Prospective Study of Colorectal Procedures with the Levita Magnetic Surgical System

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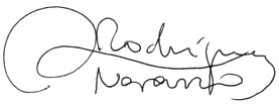
Sponsor Signature: 

Sponsor Name: Alberto Rodriguez-Navarro, MD

CONFIDENTIALITY STATEMENT

This study is confidential in nature. All information related to this study is considered proprietary and should not be made available to those not directly involved in this study. Authorized recipients of this information include Investigators and co-Investigators, other health care personnel necessary to conduct the study, and Clinical Investigation Ethics Committees and Institutional Review Boards. The personnel provided with data from this study are hereby informed of its confidential and proprietary nature. Release of these data to individuals other than those listed above requires the prior written permission of Levita Magnetics.

PROTOCOL REVIEW PAGE

STUDY TITLE: Prospective Study of Colorectal Procedures with the Levita Magnetic Surgical System
PROTOCOL: CP006
REVISION: A

Investigator's Statement: I agree to conduct this clinical study in accordance with the design and specific provisions of this protocol; modifications to the study or protocol are acceptable only with an approved protocol amendment. I agree to await Ethics Committee (EC) approval of the protocol and informed consent before initiating the study, to obtain informed consent from subjects prior to their enrollment in the study, to collect and record data as required by this protocol and case report forms, submit all reports as required by this protocol, provide the requested financial information, and to maintain study documentation for the period of time detailed in this protocol.

Investigator Signature:	***Date of Signature:***

Protocol Synopsis

Title:	Prospective Study of Colorectal Procedures with the Levita Magnetic Surgical System
Study Objective:	The purpose of this study is to evaluate the safety and effectiveness of the Levita Magnetic Surgical System in patients undergoing colorectal procedures.
Study Design:	Prospective, multicenter, single-arm, open label study designed to assess the safety and effectiveness of the Levita Magnetic Surgical System in colorectal procedures
Enrollment Size and Number of Sites:	30 subjects at up to three (3) clinical sites in Chile
Subject Population:	All patients at least 18 years of age presenting for elective colorectal surgery are potential candidates
Primary Safety Endpoint:	All adverse events will be captured and reported. Adverse events will be further summarized by relatedness to the MSS devices and/or procedure, seriousness, and level of severity.
Primary Effectiveness Endpoint:	Ability to adequately retract the colon and, as needed, peri-colorectal tissue and/or adjacent organs to achieve an effective exposure of the target tissue. Adequate retraction will be deemed to be achieved if it is not necessary to use another port to insert another instrument to retract the target tissues.
Inclusion Criteria:	*Subjects must meet <u>ALL</u> of the following inclusion criteria to be eligible for participation in the study:* • Subject is at least 18 years of age • Subject has a BMI of at least 20 kg/m^2 • Subject is scheduled to undergo elective colorectal procedure • Subject, or authorized representative, signs a written Informed Consent Form (ICF) to participate in the study, prior to any study-required procedures
Exclusion Criteria:	*Subjects must be <u>EXCLUDED</u> from participation in this study if <u>ANY</u> of the following exclusion criteria are met:* • Subject has a BMI of more than 60 kg/m^2 • Emergency procedures (e.g., obstruction, severe bleeding or perforation) • Significant comorbidities: e.g. cardiovascular, neuromuscular, chronic obstructive pulmonary disease, and urological disease (renal failure)

	• Subjects with pacemakers, defibrillators, or other electromedical implants • Subjects with ferromagnetic implants • Clinical history of impaired coagulation confirmed by abnormal blood tests • Subject has an anatomical abnormality noted after initiation of index procedure that would prevent device use • Subject is pregnant or wishes to become pregnant during the length of study participation • Subject is not likely to comply with the follow-up evaluation schedule • Subject is participating in a clinical trial of another investigational drug or device
Study Duration / Follow-up Period	Subjects will be followed for 30 days post-procedure, with follow-up visits at hospital discharge and at 7 and 30 days post-procedure.
Study Principal Investigator	I. Emre Gorgun, MD Cleveland Clinic Cleveland OH U.S.A.
Site Principal Investigators*:	Alejandro Readi, MD Hospital Salvador Santiago, Chile Alejandro Readi, MD Clinica Indisa Santiago, Chile
Sponsor:	Levita Magnetics International Corporation Alberto Rodriguez-Navarro, MD Title: CEO and Founder Email: CP006@levita.com Telephone: +1 (650) 204-0529

* The third sites is pending. An administrative update to the protocol will be made when an additional site is added.

Investigator Agreement and Certification
Levita Magnetic Surgical System Colorectal Procedures Study

I agree to participate in the clinical investigation of the Magnetic Surgical System sponsored by Levita Magnetics (hereinafter "Study Sponsor"). I agree to conduct this investigation according to the requirements of the investigational plan provided by the Study Sponsor and in accordance with Good Clinical Practice requirements as outlined in ISO 14155 and conditions imposed by the reviewing Ethics Committee (EC). I agree to ensure informed consent is appropriately obtained from all subjects prior to inclusion in this study.

I understand that this investigation will be monitored by the Study Sponsor and/or a designee employed by Study Sponsor. This monitoring will involve periodic inspection of my investigational site and ongoing review of the data that is submitted by me to Study Sponsor. I am also aware that I may be inspected by a representative of the U.S. Food and Drug Administration (FDA) or other regulatory authorities.

I am aware that Study Sponsor reserves the right to discontinue this investigation at any time.

My current curriculum vitae is attached along with the curriculum vitae of those physicians at this institution who will be using this investigational device or participating in this study as co-Investigators under my supervision. These include the extent and type of our relevant experience with pertinent dates and locations.

