

COVER PAGE

HUMAN FACTORS ACTUAL-USE CLINICAL PROTOCOL

Study Title: Human Factors Actual-Use Confirmatory Validation Study of the Eximis CS (Contained Segmentation) System (“Contain” Study)

Study Number: CIP2020-001

Study Device: Eximis™ CS (Contained Segmentation) System

Manufacturer: Eximis Surgical, Inc.
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Sponsor: Eximis Surgical, Inc.
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IDE #: G200318

**ClinicalTrials.Gov
Registration Number:** NCT04799210

Protocol Version/Date: Version 6.0 / 23 Sept 2021

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This study will be conducted according to this protocol, US Food and Drug Administration 21 CFR 812, International Organization for Standardization 14155:2020, and other regulatory requirements of the regions where the study is conducted.

Version/Date: Version 6.0 / 23 Sept 2021

Confidentiality Statement

The information contained in this document, particularly unpublished data, is the property or under control of Eximis Surgical, Inc. (Eximis) and is provided to you in confidence as an Investigator, potential Investigator, or consultant, for review by you, your staff, and applicable Institutional Review Board (IRB). The information is only to be used by you in connection with authorized clinical studies of the investigational device described in the protocol. You will not disclose any of the information to others without written authorization from Eximis Surgical except to the extent necessary to obtain informed consent from those persons who may participate in the clinical trial.

Human Factors Actual-use Clinical Protocol Signatures

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AMENDMENT SUMMARY OF CHANGES

Study Title:	Human Factors Actual-Use Confirmatory Validation Study of the Eximis CS (Contained Segmentation) System (“Contain” Study)	
CIP #:	CIP2020-001	
Amended CIP Version / Date:	Version 6.0 / 23 Sept 2021	
Replaces CIP Version / Date:	Version 5.0 / 28 Jul 2021	
Rationale:	This amendment was made to allow Eximis Surgical, Inc. to provide a commercially available electrosurgical generator capable of 200W monopolar pure cut setting for use with the Eximis CS System when requested by study site(s). Administrative changes, abbreviations, section numbering, typographical error corrections, and minor wording changes for clarity as a result of this amendment may have been made and will not be reflected in the table below.	
Section(s)	Use to Read	Now Reads
Section 16.2	Has been added	The Eximis CS System is to be used with an electrosurgical generator capable of 200W monopolar pure cut setting. Eximis will provide a commercially available electrosurgical generator capable of 200W pure cut (e.g., ValleyLab Force FX) for use with the Eximis CS System when requested by study site(s). Eximis will be responsible for ensuring the generator meets the manufacturer’s specifications. The provided generator(s) will be labeled for Clinical Trial CIP2020-001 Use Only and will be returned to the Sponsor/designee at conclusion of use in this study, or at any time per the discretion of the study site or the Sponsor.

SYNOPSIS

Study Title:	Human Factors Actual-Use Confirmatory Validation Study of the Eximis CS (Contained Segmentation) System (“Contain” Study)
Study Number:	CIP2020-001
Study Purpose:	The purpose of this study is to confirm device use safety and effectiveness of the Eximis CS (Contained Segmentation) System in actual use by representative users, use, and use environments as required for regulatory agency clearance for commercial use. This confirmatory study follows completion of a Human Factors Simulated-Use Validation Study in which gynecological surgeons utilized the Eximis CS System to contain, segment, and extract bovine tongue in a porcine model.
Investigational Device Description:	The Eximis™ CS (Contained Segmentation) is an integrated system consisting of a 900 mL Capture Bag, two Eximis Segmenters, and the Eximis RF-100 Controller. The system is to be used with an electrosurgical generator capable of 200W monopolar pure cut setting.
Indication for Use:	The Eximis™ CS (Contained Segmentation) is an integrated system intended for containment, segmentation, and extraction of tissue; indicated for use during laparoscopic gynecological surgical procedures.
Study Centers Planned:	Up to eight (8) sites in the United States. Representative use environments will include at least one large academic institution and at least one smaller community center.
Objectives:	<u>Primary Objective</u> 1. Evaluate usability to confirm device use safety and effectiveness in an actual use setting. <u>Secondary Objectives</u> 1. Evaluate integrity of the Eximis CS System Capture Bag by containment testing following use. 2. Evaluate user and subject safety.
Endpoints:	<u>Primary Endpoint</u> 1. The number of procedures where all critical tasks related to the Eximis CS are performed without serious use error. <u>Secondary Endpoints</u> 1. Number of procedures successfully completed with use of the Eximis CS device. 2. Number of Capture Bags with breach of containment. 3. The number and severity of user adverse events caused by use error. 4. The number and severity of subject adverse events caused by use error. 5. All other adverse events.
Additional Measures (Informal Evaluation):	1. Duration of the segmentation/extraction procedure (from insertion of the Eximis CS deployment instrument into the abdomen until removal of the Eximis CS Capture Bag from the abdomen) 2. Duration of the surgical procedure (from skin incision to skin closure) 3. Length of incision (mm) used for the Eximis CS device at procedure end (removal of Eximis CS Capture Bag)

	- Removed tissue weight (grams) - Number of extracted tissue segments per subject - The size (mm) of the largest segment will be recorded, defined as the segment with the largest cross-sectional area of the surface that is parallel with the incision opening - Subject's pathology results of the extracted tissue and pathologist assessment of RF-energy impact to the tissue, if any, from use of the Eximis CS device
Inclusion Criteria:	Subject will be eligible for inclusion only if all of the following criteria apply: - Age ≥ 21 and < 50 years. - Planned laparoscopic hysterectomy or myomectomy. - Tissue specimen is < 11 cm in maximum diameter based on standard preoperative assessment. - Pre-operative evaluation which may include imaging, cervical cancer screening, and endometrial biopsy has been completed. - Signed informed consent. - Willing to adhere to protocol requirements and complete follow-up.
Exclusion Criteria:	Subject will not be eligible for inclusion if any of the following criteria apply: - Subject is post-menopausal, defined as amenorrhea > 12 months in the absence of ovulation suppression. - Known or suspected malignancy of gynecological origin as determined by standard clinical practice. - Candidate for en bloc tissue removal, for example through the vagina or via a mini-laparotomy incision. - Hemoglobin < 8 g/dl within 30 days prior to surgery. - Subject has a current history of undiagnosed genital bleeding. - Subject has an implanted electronic device where use of radiofrequency (RF) energy would be contraindicated (e.g., pacemaker, internal defibrillator). - Medical condition, surgical history, or intra-operative findings, which in the opinion of the investigator, precludes utilization of the Eximis CS System. - Known allergy to polyurethane, polyethylene, thermoplastic fluoropolymer and/or chlorinated polyvinyl chloride. - Concurrent participation in another therapeutic or interventional clinical trial with investigational pharmaceutical agent(s) or medical device(s) that could impact evaluation of this study as determined by the Investigator. - Inability to comply with the study procedures or follow-up in the opinion of the investigator. - Subject is pregnant. - Intraoperative Exclusion: Abdominal wall thickness at the umbilicus incision site is > 8 cm.
Number of Device Users (Surgeons) and Study Subjects Planned:	<u>Device Users (Surgeons)</u> This study will include 15 surgeons (males and females) with a range of laparoscopic gynecological surgery experience to confirm usability of the medical device by a representative range of potential users in an actual use setting. Each of the 15 surgeons will use the device once. An additional 10 procedures will be performed by the same surgeon group with no one surgeon performing more than 3 of the 10 additional procedures to assess repeat use of the system. <u>Subjects</u>

	The study will include 25 subjects who are undergoing laparoscopic hysterectomy or myomectomy where the Eximis CS System will be utilized for segmentation, containment and extraction of the target tissue. Subjects who are consented but do not undergo use of the Eximis CS device will be considered screen failures. Subjects who are consented, enrolled and treated will be included in the analysis cohort of 25 subjects. A minimum of five (5) (20%) of the subjects are to have a body mass index (BMI) > 30 kg/m² (lbs/in²).
Device User Training	<u>Investigators (Device Users)</u> Each surgeon's participation as the device user will include training by an Eximis representative per the training plan which has previously been validated. The training will include a PowerPoint® presentation, didactic/hands on training, a device demo video, review of the Eximis CS IFU and Eximis RF-100 Controller User Manual and practice use of the device in a benchtop model. The training will be completed prior to initial use of the device and will last approximately 1.5 hours. Surgeons will have access to the training materials at will. Refresher will be provided as requested by the User. The training will take place at the institution in a location suitable to allow for use of the device in a benchtop model prior to use of the device in a human. Bovine tongue will be used as the tissue for training, if not available, pork loin or another cut of meat will be used. <u>Operating Room Circulating Nurse (Equipment Set-up User)</u> The operating room circulating nurse who will be involved in setting up the equipment and connecting cables during use of the Eximis CS device will undergo training by an Eximis representative per the training plan which has previously been validated. The training will include a device demo video, a PowerPoint® presentation, hands on demonstration, practicum use of the Eximis RF-100 Controller and review of the Eximis CS Instructions for Use (IFU) and Eximis CS RF-100 Controller User Manual. The training will be completed prior to initial use of the device by the surgeon and will last approximately 30 minutes. Circulating nurses will have access to the training materials at will. Refresher training will be provided as requested by the User.
Study Design:	This is a prospective, multi-center, single-arm study to confirm device use safety and effectiveness in an actual use setting when utilized by gynecological surgeons during surgery for containment, segmentation and extraction of uterine tissue in premenopausal women undergoing laparoscopic hysterectomy or myomectomy for non-cancer indications. Usability data collection to support evidence that the device, as designed, can be used safely and effectively will include device use performance data (observational) and subjective (interview) data from the User (surgeon). • Observations regarding device use will occur during the surgical procedure by an Eximis representative/designee. • Following the surgical procedure in each of the 25 subjects, assessment of device usability will be documented via an interview with the surgeon and the surgeon's completion of a questionnaire. This process will take approximately 30 minutes.

