**STUDY NAME:**

*Evaluat**I**ng normal values for traditiona**L** anorecta**L** f**U**nction para**M**eters with a**I**r charged a**N**d solid state HR**A**M cathe**TE**rs*

***("ILLUMINATE"** study)*

**NCT Number:**

Not Applicable

**Date of Document:**

16SEP2025

**SPONSOR:**

Laborie Medical Technologies Corporation

180 International Drive

Portsmouth, NH 03801

USA

**CLINICAL STUDY PROTOCOL**

**DEVICE:**

*Solar™ Anorectal Manometry Catheter and Solar™ Anorectal Manometry Charger*

*(Herein referred to as "Solar catheter")*

*And*

*UNITIP™ Solid State High Resolution Anorectal Manometry Catheter*

*(Herein referred to as "UNITIP catheter")*

**STUDY NUMBER:**

***Solar-01***

[redacted]

**STUDY NAME:**

*Evaluat**I**ng normal values for traditiona**L** anorecta**L** f**U**nction para**M**eters with a**I**r charged a**N**d solid state HR**A**M cathe**TE**rs*

***("ILLUMINATE"** study)*

**SPONSOR:**

Laborie Medical Technologies Corporation

180 International Drive

Portsmouth, NH 03801

USA

[redacted]

[redacted]

| | |
|---|---|
| [redacted] | [redacted] |

[redacted]

| [redacted] | [redacted] | [redacted] | [redacted] | [redacted] |
|---|---|---|---|---|
| [redacted] | [redacted] | [redacted] | [redacted] | [redacted] |
| [redacted] | [redacted] | [redacted] | [redacted] | Inclusion of Solar Compact HRM data system allows more sites to participate in the study. |

| | | | | |
|---|---|---|---|---|
| | | | [redacted] | |

This is a clinical research protocol for a post-market human research study. This study is conducted in accordance with the clinical protocol, Good Clinical Practice and with the ethical principles that have their origin in the Declaration of Helsinki.

# Table of Contents





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# 1 DEFINITIONS AND ABBREVIATIONS

The following is a list of abbreviations used in the body of this document. Abbreviations solely used in tables (e.g., table headers) are described in the table footer and are not included below.

| | |
|---|---|
| ADE | adverse device effect |
| AE | adverse event |
| ARM | Anorectal Manometry |
| ASADE | anticipated serious adverse device effect |
| CRF | case report form |
| CIP | clinical investigation plan |
| CRO | contract research organization |
| DD | device deficiency |
| DMC | data monitoring committee |
| EC | ethics committee |
| IRB | institutional review board |
| IB | investigator's brochure |
| IFU | instructions for use |
| IQR | Interquartile range |
| LAR | legally authorized representative |
| PI | Principal investigator |
| SADE | serious adverse device effect |
| SAE | serious adverse event |
| SAS | Statistical analysis software |
| USADE | unanticipated serious adverse device effect |
| HRAM | High resolution anorectal manometry |
| IAPWG | International Anorectal Physiology Working Group |
| GI | Gastrointestinal |



## 2 CLINICAL STUDY SUMMARY

| | |
|---|---|
| **Study Name** | EvaluatIng normal values for traditionaL anorectaL fUnction paraMeters with aIr charged aNd solid state HRAM catheTErs [Acronym: "**ILLUMINATE**"] |
| **Number of Sites** | Up to 5 sites |
| **Number of Subjects** | Approximately 81 subjects |
| **Objective** | Primary:<br>– obtain normative datasets for traditional measures of anorectal function with an air charged HRAM catheter in healthy subjects using the IAPWG standardized testing protocol and London classification for ARM measurement.<br>Secondary:<br>– qualitatively compare the performance of air charged and solid state HRAM catheters in determining values for traditional measures of anorectal function in a subset of study subjects using the IAPWG standardized testing protocol and London classification for ARM measurement. |
| **Inclusion criteria** | 1. Male and female volunteers, 18-65 years old<br>2. Willing to provide informed consent<br>3. Willing and able to follow instructions for ARM procedure |
| **Exclusion criteria** | 1. Documented history of gastrointestinal disorders such as:<br>a. fecal incontinence,<br>b. irritable bowel syndrome (IBS),<br>c. functional constipation, as defined by two or more of these symptoms for at least 25% of the time over the past 3 months:<br>i. excessive straining,<br>ii. hard or lumpy stools,<br>iii. sensation of incomplete evacuation,<br>iv. a feeling of anorectal blockage,<br>v. manual maneuvers to facilitate defecation,<br>vi. or fewer than 3 bowel movements per week.<br>d. functional diarrhea, as defined by the following symptoms over the past 3 months:<br>i. Loose or watery stools<br>ii. Lack of pain with diarrhea<br>iii. Diarrhea occurring in at least 75% of bowel movements<br>iv. No identifiable causes<br>2. Use of medications that may affect gastrointestinal motility as determined by healthcare professional.<br>3. Prior pelvic radiation,<br>4. Prior anorectal surgical procedures, including treatment for hemorrhoids,<br>5. Risk factors for pelvic floor trauma: |



[redacted]