I certify that I have not been involved in an investigation that was terminated for noncompliance at the insistence of Study Sponsor, this institution's Ethics Committee (EC) or any regulatory authority.

I understand that this investigation, protocol, and trial results are confidential and I agree not to disclose any such information to any person other than a representative of Study Sponsor or regulatory authority without the prior written consent of Study Sponsor.

I will provide financial information by completing a Levita Financial Disclosure Form and update it as necessary.

Accepted by

Principal Investigator Signature	Printed name	date
Co-Investigator Signature	Printed name	date
Co-Investigator Signature	Printed name	Date
Co-Investigator Signature	Printed name	date
Co-Investigator Signature	Printed name	date
Co-Investigator Signature	Printed name	date

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1 INTRODUCTION

1.1 Background and Rationale

The Magnetic Surgical System (MSS) has been shown to retract soft tissue and organs and enable a reduction in the number of ports when used in laparoscopic procedures including cholecystectomy (Rivas et al.), bariatric surgery (Guerron et al.) and prostatectomy procedures (Diaz et al) and is cleared for commercial use (FDA clearance) for these indications in the United States. In these procedures, the MSS is used to grasp and retract soft tissues and organs so that the surgeon can visualize and access the target site of the surgery (i.e., gallbladder, liver, prostate or periprostatic tissues, respectively).

Tissue retraction is also needed in colorectal surgical procedures. This study is intended to evaluate the safety and effectiveness of the Magnetic Surgical System in colorectal procedures.

As no dedicated abdominal wall port is needed to use the MSS as a tissue retractor, a reduction in the number of ports required for the surgery, with the attendant benefits of this reduction, is anticipated.

2 SURGICAL SYSTEM DEVICE DESCRIPTION

The Levita Magnetic Surgical System is composed of two hand-held instruments: a Magnetic Grasper and an external Magnetic Controller.

The Magnetic Grasper (**Figure 1**) is comprised of two main components: a detachable Grasper Tip and a Shaft. Once the Magnetic Grasper is inserted and the Grasper Tip grasps the desired tissue, the detachable Grasper Tip can be detached from the Shaft and controlled externally using the Magnetic Controller. Traction of the tissue is maintained through the magnetic field attraction between the Grasper Tip and the Magnetic Controller. The Grasper Tip may be repositioned when needed using the Magnetic Grasper shaft or conventional (non-MSS) graspers. The Magnetic Grasper is compatible with a ≥ 10 mm laparoscopic port.

The Magnetic Controller (**Figure 2**) is a single unit with handles that is held external to the body and emits a magnetic field that attracts the detachable Grasper Tip. Once the Grasper Tip is attached to the desired tissue and detached from the Shaft, the Magnetic Controller is placed external to the body to magnetically attract the Grasper Tip to manipulate the target tissue. Adjusting the distance between the Magnetic Controller and the Grasper Tip will modulate the magnetic attraction used for tissue retraction/manipulation. The Magnetic Controller can then be moved freely, facilitating unrestricted shaft-less tissue retraction. If desired, the user can connect the Magnetic Controller to a

commercially available surgical support arm that is compatible with a hexagon-shaped mounting stem.

Figure 1. Magnetic Grasper

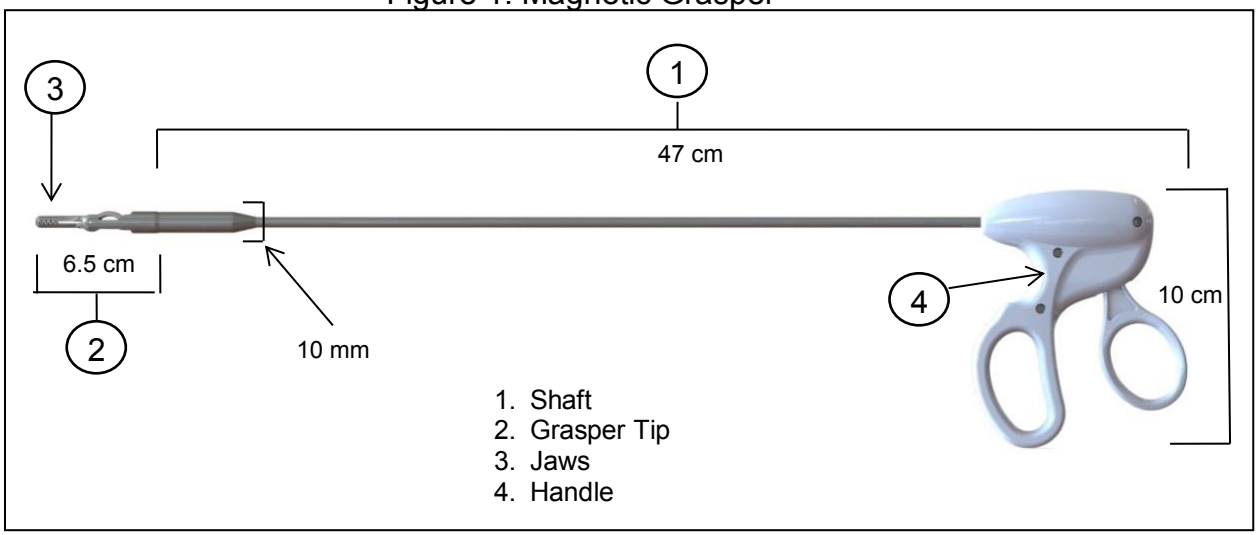
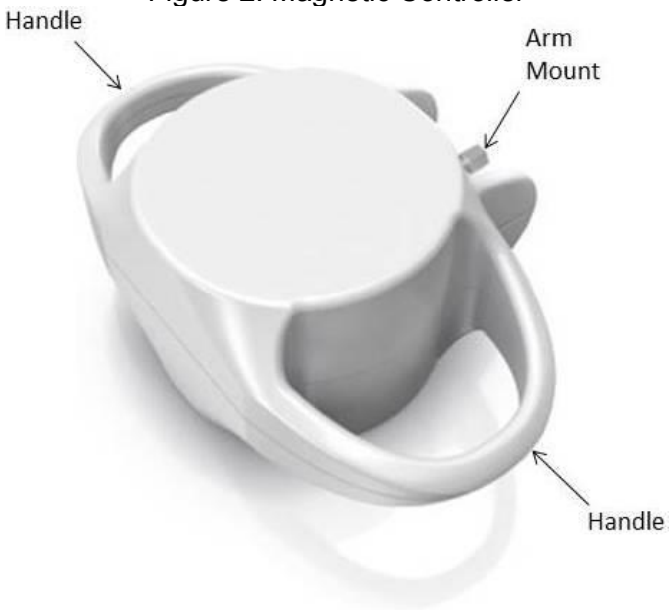