	<u>Subjects</u> Eligible subjects who have signed an informed consent form (ICF) will be enrolled. Subjects will be sequentially enrolled and assigned a study identification number. Surgeons will be assigned a unique number. Subjects will undergo the standard of care in regard to all aspects of the surgical and follow-up procedures. The aspect unique to this study is the containment, segmentation, and extraction of the target tissue will utilize one integrated device, the Eximis CS System which segments tissue via segmenting wires using RF energy, there are no sharp blades utilized with this system. The device does not provide any therapeutic effect. Screening and follow-up will be based on data collected per standard of care in preparation and follow-up for the surgical procedure. All subjects will be followed for safety for a minimum of 30 days post-operatively through the post-procedure follow-up visit per standard clinical practice (standard clinical practice is approximately 4-6 weeks).
Study Duration:	The Human Factors usability aspect of the study will consist of observation and follow-up with the device users, which will be completed the day of the surgical procedure. Subject participation will be for approximately two months; the screening assessment is based on standard of care data, and follow-up will be according to standard of care with a minimum duration of 30 days; standard of care follow-up may be up to approximately six weeks after the surgical procedure. Overall study duration is anticipated to be four (4) to six (6) months from first subject first visit (FSFV) to last subject last visit (LSLV).
Safety Assessment:	Safety will be evaluated by assessment of adverse events, unanticipated adverse device effects (UADEs) and serious adverse events (SAEs) through the standard of care 30-day follow-up visit after use of the Eximis CS device. The safety of this trial will be monitored by an independent Data Safety Monitor (DSM) operating under a ratified charter. The DSM will review SAE/UADE reports on an ongoing basis. Additionally, the DSM will review listings summarizing the frequency and severity of AEs and other relevant safety information as defined in the DSM charter. The DSM will determine if the observed AEs are acceptable for this patient population and will make recommendations to the Sponsor regarding study continuation.

Sample Size and Data Analysis Methods	<u>Usability Device Use Safety and Effectiveness</u> The safety and effectiveness associated with device use in the intended setting will be assessed through successful completion of the procedure and the evaluation of close calls and/or use errors that have the potential to result in serious harm. Frequencies and percentages of completed procedures and safety related measures will be presented using the initial procedure for the 15 surgeons. An additional 10 procedures will be used to assess repeated use of the system. Observational data will be aggregated with the interview data and analyzed to determine the root cause of any close calls, use errors or problems that occurred combined with safety related measures including Capture Bag integrity and adverse events/adverse device effects. A recommendation for use of the Eximis CS System will be obtained from this review. No single statistical analysis will be used solely to direct the recommendation. <u>Capture Bag Integrity</u> Capture bags will be assessed for breach in containment after each procedure. The bags will undergo integrity testing for containment according to a separate, validated protocol at the conclusion of the procedure. The number and percentage of bags with a breach in containment will be presented. An upper one-sided 95% confidence interval for the breach in containment rate will be provided. <u>User and Subject Safety</u> The results of all 25 procedures will be used for analysis of safety. The frequency and severity of adverse events will be used to assess user and/or subject safety. The percentages of subjects experiencing the following will be presented: 1. Serious adverse events (SAEs) 2. Unanticipated adverse device effects (UADEs) 3. Any adverse event (AE) 4. Procedure related AEs/ADEs 5. Device-related AEs/ADEs In addition to percent of subjects, the number of adverse events will also be provided. <u>Sample Size</u> This study is a human factors usability study. A sample size of n=25 was chosen as it exceeds the minimum required by regulatory guidance for a human factor's usability study (Applying Human Factors and Usability Engineering to Medical Devices), allows for the assessment of repeated use, and collects additional data to further assess Capture Bag integrity.
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List of Abbreviations

ADE	adverse device effect
AE	adverse event
BMI	body mass index
CFR	Code of Federal Regulations
CIP	Clinical Investigational Plan
cm	centimeter
CRA	clinical research associate
CRF	case report form
CTA	clinical trial agreement
DI	deployment instrument
DSM	Data Safety Monitor
EBL	estimated blood loss
EDC	electronic data capture
Eximis CS	Eximis CS (Contained Segmentation)
FAS	full analysis set
FDA	Food and Drug Administration
FSFV	first subject first visit
GCP	good clinical practice
Hct	hematocrit
Hgb	hemoglobin
HF	human factor
IB	investigator's brochure
ICF	informed consent form
ICH	international conference of harmonization
ID	identification
IFU	instructions for use
ISO	organization for standardization
IUD	intrauterine device
L	liter
LSLV	last subject last visit
LMS	leiomyosarcoma
mL	milliliter
MIS	minimally invasive surgery
N	number
OR	operating room
RF	radiofrequency
SAE	serious adverse event
SOC	standard of care
SI	segmentation instrument
UADE	unanticipated adverse device effect

Terms and Definitions

Additional Procedures	The subsequent 10 clinical procedures performed by up to 10 surgeons with the investigational device; includes usability and clinical assessment.
Adverse Device Effect	Adverse event (AE) related to the use of the investigational medical device. This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation or any malfunction of the investigational medical device. This definition also includes any event resulting from use error or from intentional misuse of the investigational medical device.
Adverse Event	An AE is defined as any untoward medical occurrence in a patient or clinical investigation subject, temporally associated with the use of a medical device, whether or not considered related to the medical device and/or procedure. Therefore, an AE can be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of the medical device and/or procedure.
Close Call	Close calls are instances in which a user has difficulty or makes a serious use error that could result in serious harm, but the user takes an action to recover and prevents the serious harm from occurring.
Correct Use	Normal use without use error.
Critical Task	A user task which, if performed incorrectly or not performed at all, would or could cause serious harm to the patient or user, where harm is defined to include compromised medical care.
En bloc	Surgical removal of tissue as a whole, without prior dissection.
Duration of Eximis CS Procedure	From time of insertion of the deployment instrument until time of capture bag removal.
Duration of the Surgical Procedure	Duration of the surgical procedure is from skin incision to skin closure.
Initial Procedure	The first surgical procedure performed by each of the 15 surgeons utilizing the investigational device; includes usability and clinical assessment.
Serious Harm	Per Eximis Risk Management Plan, serious harm was categorized as severity (S) S4 (critical) or S5 (catastrophic).
Serious Use Error	A use error associated with a critical task that did or could result in serious harm.

Use Error	User action or lack of user action that was different from that expected by the manufacturer and caused a result that (1) was different from the result expected by the user and (2) was not caused solely by device failure and (3) did or could result in harm.
User	Person who interacts with (i.e., operates or handles) the device.
Use Safety	Freedom from unacceptable use-related risk.