| | |
|---|---|
| | a. more than 4 vaginal deliveries,<br>b. vaginal delivery with birthweight greater than 4500gms (macrosomia),<br>c. known 4th degree perineal tear or known forceps use during delivery.<br>6. Contraindicated for ARM testing<br>7. Has gastrointestinal symptoms and is indicated for ARM testing<br>8. Subject is currently pregnant or plans to become pregnant during the course of their enrollment in the study, as self-reported. |
| **Anticipated Study duration** | Enrollment is expected to last up to 12 months. |
| **Follow-Up** | There is no planned follow-up period for the study.<br>However, if an AE occurs and is unresolved during the study visit, a follow-up will occur through 30 days post-procedure or until resolution, whichever is earlier. |
| **Study end point** | Primary endpoint (**all study subjects**):<br>Measure normal traditional anorectal function parameters with an air charged HRAM catheter (i.e., Solar Catheter) and Laborie's Solar GI HRAM or Solar Compact HRM data and software analysis system using the IAPWG standardized testing protocol and London classification for ARM measurement and the London Classification for anorectal function disorders.<br><br>Secondary endpoint (**sub-set of study subjects**):<br>Measure normal traditional anorectal function parameters with a solid state HRAM catheter (i.e., UNITIP catheter) and Laborie's Solar GI HRAM or Solar Compact HRM data and software analysis system using the IAPWG standardized testing protocol and London classification for ARM measurement and the London Classification for anorectal function disorders. |
| **Primary outcome** | 1. Functional anal canal length, cm<br>2. Resting anal pressure - [Time Frame: 1 min]<br>– anal pressure at rest, mmHg<br>3. Anal squeeze pressure - [Time Frame: 5 seconds]<br>– maximal pressure when a squeeze test is performed, mmHg<br>4. Push pressure - [Time Frame: 5 seconds]<br>– mean pressure during push test, mm Hg<br>5. Cough pressure - [Time Frame: 5 seconds]<br>– Cough test maximal pressure, mmHg |

# 3 INTRODUCTION

## 3.1 Background

Anorectal manometry (ARM) is a widely used diagnostic technique for the detection of abnormalities of anal sphincter function and/or anorectal coordination(Emma V. Carrington et al. 2018; E. V. Carrington et al. 2014). ARM consists of a series of pressure measurements that assess involuntary function of the



[redacted]

anal canal during rest, voluntary function during squeeze, reflex anorectal coordination during rectal distension, and anorectal coordination during simulated defecation (Emma V. Carrington et al. 2020; 2018; Rodriguez et al. 2017). ARM provides a comprehensive assessment of pressure activity in the rectum and anal canal, and is used to diagnose patients suffering from defecatory disorders and pelvic floor dysfunction resulting from fecal incontinence and constipation, especially if characterized by symptoms of disordered evacuation (Emma V. Carrington et al. 2018; Rodriguez et al. 2017).

An ARM system consists of a catheter, with pressure sensors which is inserted into the anorectal area during the procedure, and a data collection and software analysis component which displays the results of the pressure measurement. The pressure sensors in ARM catheters can be based on water-perfusion (water-perfused catheter), solid state (solid state or electronic catheter) or air compression (air charged catheter) (Emma V. Carrington et al. 2018).

An anorectal manometric system can record pressure data from single points in the anal canal in "conventional" manometry using catheters with only a few pressure sensors or can record and display pressure information from the whole anal canal and distal rectum in "high-resolution" manometry. In high resolution anorectal manometry (HRAM), the catheters have many (10-36) closely spaced pressure sensors that enable pressure measurements longitudinally and circumferentially to allow for easier evaluation of data (Banasiuk et al. 2022; Rodriguez et al. 2017; Lee and Bharucha 2016).

## 3.2 Rationale

During ARM tests, catheter design and data analysis algorithms are known to affect absolute pressure values, with parameters measured by different types of sensors differing significantly (Emma V. Carrington et al. 2020; Banasiuk et al. 2022; Staller 2015). Consequently, normal reference values for these anorectal function parameters are critical for new catheters and systems for clinical translation of diagnostic data (Emma V. Carrington et al. 2020; E. V. Carrington et al. 2014; Lee and Bharucha 2016; Oblizajek et al. 2019; Sharma et al. 2021; Bharucha et al. 2022).

For this research study, two types of catheters will be used: an air charged catheter and a solid state catheter. First, the air charged catheter will be used in an ARM procedure on all study subjects. Afterwards, the solid state catheter will be used in a second ARM procedure on some of the study subjects to collect the same ARM measurements as the first procedure. Both types of catheters will use the Solar GI HRAM or Solar Compact HRM data collection and analysis system.

The air-charged catheter to be used is the "Solar™ Anorectal Manometry Catheter". [redacted]

As a new type of HRAM catheter design with air charged pressure sensors, establishing normal reference values for anorectal function parameters for the Solar catheter is critical for clinical translation of diagnostic data. Consequently, this clinical study is primarily designed to obtain normative datasets for traditional measures of anorectal function for the Solar catheter in asymptomatic subjects using the IAPWG standardized testing protocol and London classification. The first ARM procedure using the Solar catheter on all study subjects is designed to achieve this.

The solid state catheter to be used is the "UNITIP™ Solid State High Resolution Anorectal Manometry" catheter, or "UNITIP" catheter. The UNITIP catheter is a reusable HRAM catheter developed by Laborie and has been on the market since 2008.

The Solar catheter and the UNITIP catheter are Laborie-designed HRAM catheters with different types of pressure sensors that use the same data analysis algorithms in the Laborie Solar GI HRAM or Solar Compact HRM system. It is important to understand the relative performance of the two types of catheters when determining traditional anorectal function parameters. Therefore, a secondary rationale for the clinical study is to qualitatively compare the performance of the Solar catheter and the UNITIP catheter in determining values for traditional measures of anorectal function in a subset of the study subjects using the IAPWG standardized testing protocol and London classification. To achieve this, a second ARM procedure with the UNITIP catheter will be carried out on some of the study subjects under the IAPWG standardized testing protocol and London classification. Measurement values obtained from the second ARM procedure will be qualitatively compared to that from the first ARM procedure to understand the relative performance of the two catheters.



### 3.3 Medical Device

Solar Catheter [redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

UNITIP™ HRAM Catheter [redacted]

[redacted]

Solar GI HRAM system [redacted]

[redacted]

[redacted]

Solar Compact HRM System [redacted]

[redacted]

### 3.4 Prior Literature Studies

The study of anorectal function has experienced great technical advances with conventional manometry using catheters with only a few pressure sensors being replaced by more advanced high-resolution anorectal manometry (HRAM) able to record pressures with greater resolution. [redacted]

## 3.5 Risk & Benefits

### *Risk of Study Procedure*

ARM is an established diagnostic method with risk associated with the procedure well-characterized and understood. The study procedure and follow-up tests (if necessary) will be done according to the study doctor's standard of practice and all study devices' IFUs. While there are no significant risks or side effects of the study procedure, there are some risks and discomfort that are associated with the general ARM procedure.