Figure 2. Magnetic Controller



The Magnetic Grasper is actuated via its handle with two distinct scissor-type motions to open and close the Jaws and to disengage the detachable Grasper Tip from the Shaft. The Magnetic Grasper can be used for retraction in the same manner as a conventional laparoscopic tissue grasper, or its Grasper Tip can be released and used with the external Magnetic Controller. When the Grasper Tip is detached from the Shaft, the Shaft can be removed and retraction of the tissue can be achieved through the magnetic attraction between the Grasper Tip and

the external Magnetic Controller. This access port is therefore available for use with other surgical tools. When the procedure is completed, the Grasper Tip is decoupled from the Magnetic Controller and the Shaft may be reinserted to retrieve the Grasper Tip from the patient.

3 INDICATION FOR USE

The Magnetic Surgical System is designed to grasp and retract the colon, peri-colorectal tissues, and adjacent organs in colorectal procedures to facilitate access to and visualization of the surgical site. The device is indicated for use in patients within a BMI range of 20 - 60 kg/m^2.

4 STUDY PURPOSE AND OBJECTIVE

The purpose of this study is to evaluate the safety and effectiveness of the Magnetic Surgical System as a soft tissue and organ retractor in colorectal procedures.

5 STUDY ENDPOINTS

The following endpoints will be evaluated in all enrolled subjects who undergo colorectal procedures using the Magnetic Surgical System.

5.1 Primary Safety Endpoint

All adverse events will be captured and reported. Adverse events will be further summarized by relatedness to the MSS devices and/or procedure, seriousness, and level of severity.

5.2 Primary Effectiveness Endpoint

Ability to adequately retract the colon and, as needed, peri-colorectal tissue and/or adjacent organs to achieve an effective exposure of the target tissue.

Adequate retraction will be deemed to be achieved if it is not necessary to use another port to insert another instrument to retract the target tissues.

Other Outcome Assessments

- Operative time
- Number of ports/incisions, and as compared to surgeon's standard of care (SOC) for this surgery type
- Time spent in the Post Anesthesia Care Unit (PACU)
- Length of stay (LOS) (time from admittance to post-anesthesia care unit until hospital discharge)
- Conversion rate (conversion to an open procedure due to inadequate MSS performance)
- Estimated blood loss
- Surgical Site Infection (SSI) rates

- Device malfunctions
- Subject satisfaction
- Investigator satisfaction with the MSS's ability to retract intended tissues and facilitate visualization of surgical site

6 STUDY DESIGN

6.1 Overview

This is a prospective, multicenter, single-arm, open label study designed to assess the safety and effectiveness of the Levita Magnetic Surgical System in colorectal procedures.

6.2 Sample Size and Number of Centers

The study will be conducted at up to three (3) study sites with a target maximum of 30 subjects in which the Levita Magnetic Surgical System is used for colorectal procedures.

6.3 Study Duration

Enrollment of subjects in this study is anticipated to take up to 6 months. Clinical follow-up evaluations will be conducted at discharge, and 7 and 30 days following surgery. The total study duration is expected to be approximately 7 months.

7 STUDY PROCEDURES

7.1 Subject Eligibility, Pre-Screening, and Exclusions

All subjects presenting for elective colorectal procedures are potential candidates, and will be screened for eligibility. A Screening/Enrollment Log will be provided to the study sites to maintain a cumulative tracking of all screened subjects.

Subjects must meet all study entrance criteria for enrollment in the clinical study. Reasons for screening failure(s) will be documented.

7.1.1 Inclusion Criteria

Subjects must meet ALL of the following inclusion criteria to be eligible for participation in the study:

1. Subject is at least 18 years of age
2. Subject has a BMI of at least 20 kg/m^2
3. Subject is scheduled to undergo elective colorectal procedure
4. Subject, or authorized representative, signs a written Informed Consent Form (ICF) to participate in the study, prior to any study-required procedures

7.1.2 Exclusion Criteria

Subjects must be EXCLUDED from participation in this study if ANY of the following exclusion criteria are met:

1. Subject has a BMI of over 60 kg/m^2
2. Emergency procedures (e.g., obstruction, severe bleeding or perforation)
3. Significant comorbidities: e.g. cardiovascular, neuromuscular, chronic obstructive pulmonary disease, and urological disease (renal failure)
4. Subjects with pacemakers, defibrillators, or other electromedical implants
5. Subjects with ferromagnetic implants
6. Clinical history of impaired coagulation confirmed by abnormal blood tests
7. Subject has an anatomical abnormality noted after initiation of index procedure that would prevent device use
8. Subject is pregnant or wishes to become pregnant during the length of study participation
9. Subject is not likely to comply with the follow-up evaluation schedule
10. Subject is participating in a clinical trial of another investigational drug or device

7.2 Enrollment and Written Informed Consent

Patients who meet initial eligibility criteria will be asked to sign the Informed Consent Form before any study-specific tests or procedures are performed. The Investigator will inform the potential subject of the elements of the clinical study, including risks, potential benefits and required follow-up procedures, prior to obtaining the potential subject's informed consent.