1 INTRODUCTION

1.1 Background

Uterine fibroids are the most common benign pelvic tumors in women. Prevalence estimates range from 4.5% to 68.6% depending on study populations and diagnostic methods.¹ Based on ultrasonography, the estimated cumulative incidence of fibroids in women ≤ 50 years is higher for black (>80%) versus white women (~70%).² Approximately 25% to 50% of women with fibroids are symptomatic, experiencing heavy menses, reproductive issues, pain, increased urinary frequency, constipation, fatigue and anemia.³ Uterine fibroids are one of the leading causes of hospitalizations for gynecological disorders, and are the most frequent reason for hysterectomy in the USA.¹

Hysterectomy is the surgical removal of the uterus, whereas myomectomy is the surgical removal of uterine fibroids, while preserving the uterus. Symptomatic uterine fibroids are the most common indication for hysterectomy, and the only indication for myomectomy when a patient wishes to preserve her uterus and her option for fertility. The surgical approach to hysterectomy or myomectomy depends on multiple factors, including the number, size and location of uterine fibroids. These surgeries can be performed through an abdominal incision (laparotomy), or a laparoscopic or robotic approach, in which instruments are inserted through multiple small abdominal incisions (usually each 5-10 mm in size). In certain situations, hysterectomy can also be performed vaginally (without any abdominal incisions) and myomectomy can be performed through a hysteroscope if the fibroid is almost entirely within the uterine cavity. Approximately 500,000 hysterectomies and 34,000 myomectomies are performed in the United States each year, with hysterectomy the most common surgical procedure performed in non-pregnant women.^{4, 5}

1.2 Minimally Invasive Surgical Procedures

The benefits of minimally invasive surgery (MIS) for gynecological and surgical procedures are well documented and include decreased risk of both major and minor complications including decrease blood loss, transfusion, pulmonary complications, infection, thromboembolic events, reduced hospital stay, less postoperative pain with improved quality of life, body image, return to baseline function and lower direct and indirect costs.^{3, 6-10} However, these surgeries do have a unique technological challenge, the safe removal of large masses of tissue through a small incision.

Morcellation is a mechanism to reduce the size of large tissue specimens with the intent to remove them from small openings in the body and has been used in gynecologic surgery for over 90 years.¹¹⁻¹³ Electromechanical morcellation devices were introduced into surgical practice in 1993 for use in various specialty surgeries. In recent years, the risk of dissemination of occult malignancy in the peritoneal cavity at the time of morcellation, particularly in leiomyosarcoma (LMS), has come under scrutiny and a safety communication was issued by the US Food and Drug Administration (FDA) in April 2014 informing patients and clinicians that the use of power

morcellators may increase the risk of spreading unsuspected cancerous tissue.¹⁴ In November of 2014, after a public forum and panel meeting, FDA required that manufactures of laparoscopic power morcellators with a general indication or a specific gynecologic indication include a specific “black box warning” in their labeling to inform health care providers and patients about these potential risks.^{14,15} Even in the absence of undiagnosed cancer, there is also concern about the dissemination of benign tissue, with potential consequences including disseminated peritoneal leiomyomatosis or iatrogenic endometriosis. The controversy surrounding uncontained power morcellators and the resulting reduction in the use of minimally invasive surgery in benign gynecology is reflected by the decline in laparoscopy to perform hysterectomy.^{16, 17} This decline in the use of laparoscopic hysterectomy has been associated with an accompanying increase in abdominal hysterectomy, increase in major surgical, non-transfusion complications and 30-day hospital readmission.¹⁸

To mitigate the risk of tissue dissemination while maintaining the benefits of minimally invasive hysterectomy for patients with large tissue specimens, manual or power morcellation is now often done within containment bags. However, currently available systems are cumbersome and have been associated with prolonged operative time.¹¹⁻¹³ Thus, there is a need for efficient, safe methods to collect, contain, segment, and extract tissue in a way that minimizes the risk of tissue dissemination, preserves the tissue for pathological assessment, and affords the benefits of MIS.

1.3 Novel Device

Eximis Surgical, Inc. (Eximis) has developed a new medical device that incorporates a specimen retrieval bag with an integrated electrosurgical tissue segmentation mechanism. The device allows for tissue containment and segmentation within the body cavity after the opening of the bag has been exteriorized. Once the tissue is segmented into smaller pieces, the tissue is then removed from the exteriorized bag opening located at the laparoscopic incision site.

2 DEVICE DESCRIPTION

The Eximis CS (Contained Segmentation) System consists of 3 main components as shown in Table 2-1.

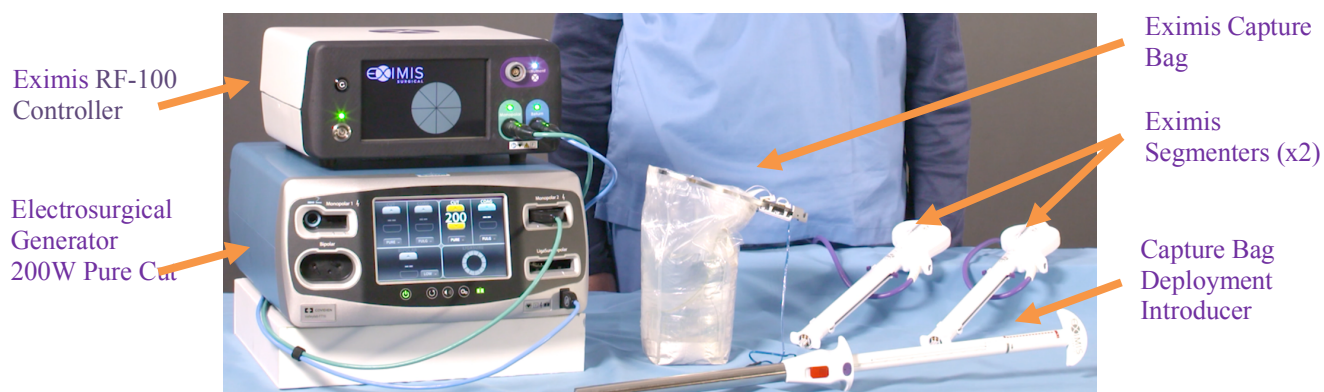
Table 2-1: Components of the Eximis CS System

Part Number	Device	Quantity	Description
CB-900-CLIN	Eximis Capture Bag	1	2.2 cm diameter introducer tube 24.4 cm introducer tube length 11 cm diameter bag opening, 900 mL 24 cm bag depth - Single-use
SI-900-CLIN	Eximis Segmenter	2	2.1 cm diameter insertion tube 17.6 cm insertion tube length - Wire receptacle for bag connection and segmentation - Single-use
RF100-CLIN	Eximis RF-100 Controller & Controller Cable	1	The controller is the interface between the Eximis Segmenter and the electrosurgical generator

The Eximis CS system is to be used with an electrosurgical generator capable of 200W monopolar pure cut setting.

The Eximis CS Capture Bag and Segmenter tissue contact materials were selected based upon performance as well as their known use in medical devices. The use of these materials is not associated with known allergic or adverse tissue reactions.

Figure 2-1: The Eximis CS System

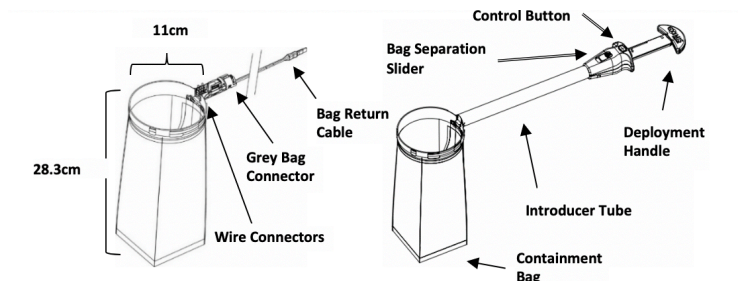


2.1 Eximis Capture Bag

The Eximis Capture Bag (Figure 2-2) is designed to be delivered into the abdomen for specimen retrieval and containment during segmentation. The Capture Bag is rolled up within the introducer tube until it is deployed in the abdomen. The Capture Bag consists of three individual bag layers whose purpose is to contain the specimen during segmentation and extraction. Two (2) sets of segmenting wires are attached to the inner surface bag. These wires are the active electrodes and are used to deliver the radiofrequency (RF) energy required to segment the tissue specimen. Once

the tissue specimen is contained in the Capture Bag, the opening of the bag is fully exteriorized and can then be connected to the Eximis Segmenter.

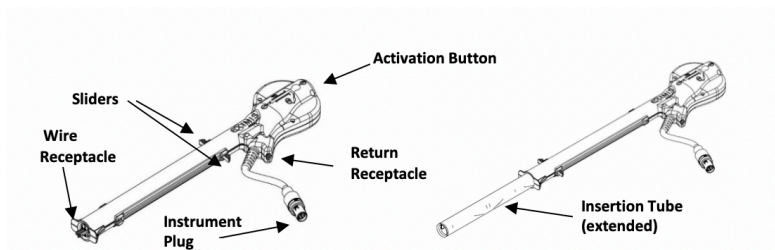
Figure 2-2: The Eximis Capture Bag



2.2 Eximis Segmenters

Two Eximis Segmenters (Figure 2-3) are required for each procedure. Each Segmenter is identical and delivers RF energy and a mechanical, controlled force to the segmenting wires to facilitate a rapid segmentation of the tissue as the wires are drawn from the Capture Bag through the tissue into the instrument. The Eximis Segmenter requires connection to the Eximis RF-100 Controller and an electrosurgical generator capable of 200W pure cut. Each instrument will activate a set of 4 segmenting wires that segment the tissue for removal through a small incision.