These include the following:

- Soreness/mild bleeding - if the anorectal area is inflamed or irritated before the procedure, subject may experience some soreness or mild bleeding after the procedure.
- Mild discomfort - from catheter insertion through the anus into the rectum. The catheter only produces as much pressure as a normal poop would.
- Bowel damage may occur due to rectal balloon over-pressurization, rectal balloon malfunction, catheter over-insertion, or a sharp/rough catheter tip
- Balloon entrapment with possible follow-up procedure may occur due to rectal ballon detachment from the catheter
- Infection or inflammation may occur due to compromised cleanliness
- Severe subject discomfort may result from overinflation of rectal balloons cause by inaccurate pressure readings or monitoring
- Pain – subject may experience pain if catheter is removed without deflating rectal balloon.

### *Risk of Study Participation*

There is a risk of violation of subject's privacy during data collection of the subject's health data. All precautions will be taken to prevent the accidental disclosure of subject's medical records. Records of subject's participation in this study will be held confidentially. Records identifying study subjects will be kept confidential to the extent allowed by the law. Disclosures required by law may include suspected child abuse, infectious disease, expression of suicidal ideas, those situations in which research documents are ordered to be produced by a court of law, and those situations in which researchers are required to report to the appropriate authorities.

Subject's private information including medical records will be accessible to individuals and organizations that conduct or watch over the research study, including:

- Study coordinator,
- Personnel working for Laborie, the study sponsor,
- Regulatory authorities or Government agencies such as the FDA, and
- Ethics representatives that reviewed this research

All data and information held by Laborie will not contain any names, only subject codes. Personal data that could be used to identify a study subject (for example name, medical record number, address,

insurance number) will be accessible by Laborie personnel only during monitoring visits. Such data will never be transferred to Laborie and stays at the hospital or clinic.

If the results of this study are published or presented at meetings, subjects will not be identified. A description of this clinical trial will be available on http://www.clinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify study subjects. At most, the website will include a summary of the results. Study subjects can search this website at any time.

***Anticipated clinical benefit***

There is no potential benefit to the participants in this study compared to having anorectal manometry done outside of the study. The data will help inform the medical community on normal values range for the device. The device, in concert with a Solar GI HRAM system or Solar Compact HRM system, allows physicians to further classify defecatory disorders and pelvic floor dysfunction due to constipation and fecal incontinence by measuring static and dynamic pressures in the lower gastrointestinal tract.

***Anticipated adverse device effects***

There are no anticipated adverse device effects as the system and procedure are well characterized and of low risks.

# 4 STUDY OBJECTIVES

Primary:

- obtain normative datasets for traditional measures of anorectal function with an air charged HRAM catheter in healthy subjects using the IAPWG standardized testing protocol and London classification for ARM measurement

Secondary:

- qualitatively compare the performance of air charged and solid state HRAM catheters in determining normative values for traditional measures of anorectal function in a subset of study subjects using the IAPWG standardized testing protocol and London classification for ARM measurement.

# 5 STUDY DESIGN

## 5.1 Description

This is a prospective, multi-center, open label post-market study. The treatment arm (i.e., ARM with Solar catheter) will consist of approximately 81 asymptomatic individuals (volunteers) recruited from the intended patient population. A subset of up to 40 study subjects will be evaluated with two ARM catheters (i.e., Solar and UNITIP catheters). The order of application of the two catheters will not be randomized. A washout period between procedures will be determined by the investigator according to their standard practice and used to mitigate potential confounding impact of patient fatigue on the primary objective.

### 5.2 Duration

The duration of each subject's participation in the study is one clinic visit, which will include the amount of time required for informed consent, screening, enrollment, and the ARM procedure(s) execution. This is estimated to be about 1 hour for subjects evaluated with one ARM procedure and about 2 hours for subjects evaluated with two ARM procedures.

There is no follow-up period planned for the study. However, if an adverse event occurs and is unresolved during the evaluation, a follow-up will occur through 30 days post-procedure or until resolution, whichever is earlier.

Expected total study duration will be about 12 months (about 1 year).

### 5.3 Suspension or Premature Termination

The research study may be suspended or terminated prematurely by the Investigator, Sponsor, or IRB depending on the circumstances. The study may be suspended if a new risk or serious health threat arises during the study requiring a risk assessment to be done to determine the risk to study subjects. If the risk is determined to be unacceptable when weighed against the benefits during study suspension, the study may be prematurely terminated, and all participants informed with appropriate follow-up.

Following a suspension, the risk assessment may determine appropriate corrective actions necessary to allow the study to resume. In that case, (1) the rationale and relevant data supporting this decision will be provided to the Investigator and IRB, as applicable, (2) the Investigator or authorized designee shall inform enrolled subjects that the study has resumed, reasons for resumption, and reminded that they may withdraw from the study at any time, without penalty, and (3) the ICF shall be updated to include any new information pertaining to risks and potential adverse events.

Other reasons for suspension or premature termination may include:

- Major or repeated protocol deviations
- Slow recruitment exceeding project timelines
- Device is not producing expected results

Early stopping or continuation of recruitment will be at sponsor's discretion depending on project timelines and whether the minimum sample size has been recruited.