7.3 Baseline Evaluation

The Baseline visit will occur within 30 days prior to the index procedure.

The following evaluations are required at this visit:

- Demographic Information: gender, race, age, weight, height, and smoking status
- Medical / Surgical History
- Pre-operative blood draw for determination of coagulation disorders
- Urine pregnancy test for women of childbearing potential. Note that if the screening test is more than 1 week prior to the index procedure, a second urine pregnancy test is required within 7 days of the index procedure.

7.4 Procedure

The Investigator will perform the surgical procedure in accordance with the methods detailed in the Instructions for Use (IFU).

The following intra-operative data will be collected:

- General anesthesia time
- Operative time (from the first incision to the last suture's placement)
- Device and procedure observations
- Conversion to open surgical procedure and reason for conversion
- Number of ports utilized
- Number of ports typically utilized according to surgeon's SOC for specific surgical procedure
- The need for an additional port to place another retractor to retract the colon, peri-colorectal tissues or adjacent organs
- Estimated blood loss
- Video recording of the overall procedure
- Adverse events

7.5 Post-Procedure / Hospital Discharge

- Investigator satisfaction with the MSS's ability to retract intended tissues and facilitate visualization and access of the surgical site

Before hospital discharge the following data will be collected:

- Length of hospital stay (time from admittance to post-anesthesia care unit until hospital discharge)
- Length of time spent in Post Anesthesia Care Unit (PACU)
- SSI
- Adverse events, if any

7.6 Follow-up

All subjects will be asked to return to the investigational site at 7 days and again at 30 days post-procedure according to the study schedule described in **Table 1**. Subjects will be queried about satisfaction with the MSS facilitated procedure at the 30 day visit and about adverse events at both study visits. Study visits should be scheduled as closely as possible to the earlier part of the visit window to allow for rescheduling if needed due to last minute schedule changes. Visits not completed within the specified visit window will be regarded as protocol deviations.

Table 1: Schedule of Assessments

Assessment	Time Frame			
	Pre-op Baseline	**Index Procedure**	**7 day follow-up**	**30 day follow-up**
Visit Window	- 30 days	NA	± 3 days	± 7 days
Informed Consent	√			
Medical History	√			
Demographics	√			
Blood Tests	√			
Pregnancy Test *	√	√		
Intra-operative assessments		√		
Adverse events		√	√	√
Investigator satisfaction		√		
Subject satisfaction				√

* Urine pregnancy test for all women of childbearing potential at pre-op visit and repeated within 7 days of index procedure unless pre-op visit/prior urine pregnancy test was within 7 days of index procedure.

7.7 Unplanned Follow-up Visits

Subjects returning for unscheduled visits will be reported on the Unscheduled Visit case report form.

7.8 Early Discontinuation / Withdrawal

All subjects will be informed of their right to withdraw from the clinical study at any time without penalty or loss of benefits to which the subject is otherwise entitled. Additionally, the Investigator may prematurely discontinue any subject's participation in the study if the Investigator believes that the subject can no longer fully comply with the requirements of the study or if any of the study procedures are deemed potentially harmful to the subject. The reason for early discontinuation will be documented in the source documents and the Study Termination case report form.

7.9 Lost to Follow-up Subjects

Every attempt will be made to have all subjects complete the follow-up visit schedule. A subject will not be considered lost to follow-up unless efforts to obtain compliance are unsuccessful. At a minimum, the effort to obtain follow-up information will include three attempts to make contact via telephone or email and if unsuccessful, then a certified letter from the Investigator will be sent to the subject's last known address. In general, the study Site Coordinator should attempt to contact the subject after each missed visit to reschedule the visit.

8 RISK / BENEFIT ANALYSIS

8.1 Benefits

Possible benefits of the Levita Magnetic Surgical System are a reduction in the number of surgical ports needed to perform the surgery, with associated reduction in post-operative pain and scarring, a shorter length of stay in the hospital, and a faster recovery.

8.2 Risks

There are risks associated with use of the Levita Magnetic Surgical System including:

- Electromagnetic field incompatibility or interference
- Malfunctioning of the device
- Breakage of the device
- Allergic reaction related to the device
- Abdominal wall/cavity/tissue and/or organ injury or damage (e.g. inflammation, redness)
- Infection
- Tissue damage, including hematoma, bleeding or petechiae
- Vascular injury
- Gastro-intestinal injury
- Organ perforation
- Need for extended surgery
- Additional surgical intervention due to any of the above factors (includes reoperation)

These adverse events do not include all adverse events, which occur with surgery in general, but are important considerations particular to laparoscopic instrumentation.

8.3 Minimization of Risk and Monitoring Procedures

The MSS has been evaluated in clinical studies of cholecystectomy, bariatric surgery, and prostatectomy and has been in commercial distribution for over two years.

Risks are mitigated in this clinical study through selection of qualified physicians with competence in minimally invasive surgery, appropriate training, and study monitoring.

- Investigators who participate in the study will be experienced and skilled in laparoscopic surgical techniques. Additionally, Investigators, in conjunction with the investigational site, will have adequate resources for participation in a clinical study.
- The study has been designed to ensure treatment and follow-up of subjects are consistent with current medical practice.

