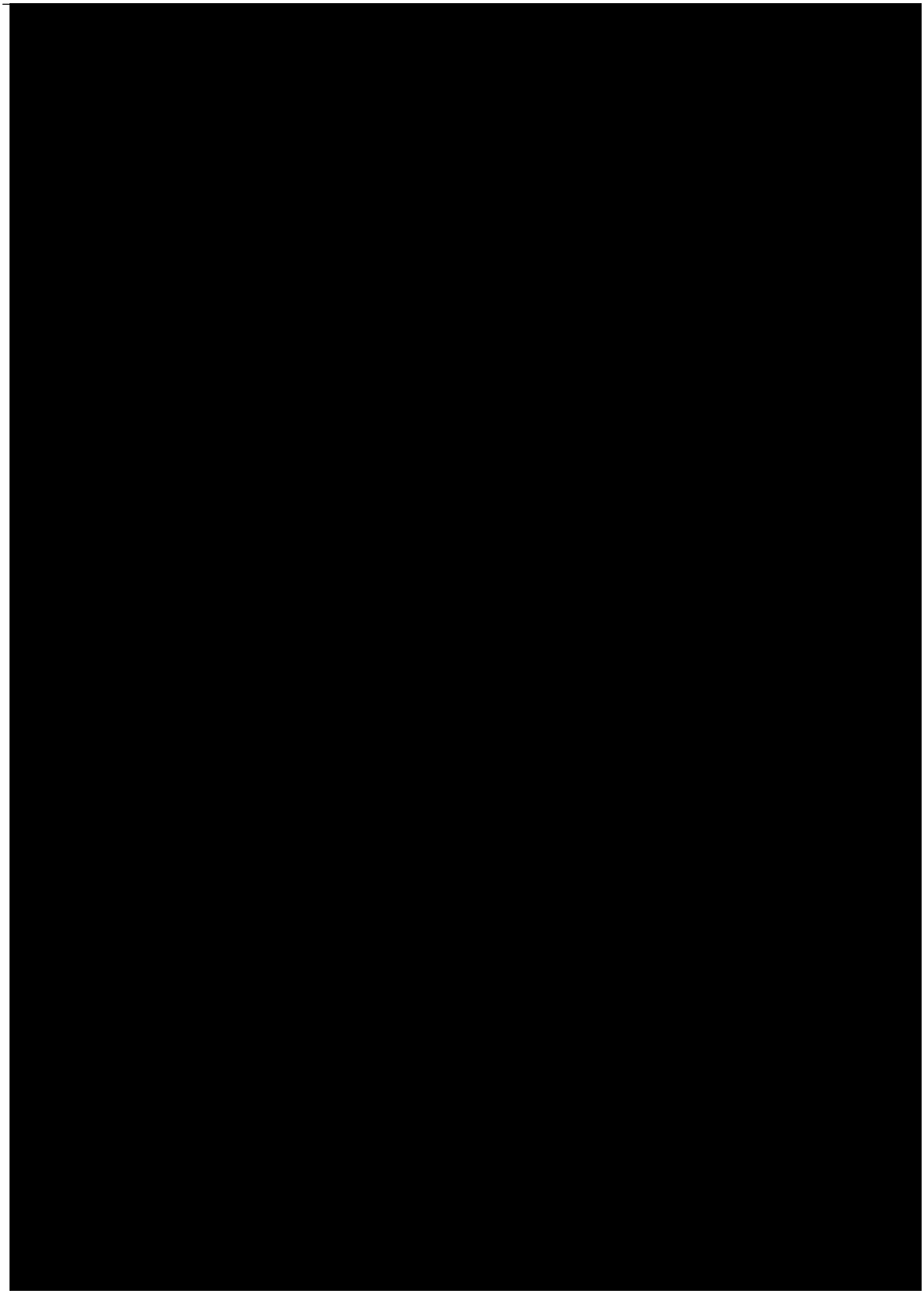

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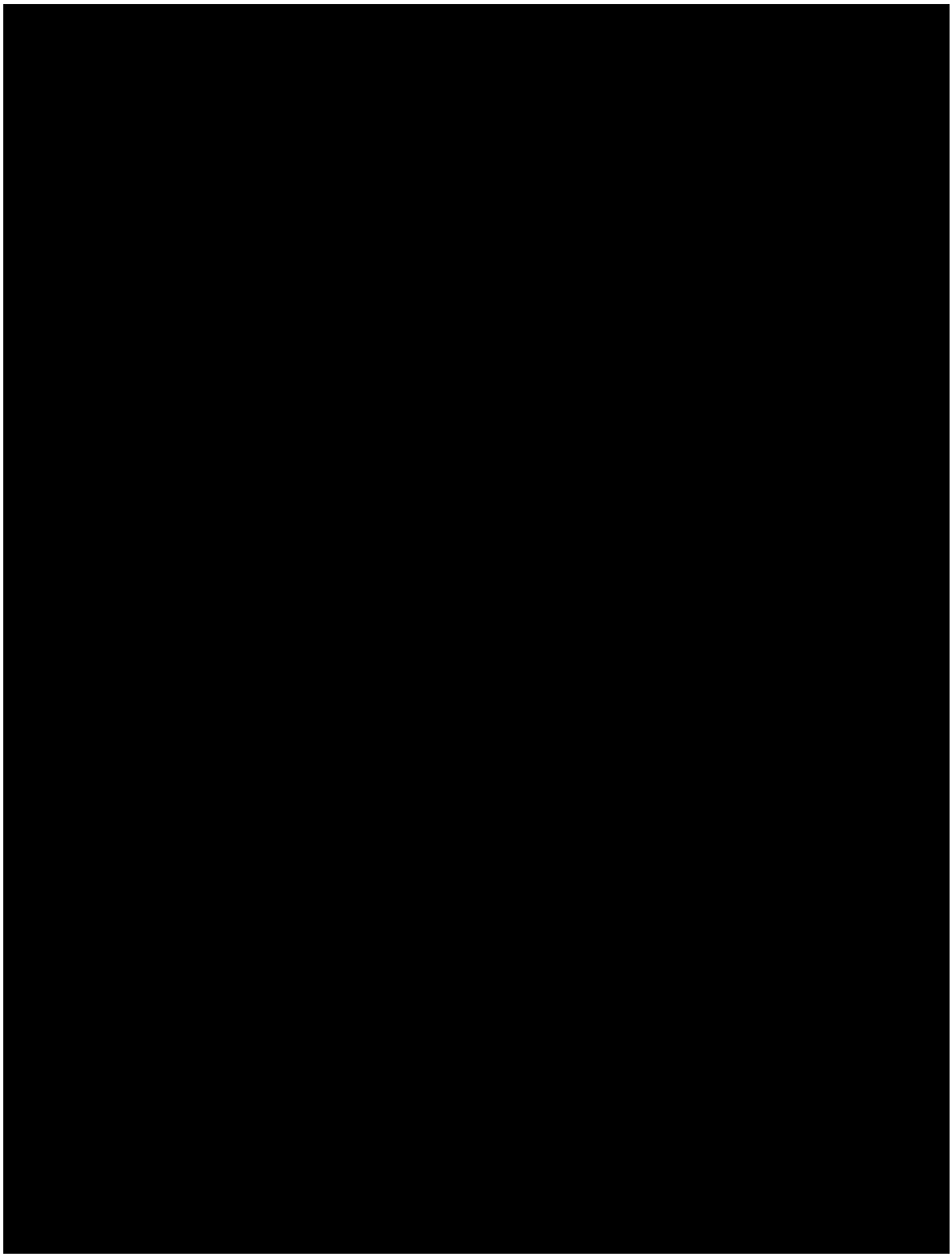

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ATTACHMENT B: SAMPLE MENORRHAGIA IMPACT QUESTIONNAIRE (MIQ)