## 6 SUBJECT SELECTION

### 6.1 Inclusion Criteria

Subject must **meet all** of the following inclusion criteria:

1. Male and female volunteers, 18-65 years old
2. Willing to provide informed consent
3. Willing and able to follow instructions for ARM procedure

### 6.2 Exclusion Criteria

Subject must **not have any** of the following exclusion criteria:

1. Documented history of gastrointestinal disorders such as:

a. fecal incontinence,
b. irritable bowel syndrome,
c. functional constipation, as defined by two or more of these symptoms for at least 25% of the time over the past 3 months:
    i. excessive straining,
    ii. hard or lumpy stools,
    iii. sensation of incomplete evacuation,
    iv. a feeling of anorectal blockage,
    v. manual maneuvers to facilitate defecation,
    vi. or fewer than 3 bowel movements per week.
d. Functional diarrhea, as defined as the following symptoms over the past 3 months:
    i. Loose or watery stools
    ii. Lack of pain with diarrhea
    iii. Diarrhea occurring in at least 75% of bowel movements
    iv. No identifiable causes

2. Use of medications that may affect gastrointestinal motility as determined by healthcare professional.
3. Prior pelvic radiation,
4. Prior anorectal surgical procedures, including treatment for hemorrhoids,
5. Risk factors for pelvic floor trauma:
    a. more than 4 vaginal deliveries,
    b. vaginal delivery with birthweight greater than 4500gms (macrosomia),
    c. known 4th degree perineal tear or known forceps use during delivery.
6. Patients contraindicated for ARM
7. Patients with gastrointestinal symptoms who are indicated for ARM testing
8. Subject is currently pregnant or plans to become pregnant during the course of their enrollment in the study, as self-reported.

## 6.3 Vulnerable Populations

The targeted subject group is not a vulnerable population.

## 6.4 Recruitment Plans and Site Selection

Target enrollment is 81 healthy volunteers accounting for a 10% dropout rate. Healthy male and female volunteers 18-65 years old will be recruited for participation in the study. It is estimated that recruitment should take approximately 12 months. Recruitment will be monitored through scheduled meetings, phone calls/text messages, and/or emails with the site coordinator. Subject enrollment will be defined as the time subject provides informed consent. Subjects will be considered part of the complete analysis population once the ARM catheter has been inserted and the procedure completed. Participants who sign informed consent but for any reason are unable to proceed with the ARM procedure will not be counted toward the target sample size.

Sites will be selected based on the availability of an adequate participant population to be included in the study and ability to perform the research with sufficient resources and in compliance with good clinical practice and other applicable guidelines and regulations. In addition, the sites must be able to comply with any requirements specified by their respective IRB, if applicable.

Principal and sub-investigators must have experience in performing anorectal manometry procedures.

### 6.5 Training

Prior to the start of enrollment at the study site, the Sponsor or designee will facilitate training for study site personnel to ensure uniform data collection and protocol compliance.

Training will include, at minimum:

- This protocol
- Instructions on data collection

No device-specific training is required, as it is not investigational in nature.

### 6.6 Informed Consent Process

The Investigator (according to applicable regulatory requirements), or a person designated by the Investigator, and under the Investigator's responsibility, fully informs the subject of all pertinent aspects of the study, including the written information given approval/favorable opinion by the IRB. New information about the study will be provided to the subject by the Site, as applicable.

Prior to a subject's participation in the study, the written ICF should be signed, name filled in and personally dated by the subject or by the subject's legally acceptable representative, and by the person who conducted the informed consent discussion. A copy of the signed and dated written Informed Consent Form will be provided to the subject.

The Informed Consent Form to be used by the Investigator for obtaining the subject's informed consent must be reviewed and approved by the Sponsor prior to submission to the appropriate IRB for approval/favorable opinion.

### Subject Withdrawal

Subjects may withdraw voluntarily from the study at any time, without penalty, or the investigator may terminate a subject's participation. The investigator will notify the sponsor when a subject is withdrawn from the study (and if possible, the reason for the withdrawal), and this will be recorded on the subject's CRF and withdrawal form. Subjects who withdraw from the trial will be allowed to be replaced by another subject.

## 7 STUDY PROCEDURE

### 7.1 Study & Visit Schedule

The anticipated data collection for the study can be found in the table below.

**Table 1: Schedule of Assessments**

| Evaluation | Enrollment | Screening | ARM Procedure | Follow-Up (0-30 Days) (Only if AEs)[#] |
|---|---|---|---|---|
| **Informed Consent** | X | | | |
| **Inclusion/Exclusion** | | X | | |
| **Demographics/Medical History** | | X | X | |
| **ARM procedure** | | | X | |
| **Adverse Events** | X | X | X | X |



[redacted]

[#]For unresolved AE at procedure discharge, follow-up through 30 days post-procedure or until resolution, whichever is earlier.

### 7.2 Recruitment and Enrollment

Sites will recruit asymptomatic volunteers for the study. The PI or designee will conduct the informed consent process with a potential study participant. Subjects signing the informed consent form (ICF) will be considered enrolled in the study.

### 7.3 Screening

After enrollment, subject eligibility will be assessed and documented during screening. Eligibility may be assessed by subject interview or through a review of the medical chart against the eligibility criteria. Subjects meeting all eligibility criteria will be considered as screen pass and will continue with the study. Subjects not meeting the eligibility criteria will be considered screen fails and exited from the study.

### 7.4 Screen Fails

Enrolled subjects who do not meet eligibility criteria will be considered screen fails and exited from the study. Screen fails will be documented on the Screen Fail CRF and will be analyzed for safety endpoints only.

### 7.5 Study Procedure – Single Clinic Visit

The study requires a single clinic visit by study subjects for up to two ARM procedures. Each subject will undergo a standard ARM procedure using the Solar Catheter in accordance with standard of care, device IFU and the IAPWG standardized testing protocol and London classification for ARM measurement where, at minimum, the following parameters are collected:

- Functional anal canal length, cm
- Anal resting pressure, mmHg
- Anal squeeze pressure, mmHg
- Push pressure, mmHg
- Cough pressure, mmHg

The International Anorectal Physiology Working Group (IAPWG) recommended IAPWG standardized testing protocol and London classification of anorectal disorders provide a standardized format for performing and interpreting ARM. No additional tests or assessments are being requested for the purposes of this data collection beyond what is considered as standard for conducting ARM measurements.

A subset of subjects will undergo a second ARM procedure using the UNITIP catheter in accordance with standard of care, device IFU and the IAPWG standardized testing protocol and London classification for ARM measurement.