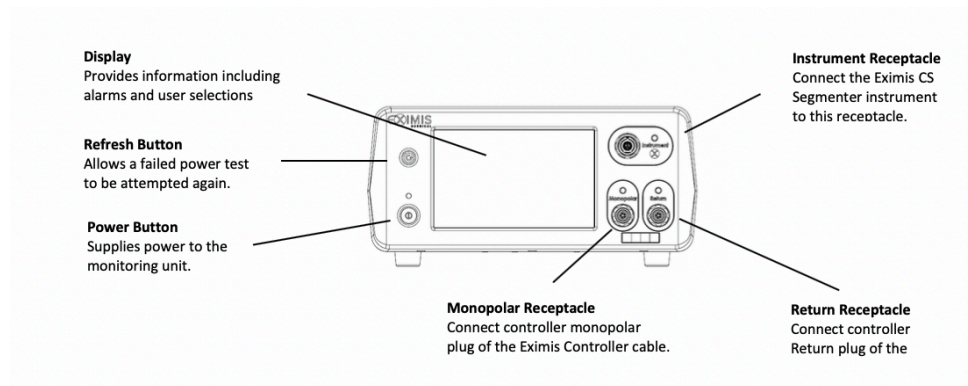
Figure 2-3: The Eximis Segmenter



2.3 Eximis RF-100 Controller

The Eximis RF-100 Controller (Figure 2-4) interfaces between the Eximis Segmenter and the electrosurgical generator. Electrosurgical generators with 200W pure cut setting are compatible with the Eximis CS. The Eximis RF-100 Controller uses the electrosurgical generator to deliver RF power to the segmenting wires. It also monitors the RF power delivered from the generator to the Eximis Segmenter to determine that sufficient power is being delivered in a safe and effective manner. The Eximis RF-100 Controller has a display and audible tones to provide information to the user during the procedure.

Figure 2-4: The Eximis RF-100 Controller

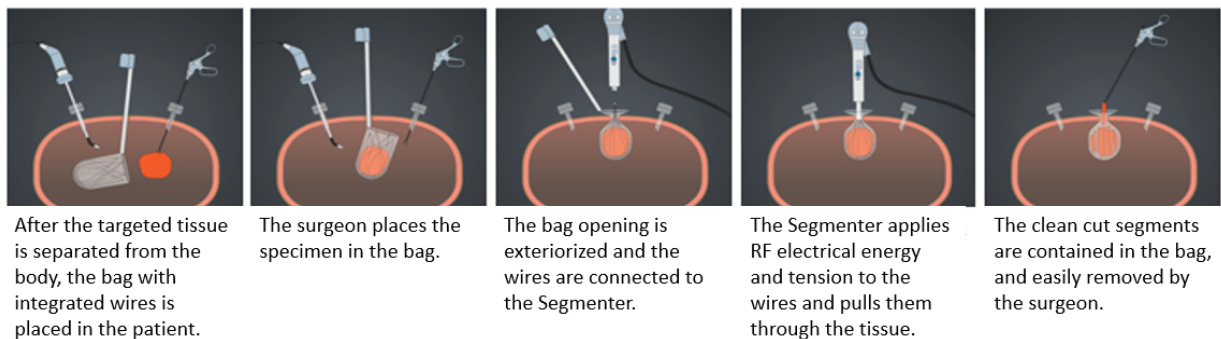


2.4 Principles of Operation

The Eximis CS System is an integrated system to provide containment, segmentation, and extraction of tissue during minimally invasive gynecological surgical procedures.

A schematic of the steps for device use are provided in Figure 2-5.

Figure 2-5: The Eximis CS System Procedures



The Eximis CS device includes an integrated bipolar electrosurgical wire cutting mechanism to allow cutting of large tissue specimens that are loaded into the Capture Bag. The Capture Bag is designed with wires and a return electrode. The cutting mechanism is automatic by press of a button on the Eximis CS Segmenter. The wire spacing is 2.2 and 2.4 cm, thus providing segmented tissue for slide preparation and pathology assessment yet able to be withdrawn through a small incision. The clean-cut tissue is removed from the Eximis CS Capture Bag using atraumatic instruments such as ring forceps.

Figure 2-6: Tissue Segmentation within Eximis CS System Capture Bag

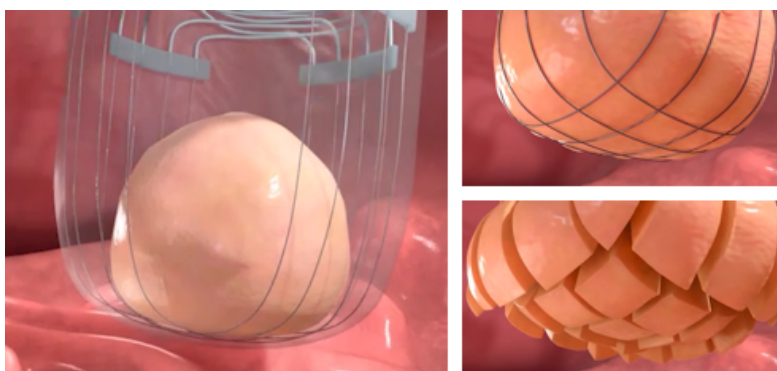


Figure 2-7: Segmented Bovine Tongue per the Eximis CS System



Detailed information and instructions are provided prior to use during the required validated training process, in the Eximis CS IFU, the Eximis CS RF-100 Controller User Manual, and the Quick Reference Card.

3 INDICATION FOR USE

The Eximis CS (Contained Segmentation) System is an integrated system intended for containment, segmentation, and extraction of tissue; indicated for use during laparoscopic gynecological surgical procedures.

4 NONCLINICAL STUDIES

The safety and efficacy of the Eximis CS System has been characterized via nonclinical, bench, usability, and performance testing studies. The nonclinical studies include evaluations of biocompatibility/materials, sterility, performance testing, thermal testing, software verification and validation, Capture Bag integrity testing, performance testing in a porcine model for training and design validation and a human factors simulated-use validation study where gynecologists utilized the device to contain, segment and extract bovine tongue in a porcine model. Taken

together, these studies support the safety of the Eximis CS System for this confirmatory usability validation study in an actual use setting.

4.1 Pre-Clinical Simulated-use Validation Study

Fifteen (15) gynecological surgeons with a broad range of experience participated in the pre-clinical human factors simulated use validation study. The surgeons utilized the Eximis CS device in a pre-clinical laboratory operating room to contain, segment, and extract bovine tongue from a laparoscopic umbilical incision in a porcine model.

The results demonstrated that first time users following completion of the validated training plan could complete all critical tasks without use errors or close calls. No design flaws were identified that could cause use errors related to harm. All users successfully completed all use scenarios and demonstrated that they understood the procedure and had adequate knowledge of the limitations noted in the product labeling (warnings). Integrity of the Capture Bag was evaluated by containment testing following use. All bags passed with the exception of one bag that was deemed unevaluable as it was clearly damaged during transport from the laboratory to the test facility. There were no observed adverse device effects with use of the device. Preclinical human factors validation was successful in demonstrating that the user interface and device operations, labeling, and training are acceptable and there was no required action to further reduce use-related risks. Post interviews with the participants provided a favorable qualitative assessment of the device use and its function.

For detailed information about the nonclinical studies, refer to the current Eximis CS System IB.

5 CLINICAL TRIAL EXPERIENCE

This will be the first in human use of the Eximis CS System.

6 RATIONALE FOR THE CURRENT STUDY

Eximis has conducted pre-clinical usability studies to evaluate if intended users are able to utilize the device without making errors that would compromise performance of the device or use safety and effectiveness. This study is to confirm the preclinical device evaluation results in an actual use setting by demonstrating that the Eximis CS System can be used by intended users without use error that could result in serious harm to the patient or user, for the product's intended use and under the expected use conditions as required for regulatory agency clearance for commercial use.

7 OBJECTIVES

7.1 Primary Objective

1. Evaluate usability to confirm device use safety and effectiveness in an actual use setting.

7.2 Secondary Objectives

1. Evaluate integrity of the Eximis CS Capture Bag by containment testing following use.
2. Evaluate user and subject safety.

8 ENDPOINTS

8.1 Primary Endpoint

1. The number of procedures where all critical tasks related to the Eximis CS are performed without serious use error.

8.2 Secondary Endpoints

1. Number of procedures successfully completed with use of the Eximis CS device.
2. Number of Capture Bags with breach of containment.
3. The number and severity of user adverse events caused by use error.
4. The number and severity of subject adverse events caused by use error.
5. All other adverse events.