- Each Investigator will ensure oversight and approval of the study by the Ethics Committee (EC) prior to initiation of the clinical study at his/her investigational site.
- The Investigator and study personnel will be trained on the clinical protocol.
- All Investigators will undergo training prior to first use during the clinical study.
- All Investigators and Operating Room (OR) support personnel will be provided with an IFU during training and as a reference for review as needed.
    - The IFU details appropriate safe working zones for use of the Magnetic Controller in an OR setting and considerations for users of a product with a strong magnet.
- Study personnel are also trained with and receive a “Magnetic Surgery Screening Checklist” and OR signage to ensure safe use of the system for subjects and users.
- Subjects will be carefully evaluated against the inclusion/exclusion criteria prior to entering the clinical study to ensure that their diagnosis and medical status are appropriate for participation in the clinical study.
- Subjects will be monitored up to the 30-day follow-up visit as defined in the study protocol. The follow-up visit will be with an Investigator to monitor the subjects’ status.
- A study Investigator will evaluate the subject for any adverse events potentially related to the device.
- Data from the investigative sites will be monitored throughout the study. Monitoring visits will be conducted at the investigative sites at the initiation of the study and periodically throughout the study to evaluate protocol compliance and to determine if there are any issues that may affect the safety or welfare of the subjects.

9 STATISTICAL SECTION

9.1 Statistical Methods

Data collected in the study will be presented using various descriptive statistics. Descriptive summaries will be the basis of study reports to generate an overall summary of the safety and effectiveness for the device.

Descriptive tables will be produced for baseline characteristics including demographics and medical history.

Missing data on study endpoints will be described.

9.2 Sample Size Justification

This is a single-arm, multicenter, investigational study. No formal sample size estimation has been performed. As safety and effectiveness have already been demonstrated in several prior indications (laparoscopic

cholecystectomy, bariatric and prostate procedures), it is expected that enrollment of 30 subjects will provide ample evidence of safe and effective use of the MSS in this additional subject population.

10 DATA MANAGEMENT

10.1 Data Collection

Data will be collected on paper case report forms (CRF) supplied by the Sponsor. The Site Principal Investigator is responsible for the accuracy and completeness of all study documentation.

Corrections to the CRF must be corrected by drawing a single line through the incorrect data, entering the correct data beside the incorrect entry, then initialing and dating the correction. Incorrect data must not be obscured. The use of pencil, erasable ink, or correction fluid on CRFs is prohibited. All fields must be completed, e.g. if the item was not done, mark “N/D”. If the item is not applicable to an individual case, mark the field “N/A”.

CRFs will be printed on 3-part NCR paper (or equivalent) so that both the site and monitor/Sponsor will have copies of the CRFs. The second copy may be sent to the Sponsor for remote monitoring. Any other subject information sent to the Sponsor must be redacted of personal identification information.

A unique study number will be assigned to each subject. All information recorded on the CRF about the subject will be recorded with the study number on it. The main database will contain only the study number to identify the subject. The code with subject name and study number will be maintained in a secured designated location at the site and will be inspected by study monitors and auditors. Any computerized data will be password protected.

The Sponsor will be responsible for database design and management.

10.2 Data Processing

Monitoring, described below, will be completed prior to data entry. In association with data entry, the data will be reviewed for further inconsistencies or incongruities. If warranted, a data clarification form or communication will be used to query the Investigator. Data will be either 100% audited or double data entry will be used to ensure accurate and complete study information.

11 MONITORING AND QUALITY CONTROL PROCEDURES

11.1 Control of Systemic Error/ Bias

Clinical monitors will verify subject data and ensure compliance with Good Clinical Practices (GCPs), clinical protocol and other study requirements. As

detailed in Section 13, an Independent Physician will adjudicate all adverse events for relatedness, severity, and seriousness. The adjudication results will be used for purposes of data analysis. The Site Investigator's analysis will also be presented in the final clinical study report.

11.2 Monitoring and Auditing

Monitoring visits to the clinical sites will be made periodically during the study, to ensure that all aspects of the current, approved protocol/amendment(s) are followed.

Prior to the enrollment of any subject in this study, site study personnel will be trained to Good Clinical Practice, the protocol and the device including Instructions For Use and management of a magnetic device. Additionally, the procedure for obtaining informed consent and the procedure for reporting adverse events will be reviewed.

Site monitoring visits will be performed by the Monitor on a regular basis during which case report forms will be 100% verified against source documentation. Data will be reviewed for safety information, legibility, completeness, accuracy, and logical consistency. Additional computer programs (e.g. edit checks) that identify selected protocol violations, out-of-range data, and other data errors may be used to help monitor the trial. Investigators will be required to make corrections to any data errors.

The Monitor is responsible for ensuring, through personal contact with the Investigator and site personnel, that the members of the clinical staff clearly understand and accept the obligations incurred in this investigation, and that these obligations are being fulfilled throughout the study. Specifically, the Monitor will interact with the site via telephone contact and periodic on-site visits to ensure that:

- Study facilities continue to be acceptable for the conduct of the study
- Regulatory and study documents are complete and current
- The protocol is appropriately followed
- Protocol amendments have been approved by the EC and the local regulatory authorities (as applicable), and the Sponsor has received the approval in writing
- Qualified subjects are enrolled in a timely manner
- Accurate, complete, and current records are maintained for all subjects
- The information recorded and submitted to the Sponsor is representative of the subject record and other supporting documentation
- Inconsistent and incomplete data are addressed and resolved
- Accurate, complete, and timely adverse event reports are being made to the Sponsor
- The site Principal Investigator continues to assume primary responsibility for the study
- Study devices are properly stored, dispensed, and accounted for

The Investigator or designee must, upon request, provide to the Monitor or regulatory authority the necessary study records for a thorough review of the study's progress. These records include, but are not limited to, case report forms and original documents and records such as hospital and clinic charts, consent forms, laboratory records, and pharmacy dispensing records.