Adverse events (AEs) and device malfunctions will be assessed and reported according to Section 12.3

### 7.6 Study Exit

Subjects' participation in the study consists of one clinic visit. Subject exit will be the conclusion of the visit and will be documented on the Study Exit CRF.



### 7.7 Follow-Up

There is no planned follow-up period for the study. However, if an adverse event occurs during the study procedure and is unresolved during the clinic visit, a follow-up will occur through 30 days post-procedure or until resolution, whichever is earlier.

## 8 MANAGEMENT OF MEDICAL DEVICE

### 8.1 Description

The following devices and equipment will be required for the study:

| Device | Description/Comments | Required for |
|---|---|---|
| Solar Catheter | [redacted] | [redacted] |
| Solar Charger | [redacted] | [redacted] |
| Solar GI HRAM System | [redacted] | [redacted] |
| Solar Compact HRM System | [redacted] | [redacted] |
| UNITIP™ Solid State Catheter [redacted] | [redacted] | [redacted] |

The Solar Catheter and Solar Charger accessory allocated for use will be from commercial stock. Each site will be responsible for tracking the receipt and disposition of the catheters and chargers. The model number and lot number/serial number of each device used will be recorded for each subject.

The study agreement will further specify the equipment and disposables that will be required and provided by Laborie.

### 8.2 Regimen

Each subject will undergo a standard ARM procedure using the Solar Catheter in accordance with standard of care, device IFU and the IAPWG standardized testing protocol and London classification for ARM measurement where, at minimum, the following parameters are collected:

- Functional anal canal length, cm
- Anal resting pressure, mmHg

- Anal squeeze pressure, mmHg
- Push pressure, mmHg
- Cough pressure, mmHg

The IAPWG standardized testing protocol and London classification as recommended by the International Anorectal Physiology Working Group (IAPWG) are outlined below:

[redacted]

[redacted]

[redacted]

[redacted]

### 8.3 Assignment to Groups

No stratification of subjects will be utilized based on study design.

### 8.4 Preparation and Handling

The manometry system including the Solar GI HRAM or Solar Compact HRM data systems, Solar Catheter, Solar Charger, and UNITIP Catheter will be prepared, and maintained by the clinician according to the IFUs and User Manuals.

### 8.5 Packaging and Labelling

The study devices are commercial devices. Packaging and labelling are per the IFUs.

### 8.6 Device Accountability

***Study Site Usage:***

All devices used in the study will be used from the site's commercial stock or provided by the Sponsor and tracked according to hospital/clinic policies. Data collection device such as Solar GI HRAM or Solar Compact HRM systems that may be placed at a site for the purposes of the study will be tracked on a case-by-case basis. For enrolled subjects, all devices used directly in the study procedure must be recorded on the CRF.

***Study Site to Laborie:***

It is not expected any equipment or unused devices will be returned to Laborie unless Solar GI HRAM or Solar Compact HRM system loaner equipment has been placed for the purposes of this study. Retrieval of loaner equipment will be arranged on a case-by-case basis after the closure of the site.

### 8.7 Concomitant Treatment

Not applicable in this study

### 8.8 Subject Compliance Monitoring

Not applicable in this study.

# 9 ASSESSMENT OF STUDY DEVICE

## 9.1 Endpoints

| OBJECTIVES | ENDPOINTS | JUSTIFICATION FOR ENDPOINTS |
|---|---|---|
| Primary | | |
| To obtain normative datasets for traditional measures of anorectal function with an air charged HRAM catheter in healthy subjects using the IAPWG standardized testing protocol and London classification for ARM measurement. | **(All study subjects):** Measure normal traditional anorectal function parameters with an air charged HRAM catheter (i.e., Solar Catheter) and Laborie's Solar GI HRAM or Solar Compact HRM data and software analysis system using the IAPWG standardized testing protocol for ARM measurement and the London classification for anorectal function disorders. | An HRAM system consists of a catheter inserted into the anorectal area and a data analysis unit which displays the results of the pressure measurements. Due to differences in catheter designs and the methods used to summarize pressures, catheter-specific normal reference values are necessary for direct clinical translation of HRAM measurements. The intent is to provide physicians with the relevant data to guide clinical translation of pressure measurements and catheter selection decisions. |
| Secondary | | |
| Qualitatively compare the performance of air charged and solid state HRAM catheters in determining normative values for traditional measures of anorectal function in a subset of study subjects using the IAPWG standardized testing protocol and London classification for ARM measurement. | **(Sub-set of study subjects):** Measure normal traditional anorectal function parameters with a solid state HRAM catheter (i.e., UNITIP catheter) and Laborie's Solar GI HRAM or Solar Compact HRM data and software analysis system using the IAPWG standardized testing protocol for ARM measurement and the London classification for anorectal function disorders. | Endpoints will be measured by recording specific anorectal pressure parameters in each healthy individual using Solar™ air charged catheter and UniTip™ solid state catheter. The goal is to compare the readings recorded for each parameter by both catheters in the same healthy individual. |

## 9.2 Methods of Assessment

A Solar air-charged catheter and/or UNITIP solid state catheter will be used to measure static and dynamic pressures in the lower gastrointestinal tract. The air charged Solar Catheter is connected to the



[redacted]

Solar GI HRAM or Solar Compact HRM data analysis unit via the Solar Charger accessory. These measurements will be recorded using a LABORIE Solar GI HRAM or Solar Compact HRM data system. The resulting interpretations will be made by the physician overseeing the subject's case. All study outcome data captured will be compiled and analyzed by the LABORIE study team to determine if the endpoints were successfully achieved.

# 10 SUBJECT SAFETY

## 10.1 Definitions

***Adverse Device Effect (ADE):***
Adverse event related to the use of an investigational medical device.

***Adverse Event (AE):***
Untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users, or persons, whether or not related to the investigational medical device and whether anticipated or unanticipated.

***Device Deficiency (DD):***
Inadequacy of a medical device with respect to its identity, quality, durability, reliability, usability, safety, or performance.