8.3 Additional Measures (For Informal Evaluation)

1. Duration of the segmentation/extraction procedure (from insertion of the Eximis CS deployment instrument into the abdomen until removal of the Eximis CS Capture Bag from the abdomen).
2. Duration of the surgical procedure (from skin incision to skin closure).
3. Length of incision (mm) used for the Eximis CS device at procedure end (removal of Eximis CS Capture Bag).
4. Removed tissue weight (grams).
5. Number of extracted tissue segments per subject.
6. The size (mm) of the largest segment will be recorded defined as the segment with the largest cross-sectional area of the surface that is parallel with the incision opening.
7. Subject's pathology results of the extracted tissue and pathologist assessment of RF-energy impact to the tissue, if any, from use of the Eximis CS device.

9 INVESTIGATIONAL PLAN

9.1 Study Design

This is a prospective, multi-center, single-arm study to confirm device use safety and effectiveness in an actual use setting when utilized by gynecological surgeons during surgery for containment, segmentation and extraction of uterine tissue in pre-menopausal women undergoing laparoscopic hysterectomy or myomectomy for non-cancer indications.

Investigators (Device Users)

Fifteen (15) gynecologists with a range of laparoscopic gynecological surgery experience will utilize the Eximis CS System during the surgical procedure for containment, segmentation, and extraction of the target tissue. Each surgeon's participation as the device user will include the following:

- Training by an Eximis representative per the training plan which has previously been validated (see Section 20.5.2).¹⁹
- Observations regarding device use will occur during the surgical procedure by an Eximis representative/designee.
- Following the surgical procedure in each of the 25 subjects, assessment of device usability will be documented via an interview with the surgeon and the surgeon will complete a questionnaire. This process will take approximately 30 minutes.

Each of the 15 surgeons will use the device once. An additional 10 procedures will be performed by the same surgeon group with no one surgeon performing more than 3 of the 10 additional procedures to assess repeat use of the system.

Operating Room Circulating Nurse (Equipment Set-up User)

The operating room circulating nurse who will be involved in setting up the equipment and connecting cables during use of the Eximis CS device will undergo training by an Eximis representative per the training plan which has previously been validated. The training will be completed prior to initial use of the device by the surgeon and will last approximately 30 minutes (see Section 20.5.2).¹⁹

Subjects (Treated Patients)

Eligible subjects who have signed an informed consent form (ICF) will be enrolled. Subjects will be sequentially enrolled and assigned a study identification number which will consist of the unique site number followed by sequential subject numbering. Surgeons will be assigned a unique number consisting of a site number and sequential surgeon numbering.

Subjects will undergo the standard of care in regard to all aspects of the surgical and follow-up procedures. The aspect unique to this study is the containment, segmentation, and extraction of the target tissue will utilize one integrated device, the Eximis CS System which segments tissue via segmenting wires using RF energy, there are no sharp blades utilized with this system. The device does not provide any therapeutic effect.

Screening and follow-up will be based on data collected per standard of care in preparation and follow-up for the surgical procedure.

All subjects will be followed for safety for a minimum of 30 days (standard clinical practice is four to six-week follow-up) post-operative, as per standard clinical practice.

9.2 Study Duration

The Human Factors usability aspect of the study will consist of observation of device use during surgery and follow-up with the device users (surgeon) which will be completed the day of the surgical procedure.

Subject participation will be for approximately two months; the screening assessment which is based on standard of care information with follow-up for a minimum duration of 30 days per standard of care (standard clinical practice is four to six-week follow-up) after the surgical procedure.

Overall study duration is anticipated to be four (4) to six (6) months from first subject first visit (FSFV) to last subject last visit (LSLV).

10 PARTICIPANTS

Device Users (Surgeons)

This study will include 15 surgeons (males and females) with a range of laparoscopic gynecological surgery experience to confirm usability of the medical device by a representative range of potential users in an actual use setting.

Subjects (Patients)

The study will include 25 subjects who are undergoing laparoscopic hysterectomy or myomectomy where the Eximis CS System will be utilized for segmentation, containment and extraction of the target tissue.

Subjects who are consented but do not undergo use of the Eximis CS device will be considered screen failures. Subjects who are consented, enrolled and treated will be included in the analysis cohort of 25 subjects.

A minimum of 20% of the subjects are to have a body mass index (BMI) $> 30 \text{ kg/m}^2$ (lbs/in^2).

10.1 Inclusion Criteria

Subject will be eligible for inclusion only if all the following criteria apply:

1. Age ≥ 21 and < 50 years.
2. Planned laparoscopic hysterectomy or myomectomy.
3. Tissue specimen is $< 11 \text{ cm}$ in maximum diameter based on standard preoperative assessment.

4. Pre-operative evaluation which may include imaging, cervical cancer screening, and endometrial biopsy has been completed.
5. Signed informed consent.
6. Willing to adhere to protocol requirements and complete follow-up.

10.2 Exclusion Criteria

Subject will not be eligible for inclusion if any of the following criteria apply:

1. Subject is post-menopausal, defined as amenorrhea >12 months in the absence of ovulation suppression.
2. Known or suspected malignancy of gynecological origin as determined by standard clinical practice.
3. Candidate for en bloc tissue removal, for example through the vagina or via a mini-laparotomy incision.
4. Hemoglobin < 8 g/dl within 30 days prior to surgery.
5. Subject has a current history of undiagnosed genital bleeding.
6. Subject has an implanted electronic device where use of RF energy would be contraindicated (e.g., pacemaker, internal defibrillator).
7. Medical condition, surgical history, or intra-operative findings, which in the option of the investigator, precludes utilization of the Eximis CS System.
8. Known allergy to polyurethane, polyethylene, thermoplastic fluoropolymer and/or chlorinated polyvinyl chloride.
9. Concurrent participation in another therapeutic or interventional clinical trial with investigational pharmaceutical agent(s) or medical device(s) that could impact evaluation of this study as determined by the Investigator.
10. Inability to comply with the study procedures or follow-up in the opinion of the investigator.
11. Subject is pregnant.
12. Intraoperative Exclusion: Abdominal wall thickness at the umbilicus incision site is > 8 cm.

11 ENROLLMENT

11.1 Recruitment Process

This is a multi-center study; each investigational site will recruit subjects according to the site's standard procedures. Recruitment material, if applicable, will be reviewed and approved by the Institutional Review Board (IRB) prior to implementation.

11.2 Informed Consent Process

Prior to subject participation in this study, the Investigator must obtain written IRB approval for the study protocol and the ICF. The approved ICF form will clearly reflect the IRB approval date.

A copy of the site-specific subject ICF form must be provided to the sponsor/designee for review and approval prior to submission to the IRB for approval. Once approved, the subject ICF form must be provided to the Sponsor prior to implementation in this study. All study subjects must provide written informed consent using the sponsor and IRB approved ICF.

Once the subject's initial eligibility has been determined, the Investigator or designee, who has been trained on the study protocol, will explain in lay terms the nature and scope of the study, potential risks and benefits of participation, answer questions for the subject and obtain informed consent if the subject is interested in participating in the study. Potential subjects will be given as much time and privacy as necessary to review the ICF, to ask any questions and to provide an opportunity to discuss potential participation with others outside the study team. If the subject agrees to participate, the ICF form must be read by the subject and signed and dated by the subject and the person completing the consent process. The ICF will be obtained prior to initiating any study specific procedure that is not considered standard of care. The original ICF form will be kept in the subject's record, and a copy will be provided to the subject. The original ICF form will remain in the study files. A note about the subject's participation will be written in the subject's medical record. Study subjects will be assured that they may withdraw from the study at any time and for any reason.

Failure to obtain a signed ICF prior to enrollment constitutes noncompliance with the Declaration of Helsinki, Good Clinical Practice (GCP), US Code of Federal Regulations (21 CFR 50 and 21 CFR 812) and International Organization for Standardization (ISO) 14155:2020.

11.3 Enrollment

Subjects who are consented but do not undergo use of the Eximis CS device will be considered screen failures. Subjects who are consented, enrolled and treated will be included in the analysis cohort of 25 subjects. The investigational site will maintain a screening/enrollment log.

12 STUDY PROCEDURES

12.1 Users (Surgeons)

1. Information collected pertaining to the Users includes the following: medical specialty, training background and volume of gynecological laparoscopic hysterectomy and/or myomectomy surgeries/year.
2. Validated training (training duration is approximately 1.5 hours) will be completed prior to initial use of the device. Date and time training completed will be documented.

12.2 Users (Operating Room Circulating Nurse)

1. The operating room (O.R.) circulating nurse, who will set up the equipment and connect cables during use, will be trained by an Eximis representative prior to use of the device during surgery. Date and time training completed will be documented.