The Monitor will provide a written report to the Sponsor after each on-site visit. The report will identify the personnel participating in the visit, the activities performed, any protocol deviations, and any action items/corrective actions identified.

If compliance problems or protocol deviations are noted, the Sponsor will recommend corrective action. If the response from the Investigator is not adequate, the Sponsor will terminate the site's participation in the study and notify the regulatory authorities (if applicable).

The study may also be subject to a quality assurance audit by the Sponsor or its designees, as well as inspection by appropriate regulatory authorities.

It is important that the Investigator and relevant study personnel are available during the monitoring visits and possible audits and that sufficient time is devoted to the process.

11.3 Device Accountability

Study devices must be used according to the protocol, Instructions for Use and Training.

The site Principal Investigator or an authorized designee shall keep records documenting the use of the study device by indicating the lot number on each subject's case report form.

12 ADVERSE EVENTS

12.1 Definitions

12.1.1 Adverse Event (AE)

AEs are any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in which subjects, users or other persons, whether or not related to the study medical device. This definition includes events related to the procedures involved. For users or other persons, this definition is restricted to events related to study medical devices.

All adverse events, regardless of relationship to the device, must be recorded on the case report forms provided. Adverse events that occur during this study should be treated by established standards of care.

Adverse events shall be assessed and documented at the time of the procedure and at all study follow-up visits. Each Investigator shall provide source documentation as requested by the Sponsor to facilitate reporting and adjudication of these events.

12.1.2 Serious Adverse Event (SAE)

An adverse event is considered a SAE if it:

- Led to death
- Led to a serious deterioration in the health of the subject, that either resulted in:
  a) A life-threatening illness or injury, or
  b) A permanent impairment of a body structure or a body function, or
  c) In-patient hospitalization, or prolongation of existing hospitalization, or
  d) medical or surgical intervention to prevent permanent life-threatening illness or injury or permanent impairment to body structure or a body function.
- Led to fetal distress, fetal death or a congenital abnormality

Planned hospitalization for a pre-existing condition, without serious deterioration in health, is not considered a serious adverse event.

12.1.3 Serious Adverse Device Effect (SADE)

A serious adverse device effect is defined as an adverse event related to the use of an study medical device that has resulted in any of the consequences characteristic of a serious adverse event.

12.1.4 Unanticipated Serious Adverse Device Effect (USADE)

An USADE is a serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the current version of the investigational plan.

12.2 Adverse Event Reporting

Any adverse event that occurs during the course of the study must be reported using the Adverse Event (AE) Form in the CRFs and the Investigator must sign each report. The Investigator must determine whether the adverse event is serious or unanticipated, its intensity, and the relationship of each adverse event to the study device or procedure. As noted in Section 13, an Independent Physician Adjudicator will also adjudicate all AE data.

Pre-existing medical conditions or symptoms occurring prior to the laparoscopic procedure involving the Levita MSS should not be reported as adverse events, unless there is a worsening of the pre-existing medical condition.

All serious adverse events, including unanticipated serious adverse device effects, must be reported to the Sponsor within 24 hours of the site first becoming aware of the event via email (CP006@levita.com). At a minimum, the AE CRF should be provisionally completed, scanned and sent via email. The Sponsor will contact the site for additional information, if required.

For any adverse event that is ongoing at the time of the initial report, periodic follow-up information is required until the adverse event is resolved or is not expected to change. The site should submit relevant follow-up information related to the adverse event as soon as it is available.

Depending upon the nature and seriousness of the adverse event, the Sponsor may request the Investigator to provide copies of the subject's medical records (such as the subject's laboratory tests and hospital records, Investigator summaries, etc.) to document the adverse event. The Sponsor and/or Sponsor designated clinical/medical personnel are available to respond to any medical issues that arise during the conduct of this study.

The Investigator will report all serious adverse events, including unanticipated serious adverse device effects, to the EC according to the EC requirements. A copy of this EC communication should be sent to the Sponsor.

Within 10 working days of notification, the Sponsor will report all unanticipated adverse device effects to the appropriate authority, all participating Investigators, and all reviewing ECs. The Sponsor will ensure that safety reporting for the study is conducted in compliance with all pertinent requirements and regulations.

12.3 Adverse Event Severity

The Investigator must determine the severity of the adverse event according to the following definitions:

Mild The adverse event is noticeable to the subject, but does not interfere with routine activity; the symptoms are easily tolerated and transient in nature.

Moderate The adverse event interferes with routine activity but responds to symptomatic therapy or rest; the symptoms are poorly tolerated and sustained.

Severe The adverse event significantly limits the subject's ability to perform routine activities despite symptomatic therapy. The adverse event requires

medical or surgical treatment or results in hospitalization.

Life-Threatening The subject is at immediate risk of death.

12.4 Event Relationship

The following lists the potential event attribution categories.

12.4.1 Device Related

An adverse event is considered device-related when the clinical event has a reasonable time sequence associated with use of the study device and is unlikely to be attributed to concurrent disease or other procedures or medications. It is reasonable to believe that the device directly caused or contributed to the adverse event.

The Investigator will evaluate the relationship of the adverse event to the Levita MSS according to the following definitions:

Definite The adverse event is clearly related to the study device: the event has a temporal relationship to the study device, follows a known pattern of response, or is otherwise logically related to the study device, and no alternative cause is present.

Probable The adverse event is likely related to the study device: the event has a temporal relationship to the study device, follows a known or suspected pattern of response, or is otherwise logically related to the study device, but an alternative cause may be present.

Not likely The adverse event is unlikely related to the study device: the event does not follow a clear temporal relationship to the study device or does not follow a known pattern of response, or is otherwise likely to be due to the subject's clinical state or other modes of therapy.