***Serious Adverse Event:***
An adverse event that led to any of the following:

1) death,
2) serious deterioration in health of the subject, user, or others as defined by one or more of the following:
    a) a life-threatening illness or injury, or
    b) a permanent impairment of a body structure or a body function including chronic disease, or
    c) in-patient or prolongation hospitalization, or
    d) medical or surgical intervention to prevent life-threatening illness or injury, or permanent impairment to a body structure or a body function,
3) fetal distress, fetal death, a congenital abnormality, or birth defect including physical or mental impairment

***Unanticipated Adverse Device Effect (UADE):***
Any serious adverse effect on a subject's health or safety, or any life-threatening problem or death caused by, or associated with, a device, that was not previously identified in nature, severity, or degree of incidence in the investigation protocol or application, or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

## 10.2 Data Collection

Adverse events, device deficiencies, and serious adverse events shall be recorded on the CRF.

## 10.3 Reporting

For the purposes of this study, all adverse events will be collected upon subject enrollment. All adverse events, device deficiencies and any other potential unanticipated safety concern shall be recorded and

reported to the sponsor on the appropriate CRF according to the reporting table below. Details of reporting and analysis are described in the statistical analysis plan (Refer to [redacted]LLUMINATE clinical study Statistical Analysis Plan).

<table>
<tr><th>Safety Event</th><th>Reporting Timeframe</th><th>Report to Laborie</th><th>Report to local IRB (if applicable)</th></tr>
<tr><td>SAE</td><td rowspan="2">24 hours</td><td rowspan="3">Email:<br>[redacted]</td><td rowspan="4">In accordance with local IRB procedure if applicable</td></tr>
<tr><td>SADE</td></tr>
<tr><td>AE</td><td rowspan="2">According to clinical site policy or as soon as reasonably possible.</td></tr>
<tr><td>ADE</td></tr>
<tr><td colspan="4">Sponsor communication to Central IRB</td></tr>
<tr><td colspan="2">SAE</td><td colspan="2" rowspan="2">Laborie will communicate SAEs to Central IRB in accordance with the IRB policy</td></tr>
<tr><td colspan="2">SADE</td></tr>
</table>

### 10.4 Foreseeable Events

The residual risks have been deemed acceptable and the benefits overweighs the risks. Please also refer to Section 5.0 above for assessment of risks and adverse device effects.

### 10.5 Follow-Up

If an adverse event occurs, any follow-up intervention prescribed is at the discretion of the Investigator, and the site must notify Laborie of the outcome of the follow-up.

## 11 STATISTICAL CONSIDERATIONS

### 11.1 Statistical Method

This is a descriptive study aimed at estimating parameters used in diagnostic evaluation of gastrointestinal disorders. No formal hypothesis tests are planned for any endpoint. Descriptive statistics will be used to analyze data from this study. Continuous variables will be summarized with means, median, standard deviations, IQR, sample size (N), minimums, and maximums. If included, categorical variables will be summarized in frequencies and percentages in the category of interest. Statistical analysis will be conducted using a validated statistical software package. A Statistical Analysis Plan outlining the details of the analyses and hypothesis testing is available [redacted]ILLUMINATE clinical study statistical analysis plan) and will be finalized prior to database lock.

### *11.2* Sample Size Determination & Power

The sample size is calculated for estimating the mean for specific parameters with a specified precision. Anal resting pressure was selected for calculating the minimum sample size as it is more indicative of catheter behavior and one of the main parameters of interest for physicians. Details are described in the statistical analysis plan (Refer to: [redacted] ILLUMINATE clinical study Statistical Analysis Plan).

Briefly, the sample size was determined based on the following formula and assumptions:

[redacted]

[redacted]

### 11.3 Randomization / Blinding

The ARM procedures during the study will be conducted in an open label setting so no blinding will be possible. Also, there will be no randomization. For all study subjects, the Solar catheter will be first in the order of catheter insertion during ARM procedures. The Solar catheter will be the first catheter that will be used in all study subjects, even for the subset of study subjects undergoing ARM procedures with both the Solar and UNITIP catheters. A washout period between procedures to be defined by the investigator in accordance with their standard of practice will be used to mitigate potential confounding impact of patient fatigue on the primary objective.

### 11.4 Analysis Population

All consented subjects, including screen fails will be considered in the Enrolled analysis population with Safety endpoint(s). Enrolled subjects initiating catheter insertion but not completing the ARM procedure will be considered in the Attempted analysis population, also with Safety as the endpoint(s). Enrolled

subjects completing the ARM procedure will be considered in the Completed analysis population and will be analyzed for the study endpoints.

### 11.5 Handling Missing Data

All attempts will be made to limit the amount of missing data. If any CRFs are found to be incomplete, the study monitor will follow up as to the reason. No attempt will be made to impute missing data. If a data point is missing, that data point will not contribute to that portion of the analysis. The number of evaluable observations will be reported in each analysis so that the extent of missing data can be assessed.

### 11.6 Deviations

Any changes to the planned statistical analyses or additions to the endpoints analyzed will be documented and justified in the final report. Any other deviations or changes from the planned analyses deemed necessary due to violation of critical underlying statistical assumptions, data characteristics, or missing data will be clearly described in the clinical study report with justification and rationale.

### 11.7 Early Stopping

There are currently no criteria for stopping the study early on statistical grounds, however you may refer to Section 7.3 for details about suspension or premature termination for non-statistical reasons.

### 11.8 Interim Analysis

No interim analysis is planned for this study. However, interim data may be summarized for the purpose of providing reports for internal review and assessment.

## 12 DATA HANDLING & RECORD KEEPING

### 12.1 Direct Access

The investigator/institution will permit trial-related monitoring, audits, IRB review, and regulatory inspections by providing direct access to the source data/documents as needed. Regarding the subjects' personal data including health data, such data is provided in a de-identified form wherever possible and not otherwise necessary.