12.3 Subject Screening

Patients will have undergone standard procedures and testing per clinical practice in preparation for surgery, which is unrelated to the potential use of the Eximis CS medical device. Retrospective review of data will be used to determine potential subjects for study participation and to obtain screening data from standard of care procedures. Subject data will be reviewed by the study team to assess eligibility for study participation. Limited de-identified data will be documented for screen failures. Subject information may not be captured for the study until informed consent has been obtained.

Data from the following standard of care procedures in preparation for surgery will be collected.

1. Review eligibility for study participation
2. Obtain consent
3. Medical and surgical history
4. Demographic information (date of birth, race, ethnicity)
5. Subject's height and weight; body mass index (BMI) will be calculated
6. Gynecological examination
7. Characterization of target tissue
 - a. Target tissue (uterus or uterine fibroids)
 - b. Uterine dimension (length, width, anteroposterior diameter in cm)
 - c. Total number and size of each measured fibroid (cm), if applicable
 - d. Additional characterization of tissue (e.g., calcification as identified per scans, adenomyosis), if applicable

Note: The Eximis CS should not be used with tissue specimens that contain foreign materials except for surgical staples and non-metal sutures. Damage to the bag, inability to segment the specimen, poor segmentation performance or higher than normal temperatures in the tissue specimen may occur

8. Preoperative evaluation diagnostic results as done per standard clinical practice per surgeon assessment²⁰:
 - a. Cervical cancer screening
 - b. Endometrial biopsy
 - c. Imaging
9. Hemoglobin (Hgb) concentration (g/dL) and/or hematocrit (%) (Hct) within 30 days prior to surgery
10. Pregnancy test results on day of surgery

12.4 Day of Surgery

12.4.1 Subject Information

1. Surgical procedure (e.g., laparoscopic hysterectomy vs myomectomy)
2. Measure abdominal wall thickness at the umbilicus incision site. If > 8 cm, an alternate method of segmentation and extraction should be used as the Eximis Segmentation instrument may not be long enough to work effectively.
3. Duration of the surgical procedure (minutes) (from skin incision to skin closure)
4. Location of incision used for Eximis CS device (e.g., umbilicus)
5. Length of incision (mm) used for the Eximis CS device at procedure end (removal of Capture Bag)
6. Record if additional tissue removal technique was utilized for multiple specimens:
 - a. Method used
 - b. Reason used
 - c. Length of incision (mm) upon completion of all tissue extraction
7. Method of fascial closure of incision used for Eximis CS device (type of suture, use of fascial closure device, running or interrupted suture, number of stitches if interrupted sutures used)
8. Estimated blood loss (EBL) (mL) at procedure end
9. Record AEs, SAEs and UADEs. All AEs will be recorded from use of the Eximis device during surgery through the final follow-up or early termination visit (see Section 17)
10. Pathology results of the extracted tissue
11. Pathologists assessment of impact of RF-energy, if any, to the tissue from use of the Eximis CS Device

12.4.2 Device Usability and Performance Information

Eximis representatives/designees will capture the following during and following the surgical procedure (see Section 14).

1. Eximis CS equipment lot and serial numbers
2. Off the shelf generator manufacturer and model
3. Power setting of the electrosurgical generator during device use
4. Device used to load specimen into Capture Bag
5. Eximis CS procedure duration (from insertion of the Eximis deployment instrument into the abdomen until removal of the Capture Bag from the abdomen)
6. Device used to remove segmented tissue from Capture Bag
7. Usability will be evaluated via
 - a. Observation of device use during the surgical procedure documenting correct use, close call or use error
 - b. Post-procedure interview and completion of questionnaire with each User (surgeon)
8. Specimen characteristics per subject

- a. Characterization of extracted tissue (e.g., soft, firm, calcified, grainy, dispersed, degenerated) as assessed by the surgeon
 - b. Removed tissue weight (grams)
 - c. # segments
 - d. The size (mm) of the largest segment will be recorded, defined as the segment with the largest cross-sectional area of the surface that is parallel with the incisional opening.
9. Photograph of the segmented tissue
 10. Surgeon inspection of used Capture Bag for evidence of breach in containment
 11. Photographs of the used Capture Bag
 12. Integrity of the Capture Bag by containment testing following use (see Section 15)
 13. Any complications (adverse device effects) observed during use of the device
 14. Device malfunction(s) observed during use of the device

12.5 End of Study/Early Termination

Standard of care assessment data will be collected for all subjects for whom the Eximis CS System was utilized during surgery, which will occur a minimum of 30 days post-operatively as per standard of care (standard clinical practice is follow-up four to six-weeks post-procedure).

In the event that a subject withdraws consent for study participation, an early termination assessment should be completed as close as possible to the time when consent was withdrawn.

The following will be completed for the follow-up and/or the early termination assessment:

1. Gynecological examination
2. Record AEs, ADEs, SAEs, and UADEs (see Section 17)

Table 12-1: Schedule of Procedures

Study Requirements	Screening (per SOC*)	Prior to Initial Device Use	Day of Surgery (Day 0)	Study Term (≥ 30 days [SOC approx. 4-6 wks.]
Surgeons (Users)				
Record medical specialty, training background and practice data on Form provided	X			
Validated training (~1.5 hours) completed prior to first use of the device. Date and time training completed will be documented.		X		
Post-op interview with User (surgeon)			X	
Completion of HF Form: Post-Procedure User Questionnaire (open fields)			X	
OR Circulating Nurse (User)				
Validated training (~30 mins) completed prior to first use of the device. Date and time training completed will be documented.		X		
Subjects (Patients undergoing Surgery)				

Study Requirements	Screening (per SOC*)	Prior to Initial Device Use	Day of Surgery (Day 0)	Study Term (≥ 30 days [SOC approx. 4-6 wks.])
Eligibility and Informed Consent	X			
Medical/surgical history	X			
Demographics (date of birth, race, ethnicity)	X			
Height and weight	X			
Gynecological examination	X			X
Characterization of target tissue	X			
Cervical cancer screening results	X ¹			
Endometrial biopsy results	X ¹			
Imaging results	X ¹			
Hgb and/or Hct within 30 days of surgery	X			
Pregnancy test results the day of surgery	X			
Subject pathology results			X	
Pathologists assessment of impact of RF-energy, if any, to the tissue from use of the Eximis CS Device			X	
Record AEs, ADEs, SAEs, UADE			X	X
Surgery and Device Performance Information				
Surgical procedure (lap hysterectomy vs myomectomy)			X	
Measure abdominal wall thickness prior to use of the Eximis CS device			X	
Duration of the surgical procedure (minutes)			X	
Location of incision used for Eximis CS device			X	
Length of incision used for Eximis CS device at procedure end (removal of Capture Bag)			X	
Record if additional tissue removal technique was utilized for multiple specimens (method used, reason used and length of incision upon completion of all tissue extraction)			X	
Method of fascial closure of incision used for Eximis CS device			X	
Estimated blood loss (EBL) at procedure end			X	
Eximis CS equipment lot and serial numbers			X	
Off the shelf generator manufacturer and model			X	
Power setting of the electrosurgical generator during use			X	
Device used to load specimen into Capture Bag			X	
Eximis CS procedure duration			X	
Device used to remove segmented tissue from Capture Bag			X	
Observational data collection of device use			X	
Specimen characteristics			X	
Characterization of the extracted tissue per surgeon's assessment			X	

Study Requirements	Screening (per SOC*)	Prior to Initial Device Use	Day of Surgery (Day 0)	Study Term (≥ 30 days [SOC approx. 4-6 wks.])
Photograph of the segmented tissue			X	
Surgeon inspection of used Capture Bag			X	
Photographs of the used Capture Bag			X	
Integrity testing of Capture Bag following use			X	
Any complications (adverse device effects) observed during device use			X	
Device malfunctions			X	

*SOC = standard of care ¹As done per standard clinical practice per surgeon assessment.

13 STUDY DISCONTINUATION

All subjects are free to withdraw from study participation at any time and for any reason, specified or unspecified, and without prejudice. Similarly, an Investigator may discontinue any subject from study participation for any reason. The reason for the study discontinuation will be recorded in the CRF.

13.1 Early Discontinuation/Study Termination

Reasons for a subject's withdraw from study participation or termination of the study by the Sponsor may include, but are not limited to the following:

1. Subject refuses follow-up and withdraws consent
2. Investigator decision
3. Sponsor decision
4. Subject is lost to follow-up
5. Subject death

14 HUMAN FACTORS METHODOLOGY

Usability data will be collected on all 25 procedures to support evidence that the device, as designed, can be used safely and effectively will include device use performance data (observational) and subjective (interview) data from the User (surgeon).

The usability portion of the clinical protocol will begin at the start of the Eximis CS procedure and will be complete once the Eximis CS Capture Bag is removed from the subject.