Not related The adverse event is clearly not related to the study device: the event has no temporal or other relationship to the administration of the study device, follows no known or suspected pattern of response, and an alternative cause is present.

Unknown Unable to determine the relationship based on all available information.

12.4.2 Procedure-Related

An adverse event is considered to be procedure-related when it is reasonable to believe that the event is associated with the index procedure and is not specific to the study device. Other products,

surgical techniques, or medications required specifically for the procedure may have contributed to the occurrence of the event.

The Investigator will evaluate the relationship of the adverse event to the procedure according to the following definitions:

Definite The adverse event is clearly related to the procedure: the event has a temporal relationship to the procedure, follows a known pattern of response, or is otherwise logically related to the procedure, and no alternative cause is present.

Probable The adverse event is likely related to the procedure: the event has a temporal relationship to the procedure, follows a known or suspected pattern of response, or is otherwise logically related to the procedure, but an alternative cause may be present.

Not likely The adverse event is unlikely related to the procedure: the event does not follow a clear temporal relationship to the procedure or does not follow a known pattern of response, or is otherwise likely to be due to the subject's clinical state or other modes of therapy.

Not related The adverse event is clearly not related to the procedure: the event has no temporal or other relationship to the procedure, follows no known or suspected pattern of response, and an alternative cause is present.

Unknown Unable to determine the relationship based on all available information.

12.5 Subject Death

Any subject death during the investigation must be reported to the Sponsor within 24 hours of Investigator's knowledge of the death. The Adverse Event CRF must be completed and include a complete description of the relevant details of the death. A copy of the death records, death certificates and an autopsy report (if performed) are required to be sent to the Sponsor. In addition, subject death must be reported to the EC in accordance with EC requirements.

12.6 Device Deficiency

All device deficiencies related to the identity, quality, durability, reliability, safety or performance (includes malfunctions, use errors, and inadequate labeling) of the device shall be documented. Sponsor will assess all device

deficiencies that could have led to a serious adverse device effect for potential regulatory reporting requirements.

In the event of a suspected malfunction or device deficiency, the study device should be returned to the Sponsor for analysis. Instructions for returning the study device will be provided by the Sponsor.

13 STUDY OVERSIGHT

13.1 Physician Adjudicator

An Independent Physician Adjudicator will be responsible for the adjudication of all reported adverse events. The Independent Physician Adjudicator will be a General Surgeon familiar with laparoscopic surgery who is not an Investigator in the trial and does not have a financial conflict of interest with the Sponsor. The adjudication process will include determination of device and procedure relatedness, seriousness, and severity of the adverse event. If there is insufficient evidence to make these determinations, the Physician Adjudicator may choose to request additional information. All available data will be presented for review to the Independent Physician Adjudicator.

14 STUDY ADMINISTRATION

14.1 Statement of Compliance

The clinical investigations will be in accordance with the ethical principles of the Declaration of Helsinki (October 2013), ISO 14155:2011 and ICH-GCP Guidelines. The clinical investigation shall not commence until approval by the EC. Any additional requirements imposed by the EC or regulatory authority shall be followed. The Sponsor shall maintain a Clinical Trial Liability Policy with an insurance company.

14.2 Ethics Committee (EC) Approval

The study protocol shall be reviewed and approved by the Investigator's EC prior to subject enrollment. All proposed changes to the investigational plan must be reviewed and approved by the Sponsor in writing prior to implementation. Significant changes to the investigational plan must be approved in writing by the Sponsor and the EC prior to implementation. A significant change is one which may increase the risk or present a new risk to a subject, or which may adversely affect the scientific validity of the study.

Prior to shipment of study devices, a signed copy of the EC approval letter identifying the clinical study and investigational site is required to be submitted to the Sponsor. Investigators are responsible for obtaining and maintaining annual renewal of the study by their EC (or according to renewal schedule imposed by the EC). Evidence of renewal and continued EC approval must be provided to the Sponsor accordingly.

14.3 Informed Consent

Written informed consent is mandatory and must be obtained from all subjects as per local regulations, prior to their participation in the study. A sample of the Informed Consent is provided to each investigational site.

It is the responsibility of the Investigator to ensure written informed consent from each subject, or the legally authorized representative of the subject, is obtained prior to the initiation of any study-related procedures.

Study participation is voluntary, and refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled.

Study personnel fully knowledgeable in the purposes and procedures of the study will approach all prospective study participants. The facilities and settings in which prospective participants will be presented with the opportunity to learn about and consent to participation in the study will provide them sufficient quiet and unhurried time to be informed of the study and to ask questions prior to the initiation of study procedures. Study personnel will, after presenting the study to prospective participants, assess the subject's understanding and autonomy by asking the subject to explain the study in his/her own words.

Once that step is completed, consent will be able to be given by the subject signing the consent form. A copy of the consent form will be given to all consented participants.

Signed subject consent forms must be retained in the study files by the Investigator, and be available for review by the Sponsor and/or regulatory agencies, as applicable.

The informed consent form and any other written information provided to subjects will be revised whenever important new information becomes available, or if there is an amendment to the protocol which necessitates a change to the content of subject information and/or to the consent form. The Investigator will inform the subject of changes in a timely manner, and will ask the subject to confirm his/her continuation in the study by signing a revised consent form.

Any revised informed consent form and other written information provided to subjects must receive approval from the EC and Sponsor prior to use.

14.4 Amending the Protocol

This protocol is to be followed exactly, and will only be altered by written amendments. Amendments must be approved by all parties responsible for approving the protocol prior to implementation. The Informed Consent and CRFs will be reviewed to ensure these are amended if necessary.