### 12.2 Confidentiality & Security

All information disclosed or provided by the Sponsor (or any company/institution acting on their behalf), or produced during study, including, but not limited to, the Protocol, the CRFs, and the results obtained during the course of the study, is confidential. The Investigator or any person under his/her authority agrees to undertake to keep the information confidential. In particular, the Investigator undertakes (1) not to make the information accessible to third parties - directly or indirectly, in writing, orally or in any other way - without the prior written approval of the Sponsor, (2) to use it exclusively within the scope defined by this Protocol and (3) to take all necessary measures to prevent third parties from becoming aware of and exploiting the information (obligation to secrecy, non-use and security).

However, the submission of this Protocol and other necessary documentation to the IRB is expressly permitted, the IRB members having the same obligation of confidentiality. The Sub-Investigators shall be bound by the same obligation as the Investigator. The Investigator shall inform the Sub-Investigators of the confidential nature of the Study. The Investigator and the Sub-Investigators shall use the

information solely for the purposes of the Study, to the exclusion of any use for their own or for a third party's account.

All data to Laborie will be confidential and all subject identifiers will be redacted before being sent to Laborie. Documents will be kept in a secure location and all digital information will be kept following local government regulations.

### 12.3 Data Handling

Data quality may be monitored via centralized data monitoring and edit checks. Centralized data monitoring may include individual subject and aggregate data analysis and review to identify outliers for confirmation by the site.

### 12.4 Case Report Form (CRF) & Source Documents

All study staff will be trained on the protocol requirements and CRF completion. It is the responsibility of the Investigator to maintain adequate and accurate CRFs designed by Laborie to record all observations and other data pertinent to the clinical investigation. All CRFs should be completed in their entirety in a neat, legible manner to ensure accurate interpretation of data. Should a correction be made, the information to be modified must not be overwritten. The corrected information will be transcribed by the authorized person using the correction section of the CRF. Source documents templates are present at the sites. Data from the source documents should be entered into the CRF after each subject's visit.

### 12.5 Record Retention

Each Investigator must maintain accurate, complete, and current records relating to the conduct of the study. The final responsibility for maintaining such records remains with the Investigator. These records include, but not limited to:

- All signed agreements
- IRB approval letters
- Signed ICF
- Records of each subject's case history, including study required CRFs,
- Signed delegation of authority logs
- Any other records applicable to the clinical study

An investigator or sponsor shall maintain the records required by 21 CFR Part 812.140 during the investigation and for a period of 2 years after the investigation is terminated or completed. The Investigator must maintain confidential all study documentation and take measures to prevent accidental or premature destruction of these documents. All essential documents from the Investigator will be kept in the Investigator binder. All sponsor essential documents will be kept in the study master file. The investigator and sponsor shall also maintain a record of their location of the respective essential documents. If the Investigator's personal situation is such that archiving can no longer be ensured by him/her, the Investigator shall inform the Sponsor and the relevant records shall be transferred to a mutually agreed upon designee.

### 12.6 Performance Monitoring

A quality control procedure will be reviewed prior to study procedure execution to ensure that all equipment is working within its specified performance. In the event that this is not the case, alternative equipment will be supplied where possible provided the alternative equipment will not jeopardize the



outcome of the study data. Monitors will periodically check CRF data to ensure all fields are entered as far as possible and inquire as to whether any usability issues are being encountered as the study progresses.

# 13 MONITORING, AUDITING, AND INSPECTING

## 13.1 Study Monitoring Plan

The Investigator agrees to provide reliable data and all information requested by the clinical trial protocol (with the help of the Case Report Form [CRF] or other appropriate instrument) in an accurate and legible manner according to the instructions provided and to ensure direct access to source documents to Sponsor representatives.

The Sponsor of this Clinical Trial is responsible to Health Authorities for taking all reasonable steps to ensure the proper conduct of the Clinical Trial Protocol as regards ethics, Clinical Trial Protocol compliance, integrity and validity of the data recorded on the Case Report Forms. Thus, the main duty of the Monitoring Team is to help the Investigator and the Sponsor maintain a high level of ethical, scientific, technical, and regulatory quality in all aspects of the Clinical Trial.

At regular intervals during the Clinical Trial, the site will be contacted, through monitoring visits, letters, or telephone calls, by a representative of the Monitoring Team to review study progress, Investigator and subject compliance with Clinical Trial Protocol requirements, and any emergent problems (as per the sponsor's monitoring plan). During these monitoring visits, the following but not exhaustive list of points will be scrutinized with the Investigator: subject informed consent, subject recruitment and follow-up, Serious Adverse Event documentation and reporting, outcome events documentation and reporting, and quality of data.

## 13.2 Auditing and Inspecting

For the purpose of ensuring compliance with the Clinical Trial Protocol, Good Clinical Practice and applicable regulatory requirements, the Investigator should permit auditing by or on the behalf of the Sponsor and inspection by applicable regulatory authorities.

The Investigator agrees to allow the official inspectors to have direct access to his/her study records for review, who are bound by professional secrecy and as such, are not entitled to disclose any personal identity or personal medical information.

The Investigator will make every effort to help with the performance of the audits and inspections, granting access to all necessary facilities, data, and documents to the designated auditors/inspectors.

As soon as the Investigator is notified of a future inspection by the authorities, the Investigator will inform and authorize the Sponsor to participate in the planned inspection.

The confidentiality of the data verified, and the protection of the subjects should be respected during these inspections.

Any result and information arising from the inspections by the regulatory authorities will be immediately communicated by the Investigator to the Sponsor. The Investigator shall take appropriate measures required by the Sponsor to take corrective actions for all problems found during the audit or inspections.

# 14 DEVIATIONS

All departures from the approval protocol shall be documented by the investigator. All deviations will be recorded on the subject CRF, and a deviation report will be sent to Laborie and the ethics board, as required. Timelines for notification will be subject to IRB standard operation procedures. Deviations will be reviewed and signed off by the sponsor. If deviations are observed/reported that significantly affect or have the potential to significantly affect human subject protection or reliability of the trial results, then Laborie will conduct a root cause analysis and implement appropriate corrective and preventative actions.