MIQ concept	MIQ item		Response scale
Perception of amount of blood loss	**MIQ 1** 'During your most recent menstrual period, your blood loss was':	□	1. Light
		□	2. Moderate
		□	3. Heavy
		□	4. Very Heavy
Limitations in work outside or inside the home	**MIQ 2** 'During your most recent menstrual period, how much did your bleeding limit you in your work outside or inside the home?'	□	1. Not At All
		□	2. Slightly
		□	3. Moderately
		□	4. Quite A Bit
		□	5. Extremely
Limitations in physical activities	**MIQ 3** 'During your most recent menstrual period, how much did your bleeding limit you in your physical activities?'	□	1. Not At All
		□	2. Slightly
		□	3. Moderately
		□	4. Quite A Bit
		□	5. Extremely
Limitations in social or leisure activities	**MIQ 4** 'During your most recent menstrual period, how much did your bleeding limit you in your social or leisure activities?'	□	1. Not At All
		□	2. Slightly
		□	3. Moderately
		□	4. Quite A Bit
		□	5. Extremely
Global assessment of change in blood loss	**MIQ 6/6a/6b** Compared to your previous menstrual period, would you say your blood loss during this period was':	□	**0. About the same**
			1. Better (7-item scale):
		□	1. Almost the same, hardly better at all
		□	2. A little better
		□	3. Somewhat better
		□	4. An average amount better
		□	5. A good deal better
		□	6. A great deal better
		□	7. A very great deal better
			2. Worse (7-item scale):
		□	1. Almost the same, hardly worse at all
		□	2. A little worse
		□	3. Somewhat worse
		□	4. An average amount worse
		□	5. A good deal worse
		□	6. A great deal worse
		□	7. A very great deal worse
Meaningfulness of perceived change in blood loss	**MIQ 6c** 'Was this a meaningful or important change for you?'	□	0. No
		□	1. Yes

*MIQ1: If none of the choices are appropriate, subject should specify blood loss as □ none or □ spotting.
**MIQ6/6a/6b: To be completed at the follow-up visits (not required for Screening/Baseline). Also, the perception of amount of blood loss for the most recent menstrual period should be compared to the perception of amount of blood loss assessed at Screening/Baseline.

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ATTACHMENT C: SAMPLE NUMERICAL RATING SCALE (NRS) FOR DYSMENORRHEA-RELATED PAIN AND PROCEDURE-RELATED PELVIC PAIN

Numerical Rating Scale (NRS) for Dysmenorrhea-related Pain

On a scale of 0 to 10, with 0 being no pain and 10 being the worst pain possible, please mark the appropriate box that best describes your menstrual pain.

□0	□1	□ 2	□ 3	□ 4	□ 5	□ 6	□ 7	□ 8	□ 9	□ 10
No Pain					Moderate Pain					Worst Pain Possible

Numerical Rating Scale (NRS) for Procedure-related Pain

On a scale of 0 to 10, with 0 being no pain and 10 being the worst pain possible, please rate your **procedure-related pain** by marking the appropriate box that best describes your pain NOW.

□0	□1	□ 2	□ 3	□ 4	□ 5	□ 6	□ 7	□ 8	□ 9	□ 10
No Pain					Moderate Pain					Worst Pain Possible

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ATTACHMENT D: SAMPLE RATING SCALE FOR PATIENT AND USER (INVESTIGATOR) GLOBAL EVALUATION OF SATISFACTION WITH THE STUDY TREATMENT

Patient Global Evaluation (PGE)

Are you satisfied with the treatment you received for menorrhagia?

☐ Very Satisfied ☐ Satisfied

☐ Not Sure ☐ Dissatisfied ☐ Very Dissatisfied

How would you describe your menstrual status?

☐ No Bleeding (Amenorrhea)

☐ Spotting

☐ Light Bleeding (Hypomenorrhea)

☐ Medium or Normal Bleeding (Eumenorrhea)

☐ High or Heavy Bleeding (Menorrhagia)

Would you recommend this procedure to your friends?

☐ Yes

☐ No

Investigator Global Evaluation (IGE)

Are you satisfied with the treatment this patient received for menorrhagia?

☐ Very Satisfied ☐ Satisfied

☐ Not Sure ☐ Dissatisfied ☐ Very Dissatisfied

How would you describe the patient's menstrual status?

☐ No Bleeding (Amenorrhea)

☐ Spotting

☐ Light Bleeding (Hypomenorrhea)

☐ Medium or Normal Bleeding (Eumenorrhea)

☐ High or Heavy Bleeding (Menorrhagia)

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