Eximis representatives will be present during use of the Eximis CS system, with roles as outlined below:

Eximis Trainer/Representative: This person will conduct validated training for the Users and will be present during use of the device in surgery.

Observer/Scribe: This person is responsible for observations of device use (correct use, close calls or use error) and any observed adverse device effects during use as well as to conduct a post-use debriefing interview with each User (surgeon).

Engineer: The Engineer documents equipment details, performs extracted tissue assessment (weight, measurement, count, photo of segmented tissue and photographs of the used Capture Bag), and performs Integrity of the Capture Bag by containment testing following use.

As outlined in the Eximis CS IFU and the Eximis RF-100 Controller User Manual, the natural workflow for use of the Eximis CS System is as follows:

- System set-up, connecting the Eximis RF-100 controller to the electrosurgical generator, attaching cables and preparing devices for use
- Insert Capture Bag Introducer Tube into incision;
- Deploy the Capture Bag in the subject's peritoneal cavity;
- Load the target tissue specimen into the Capture Bag, retract bag and exteriorize the bag opening;
- Prepare bag; release DI from bag, inflate and inspect
- Receive first Segmentation Instrument (SI1), attach to controller and to bag. Extend insertion tube into bag;
- Perform segmentation with Segmentation Instrument;
- Receive second Segmentation Instrument (SI2), attach to controller and to bag. Extend insertion tube into bag;
- Perform segmentation with Segmentation Instrument (SI) 2;
- Remove the segmented tissue from the Capture Bag, and;
- Remove the Capture Bag from the abdomen.

Critical tasks are user tasks that, if performed incorrectly or not performed at all, would or could cause serious harm to the patient or user, where harm is defined to include compromised medical care. Per Eximis Risk Management Plan (RMP-001²¹), serious harm was categorized as S4 (critical) or S5 (catastrophic) as outlined in

Table 14-1 below.

Table 14-1: Severity Scale of Harm

Qualitative	DESCRIPTION	Quantitative
Negligible	User or patient inconvenience/nuisance or minor temporary discomfort. [Note: failure modes that have no effect to the user or patient are included in this severity ranking as a conservative estimation]	1
Minor	Minor impact on patient, user or third person, recoverable. Requires minimal professional medical attention.	2
Major	Injury/damage to patient, user or third person's health. Requires medical attention without sequelae (renders a condition that is permanent and always requires treatment).	3
Critical	Serious injury or permanent physical impairment to the patient or user, to patient, user or third person's health, requires surgical intervention. Injury may be life threatening if not treated by the physician. Might need to return for additional treatment/surgery.	4
Catastrophic	Death of patient, user or third person.	5

Critical tasks have been determined by the Sponsor per the use-related risk analysis as use errors that have the potential to result in serious harm (S4 or S5) (per internal documents Risk-003²² and RMP-001²¹) which are outlined in Table 14-2 below. The Task ID number is for correlation with Eximis internal documents. The potential effect (harm) is the worst-case scenario.

Table 14-2: Critical Task Associated Use Errors

Task	Associated Use Error	Potential Hazard	Potential Effect (Harm)
Task 10: Insert Capture Bag Introducer Tube into incision	U2.08 User aggressively inserts Capture Bag deployment instrument (DI) deep into peritoneal cavity	Capture Bag Tube damages intraperitoneal organs /structures/vessels	Non-target tissue injury (critical)
Task 022 Perform Segmentation with SI 1	U3.26 User proceeds to segmentation with partially exteriorized bag	Loss of containment	Intraperitoneal tissue dissemination (malignant)
Task 028 Perform Segmentation with SI 2	U3.58 User does not keep the scissor away from the Capture Bag while cutting the exposed wire to release	Loss of containment	Intraperitoneal tissue dissemination (malignant)
	U3.59 User does not ensure the SI Insertion Tube remains through the incision and in contact with tissue during tensioning or segmentation	Loss of containment	Intraperitoneal tissue dissemination (malignant)
	U3.62 Other electrosurgical instruments used simultaneously in second monopolar port, and contact of bag to surrounding peritoneum	Heat generation	Alternate site burn (irreversible)

Task	Associated Use Error	Potential Hazard	Potential Effect (Harm)
Task All: Can Occur at Multiple Steps	U8.02 User penetrates or grasps Capture Bag with non-traumatic instrument in an aggressive manner	Loss of containment	Intraperitoneal tissue dissemination (malignant)
	U8.03 Excessive manipulation or forces cause stretching and deformation to the Capture Bag until it ultimately rips (or is damaged)	Loss of containment	Intraperitoneal tissue dissemination (malignant)
	U8.04 User does not protect the Capture Bag while extending the incision	Loss of containment	Intraperitoneal tissue dissemination (malignant)
	U8.05 User places laparoscope in contact with the Capture Bag for a prolonged period of time	Loss of containment	Intraperitoneal tissue dissemination (malignant)

Eximis representatives will be present for device use during surgery. In the event that the company representatives observe the user about to perform a use error that could result in a potential serious harm, the representative would intervene and instruct the user accordingly. This would be captured as a close call on the study HF CRFs with the required intervention captured. A debrief interview will be conducted with the User to help determine root cause.

14.1 Direct Observations

The study observer will observe the device users and record their performance on each critical task as correct use, close call or use error. Any issues encountered related to the device use or performance will be recorded in the Sponsor HF Usability CRF. As well, any adverse device effect presenting during use of the device will be captured.

14.2 Post-Procedure Debrief Interview

Following each procedure, a debrief interview will be conducted with each User (surgeon) as follows:

- When a “close call” or “use error” box was checked on the HF Usability Case Report Form, the surgeon will be asked follow-up questions to better determine if a use error has occurred, and what might be the root cause.
- A set of general open-ended questions intended to allow for the collection of unbiased feedback will be completed by the User.

15 EXIMIS CAPTURE BAG INTEGRITY TESTING

The integrity of the Capture Bags will be tested according to internal Eximis protocol TP2020-021 by an Eximis representative via a validated test method (internal Eximis document WI-7.3-23) following utilization in an actual use setting. The test method uses electrical resistance

measurements to determine if a path exists for the transfer of fluid from the inside of the Capture Bag to the outside of the Capture Bag through holes greater than or equal to 1 micron. For the Capture Bag to pass, the electrical resistance reading must be greater than or equal to 9150 kΩ.

The test method utilizes 0.9% saline solution with 0.25 mM Polysorbate 20; a large capacity syringe, a reservoir with at least 2 L capacity, a Test Fixture, and a digital multimeter and connection accessories. All equipment for testing will be provided by Eximis and returned to Eximis upon completion of use. All tested bags will be retained by Eximis.

16 MEDICAL DEVICES

16.1 Investigational Device

16.1.1 Packaging and Labeling

The investigational device will be provided to the investigator(s) by the Sponsor. The Eximis CS Capture Bag and Segmenters are supplied sterile and are intended and labeled for single use. The Eximis CS system will be clearly labeled as an investigational device.

16.1.2 Storage

The investigational devices are to be stored in a cool, dry, secure place with access limited to the investigators and their designees. Devices should be with their original shipping materials. Proper care should be taken to ensure that the devices will not be damaged.

16.1.3 Accountability

The investigator or designee will maintain an inventory record of investigational devices received, used for treatment, otherwise discarded, and returned to the Sponsor.

The Investigator will not supply medical device materials to any surgeon who is not participating in the study.

Used Capture Bags will be retained by the Sponsor. Used materials (e.g., Segmentation Instruments and/or Deployment Instruments) may be retained by the Sponsor in the event further investigation is warranted as determined by Eximis representatives. Materials to be disposed of at the site are to be handled as per the study site's standard procedures. At the conclusion of the study, the Eximis RF-100 Controllers and controller cables and all unused materials will be returned to the Sponsor.

16.1.4 Devices for Training

Devices to be used for the benchtop training will be clearly labeled for training use only. Management and accountability of training devices will be done by Eximis representatives.

16.1.5 Device Concerns and Malfunctions

The study site will examine device shipments upon receipt to ensure that packaging and labeling is intact. Any potential damages or device malfunctions must be reported to the Sponsor. The Sponsor will document any device malfunctions/deficiencies observed during use of the device. The Sponsor will investigate all reported device concerns and malfunctions.

16.2 Electrosurgical Generator

The Eximis CS System is to be used with an electrosurgical generator capable of 200W monopolar pure cut setting. Eximis will provide a commercially available electrosurgical generator capable of 200W pure cut (e.g., ValleyLab Force FX) for use with the Eximis CS System when requested by study site(s).

Eximis will be responsible for ensuring the generator meets the manufacturer's specifications. The provided generator(s) will be labeled for Clinical Trial CIP2020-001 Use Only and will be returned to the Sponsor/designee at conclusion of use in this study, or at any time per the discretion of the study site or the Sponsor.