Significant risk deviations from the approved protocol are those which impact subject rights and safety, or data integrity and data security. Serious or repeated protocol deviations on the part of the investigator may be grounds for termination of the clinical investigation. The sponsor may also consider other corrective actions including protocol re-training, site visit, conference call or a formal warning letter.

Investigators may request prior, written approval for a study deviation or change in protocol. A protocol amendment may be required, and IRB/regulatory authorities notified where applicable.

Deviations from the protocol to protect the rights, safety, and well-being of subjects under emergency circumstances may proceed without prior approval from the sponsor, IRB, or regulatory authority. Such deviations shall be documented and reported to the sponsor and IRB as soon as possible.

# 15 AMENDMENTS

If there are any significant changes to the protocol during the clinical study application process or during the length of the clinical study in progress, the protocol with amendments will be completed and sent to the IRB for notification and review. If an amendment is made to the protocol during an ongoing study, the amended protocol will be sent to the applicable institution within the timelines required. The Investigator should not implement any deviation from or changes to the clinical protocol without agreement by the Sponsor and prior review (and documented approval/favorable opinion) from the IRB of an amendment, except when necessary to eliminate an immediate hazard(s) to a clinical study subject. In some instances, an amendment may require a change to the Informed Consent Form. The Investigator must receive an IRB approval/favorable opinion concerning the revised Informed Consent Form prior to implementation of the change.

# 16 STUDY ADMINSTRATION

## 16.1 Funding Sources and Conflicts of Interest

Laborie will be the sponsor and the financial details are covered in the Investigator Agreement.

## 16.2 Subject Stipends or Payments

Subjects will be offered a stipend for their participation in the study. The Sponsor has covered this study by means of an insurance covering bodily injury or property damage arising out of the clinical trial. The certificate of insurance evidencing the coverage, insurance company, policy number and the sum insured are provided in the Study's File.

### 16.3 Committees

A Data Monitor Committee will not be utilized in this study based on the evaluation of the level of potential risks.

## 17 ETHICS AND REGULATORY APPROVAL

This study will not begin until the appropriate approvals from the IRB have been obtained. Any additional requirements imposed by the IRB will be followed. This study will be conducted in compliance with all laws and regulations governing human studies, as well as any applicable guidelines.

The study will be registered on www.clinicaltrials.gov, as appropriate.

## 18 PUBLICATION POLICY

The results of the study may be submitted for publication, whether peer-reviewed or marketing materials. Publication rights and details are covered in the Investigator Agreement, there may be other authors involved in the creation of the publication.

The data and results from the trial are the sole property of the Sponsor. The Sponsor shall have the right to access and use all data and results generated during the study. The Investigators will not use the study/investigation-related data without the written consent of the Sponsor for any other purpose than for study/investigation completion or for generation of publication material, as referenced in the Study Agreement/Investigator Agreement.

The Sponsor acknowledges that the trial's Principal Investigators intend to publish a multi-center publication regarding the study/investigation results, and numerous secondary publications. The Sponsor must receive any proposed publication and/or presentation materials at least 30 days prior to the proposed date of the presentation or the initial submission of the proposed publication in order for the materials to be reviewed by the Sponsor in compliance with the Sponsor's publication policy set forth in the Study Agreement/Investigator Agreement.

The study will be registered on the ClinicalTrials.gov website upon approval by an IRB in order to meet the criteria of the International Committee of Medical Journal Editors. Institution(s) and/or Principal Investigator(s) shall not take any action to register the trial.

## 19 RELATED STUDY DOCUMENTS

### 19.1 Informed Consent Form

[redacted]

### 19.2 Case Report Forms

[redacted]

## 20 REFERENCES

1. Carrington EV, Scott SM, Bharucha A, et al. Advances in the evaluation of anorectal function. *Nat Rev Gastroenterol Hepatol*. 2018;15(5):309-323. doi:10.1038/nrgastro.2018.27

2. Carrington EV, Brokjær A, Craven H, et al. Traditional measures of normal anal sphincter function using high-resolution anorectal manometry (HRAM) in 115 healthy volunteers. *Neurogastroenterol Motil*. 2014;26(5):625-635. doi:10.1111/nmo.12307

3. Carrington EV, Heinrich H, Knowles CH, et al. The international anorectal physiology working group (IAPWG) recommendations: Standardized testing protocol and the London classification for disorders of anorectal function. *Neurogastroenterol Motil Off J Eur Gastrointest Motil Soc*. 2020;32(1): e13679. doi:10.1111/nmo.13679

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5. Banasiuk M, Dobrowolska ME, Skowrońska B, Konys J, Banaszkiewicz A. Comparison of Anorectal Function as Measured with High-Resolution and High-Definition Anorectal Manometry. *Dig Dis*. 2022;40(4):448-457. doi:10.1159/000518357

6. Lee TH, Bharucha AE. How to Perform and Interpret a High-resolution Anorectal Manometry Test. *J Neurogastroenterol Motil*. 2016;22(1):46-59. doi:10.5056/jnm15168

7. Staller K. Role of Anorectal Manometry in Clinical Practice. *Curr Treat Options Gastroenterol*. 2015;13(4):418-431. doi:10.1007/s11938-015-0067-6

8. Oblizajek NR, Gandhi S, Sharma M, et al. Anorectal pressures measured with high-resolution manometry in healthy people-Normal values and asymptomatic pelvic floor dysfunction. *Neurogastroenterol Motil*. 2019;31(7): e13597. doi:10.1111/nmo.13597

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10. Bharucha AE, Basilisco G, Malcolm A, et al. A Review of the Indications, Methods, and Clinical Utility of Anorectal Manometry and the Rectal Balloon Expulsion Test. *Neurogastroenterol Motil Off J Eur Gastrointest Motil Soc*. 2022;34(9): e14335. doi:10.1111/nmo.14335