Administrative changes that do not affect the benefit/risk ratio or scientific validity of the study (e.g., editorial changes for clarity) may be made with just approval from the Sponsor and will be documented as a protocol revision.

14.5 Protocol Deviations/Violations and Medical Emergencies

A protocol deviation or violation is a failure to comply with the requirements of the clinical study as specified in the protocol. Examples of protocol deviations include late visits, missed visits, and required follow-up testing not completed. An example of a protocol violation includes enrollment of a study subject who fails to meet inclusion/exclusion criteria as specified in the protocol or failure to obtain informed consent. Each Investigator shall conduct this clinical study in accordance with the study protocol and any conditions required by the reviewing EC.

Deviations/violations from clinical protocol requirements will be reviewed and evaluated on an ongoing basis and, as necessary, appropriate corrective actions put into place. The Sponsor accepts the right of the Investigator to deviate from the protocol in an emergency when necessary to safeguard the life or the physical well-being of a study subject but such deviation must be reported within **24 hours** of implementation to the EC and Sponsor.

14.6 Pre-Study Documentation Requirements

Prior to study enrollment, the following documents must be provided to the Sponsor:

- Signed protocol/protocol amendments
- Signed and dated Investigator Agreement(s)
- A copy of the written EC approval of the protocol
- A copy of the written EC approval of the Informed Consent Form
- Signed and dated Curriculum Vitae of the Investigator(s)
- Copy of the Investigator(s)' current medical license(s), or equivalent
- Signed and dated Non-disclosure Agreement(s), if required
- Signed and dated Financial Disclosure Form(s)

14.7 Record Retention

The Investigator will maintain all essential trial documents and source documentation that support the data collected on the study subjects in compliance with ICH/GCP guidelines. Documents must be retained until at least 2 years have elapsed since the date the investigation is completed or terminated or the records are no longer required to support a regulatory submission, whichever date is later. These documents will be retained for a longer period of time by agreement with the Sponsor or in compliance with other regulatory requirements. 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, custody must be transferred to an individual who will

assume responsibility. The Sponsor must receive written notification of this custodial change.

14.8 Criteria for Terminating Study

The Sponsor reserves the right to terminate the study but intends only to exercise this right for valid scientific or administrative reasons or reasons related to protection of subjects. Investigators and associated ECs will be notified in writing in the event of termination.

Possible reasons for study termination include:

- The discovery of an unexpected, significant, or unacceptable risk to subjects enrolled in the study.
- A decision on the part of the Sponsor to suspend or discontinue further regulatory submissions for the device.

14.9 Criteria for Suspending/Terminating an Investigational Site

The Sponsor reserves the right to stop the enrollment of subjects at an investigational site at any time after the study initiation visit if no subjects have been enrolled or if the center has multiple or severe protocol violations without justification or fails to follow remedial actions.

Possible reasons for suspending/terminating a study center include:

- Failure to obtain written Informed Consent.
- Failure to report SAE or USADE to the Sponsor within 24 hours of knowledge.
- Failure to complete data forms prior to the scheduled monitoring visits.
- Loss of (or unaccounted for) study product inventory.

14.10 Publication Policy

It is anticipated that the Investigators involved will publish the results of this study. Listing of authors shall follow accepted standards of authorship, such as those established by International Committee of Medical Journal Editors (ICMJE). Any manuscripts pertaining to this study shall be reviewed for technical and scientific accuracy by the Sponsor prior to submission for publication. The Sponsor shall be responsible for approving the peer-reviewed journals for submission of the manuscript and for requesting edits prior to submission.

14.11 Sponsor Responsibilities

The Sponsor, Levita Magnetics, is responsible for selecting qualified Investigators and providing them with the information and materials necessary to conduct this trial appropriately, ensuring proper monitoring of the investigation, that EC review and approval are obtained, and ensuring that the Investigators and the reviewing EC are promptly notified of significant new information about this investigation.

Specifically, the Sponsor will be responsible for:

- Securing compliance with the clinical protocol, Investigators' agreement, and local regulations;
- Conducting evaluations of all adverse events;
- Maintaining records and reports;
- Analyzing and reporting data;
- Designating appropriately qualified medical personnel to be available to advise on study related medical questions or problems

This study may be used to support regulatory submissions to the United States Food and Drug Administration or to regulatory agencies in other countries. If so used, it is the responsibility of the Sponsor to complete such applications.

14.12 Investigator Responsibilities

Selected Investigators are responsible for items as detailed below:

- Agree to sign and adhere to the Investigator Agreement.
- Obtain approval from the EC including subsequent protocol amendments and changes to the Informed Consent form and obtaining annual EC approval and renewal throughout the duration of the study.
- Await EC approval, as well as, any additional hospital requirements prior to requesting written informed consent from any potential study subject or prior to allowing any subject to participate in the study.
- Complete and provide signed Financial Disclosure information prior to the study and maintain this information for the duration of the study.
- Agree to participate in Investigator meetings, if scheduled, by The Sponsor.
- Be willing to perform and be capable of performing treatment procedures as outlined in this protocol.
- Comply with all required elements of this protocol (e.g., perform testing and follow-up as specified, especially during personnel transitions).
- Agree to obtain written Informed Consent before any study specific procedures are performed.
- Control any study device(s) stored at their site.
- Be aware of, and comply with, GCP and applicable regulatory requirements.
- Permit monitoring and auditing by the Sponsor, and inspection by the appropriate regulatory authorities.
- Have available an adequate number of qualified staff and adequate facilities to properly conduct the study.
- Ensure study personnel are adequately informed about the protocol, the study device and study-related duties and functions.

15 REFERENCES

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16 REVISION HISTORY

Revision	Date	Description of Change
A	21 May 2019	Initial release