17 ADVERSE EVENTS/ADVERSE DEVICE EFFECTS

17.1 Potential Adverse Events of Laparoscopic Hysterectomy/Myomectomy

Hysterectomy and myomectomy are generally safe, but as with all major surgeries, complications can arise. Approximately 7.9% of women who undergo hysterectomy for a benign indication²³ and 11.7% of women undergoing myomectomy experience a complication related to surgery.²⁴ While many of these complications can be managed as an outpatient, 3% and 1.7% of all hysterectomy and myomectomy patients require readmission, respectively.^{24, 25} As described in the literature, the potential risks of hysterectomy and/or myomectomy include blood loss, transfusion, superficial and deep wound infection, venous thrombo-embolism, vascular, intestinal, and/or urinary tract injury, gas embolism, pain, nerve injury, and incisional hernia.²⁶⁻²⁹ It is well established that women undergoing a minimally invasive approach to hysterectomy or myomectomy have shorter hospital stay, less postoperative pain and less perioperative morbidity compared to those who undergo laparotomy.³⁰ Yet, in order to remove large tissue specimens without performing a laparotomy and incurring their associated risk, the tissue must be cut into tissue fragments and removed through small incisions.

As described in the literature, potential risks with manual or electromechanical tissue extraction methods include dissemination of previously unknown malignant tissue within the peritoneal cavity (which may worsen prognosis); dissemination of benign tissue (which may result in disseminated leiomyomatosis and iatrogenic endometriosis); rendering complete pathologic

evaluation of tissue specimen more difficult; and injury to adjacent organs unique to the technique of morcellation.^{12,31}

17.2 Potential Risks with Use of the Eximis CS System

This study is being conducted on an investigational device designed to contain and segment tissue to facilitate removal of large tissue specimens. The device does not provide any therapeutic effect for their underlying diagnosis for which they are undergoing hysterectomy or myomectomy. The subjects are following standard of care in the decision to perform hysterectomy and the surgical approach to hysterectomy or myomectomy, meaning the patients enrolled in the study are undergoing the surgical procedure whether the device is used or not. Therefore, the potential risks associated with this study are limited to the risks associated with the use of the device and confidentiality. Furthermore, because this is a follow-on study of a pre-clinical simulated use usability study, the actual risk in terms of likelihood of occurrence is believed to be sufficiently low and acceptable for clinical use. As with any medical device, there is always risk of extremely rare or previously unknown side effects developing from use of the device.

Table 17-1: Possible Risks to the Subject

Possible risks associated with RF energy
Thermal damage to adjacent tissue. In order for this to occur, the following sequence of events would need to happen: 1. A second monopolar instrument must be in the SAME generator as the Eximis CS (this risk does not occur if they are activating from a different generator) 2. The Containment Bag must be exteriorized, the Segmenter connected to the Controller AND the return cable connected to the Segmenter (the return is the last connection to the Segmenter and first connection to be removed after use) 3. The monopolar instrument must be activated in Coag mode (Cut does not pose a risk) 4. The activation must occur when the setup described in step 2 is created but will be disallowed while the Eximis CS activates (generator will not allow two activations to occur at the same time) 5. The return electrode portion of the bag would need to be in intimate contact with the patient tissue.
Risks related to single use medical devices (Capture Bag, Segmenter)
Sterility breach leading to infection.
Reaction or allergy to materials leading to adverse tissue reaction. Though not known to be allergens, the following are the device materials which are in contact with tissue: polyurethane, polyethylene, thermoplastic fluoropolymer and/or chlorinated polyvinyl chloride.
Aggressive insertion of the deployment instrument with potential for mechanical injury to adjacent structures.
Device failure and/or incomplete/inadequate segmentation that requires increasing the incision wider than what was intended.
Risks related to Capture Bag

Inadvertent damage to bag raising the potential of benign or previously unknown malignant intraperitoneal tissue dissemination.

17.3 Potential Risk to Users

The Eximis CS System may generate a minor amount of smoke during segmentation similar to other electrosurgical devices which could cause respiratory irritation. Electric shock may occur if the Eximis Controller RF-100 malfunctions, use of damaged or improperly maintained Controller cable, or if there are mitigation failures of the Eximis Segmenter and/or software. The electric shock would be of similar or lower magnitude to other devices.

17.4 Risk Mitigation

Each User will undergo formal device training by an Eximis representative prior to initial use of the device. Eximis representatives will be present during surgery to monitor device use and performance of the device. In the event that the company representatives observe the user about to perform a use error related to a potential serious harm, the representative would intervene and instruct the user accordingly. This would be captured as a close-call on the study HF CRFs with the required intervention captured. A debrief interview will be conducted with the User to help determine root cause. The study will be monitored to ensure the identification, documentation and analysis of adverse events, compliance with the protocol, and ethical requirements are in place for conducting research to protect the safety and well-being of all subjects.

Additionally, the Eximis CS System has design features built in to reduce or eliminate potential risks, as briefly outlined below.

17.4.1 Patient Selection

The indications for use limit enrollment in this study to patients who meet the inclusion/exclusion criteria. The device indications for use and patient selection criteria are specifically designed to reduce the risk of device use in patients with known or suspected malignancies. Subjects will be monitored before, during and after use of the device during surgery to help ensure their safety.

17.4.2 Eximis Capture Bag

The Capture Bag is intended to contain the target tissue once loaded into the bag, throughout segmentation and extraction. The bag consists of three individual bag layers, which are attached at the top, to mitigate potential transfer of cells and/or loss of containment. The outer bags are made of polyurethane and the middle bag is made of polyethylene. As noted in the IFU, only blunt objects such as ring forceps should be utilized to remove the segmented tissue; sharp surgical instruments such as scissors, scalpels or tenaculum's and power morcellation devices should not be used within or near the Capture Bag under any circumstance.

17.4.3 Eximis RF-100 Controller

The Eximis RF-100 Controller monitors the RF delivery with the following features:

- Senses the RF output of the electrosurgical generator to ensure proper energy is being delivered to the Eximis Segmenter
- Ensures proper contact of the tissue specimen with the return electrode within the Eximis Capture Bag with an internal specimen neutral electrode contact quality system
- Uses Arc Detect technology to ensure an efficient low temperature cut is being performed
- Ensures that the segmenting wires are progressing through tissue and not stalling
- If any of the previous conditions are not satisfied, the Eximis RF-100 Controller will disable RF delivery to that specific wire and will proceed to the next one

17.4.4 Thermal Risks

The Eximis CS device employs bipolar energy, an established effective modality for use in laparoscopic and open surgery.^{32,33} Bipolar energy results in very low surface temperatures on the outside of the bag during use. These temperatures remain well below other energy-based devices such as vessel sealing, bipolar and monopolar cutting and coagulation and ultrasonic dissectors.

The metal ring at the opening of the Capture Bag is completely isolated from the active and return electrodes in the bag so there is no risk of burn or shock.

For detailed information about the device, refer to the current Eximis CS IB, Eximis CS IFU and the Eximis RF-100 Controller User Manual.

17.5 Risk-Benefit Assessment

The Eximis CS was designed to provide an integrated, controlled containment, segmentation and extraction of tissue system indicated for use in minimally invasive gynecological and surgical procedures for which the benefits are well known and include significant improvements in morbidity and mortality compared with open surgery. The technology is designed to offer a unique solution as a fully integrated tissue containment, segmentation and extraction system which segments tissue via segmenting wires using RF energy, there are no sharp blades utilized with this system. The Eximis CS System employs bipolar energy, an established effective modality for use in laparoscopic and open surgery. This approach is designed to minimize the risk of tissue dissemination, a primary concern for women undergoing total hysterectomy where malignancy may be undiagnosed, results in reliably short procedure times and affords the significant clinical benefits associated with minimally invasive surgery. The three individual bag layers were designed to mitigate potential transfer of cells and/or loss of containment. Also, since the Eximis CS procedure results in clean-cut tissue segments for removal, a potential benefit is an improved tissue quality for histopathology.

17.6 Adverse Event Recording/Reporting

17.6.1 Adverse Event

An AE is defined as any untoward medical occurrence in a patient or clinical investigation subject, temporally associated with the use of a medical device, whether or not considered related to the medical device and/or procedure. Therefore, an AE can be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of the medical device and/or procedure.

Abnormal laboratory results must be recorded as AEs if any of the following conditions are met:

- The abnormal laboratory value leads to a therapeutic intervention.
- The abnormal laboratory value is considered to be clinically significant by the investigator.
- The abnormal laboratory value is considered to be related to use of the medical device by the investigator.

Examples of an AE **do not include**:

- Expected outcomes of the procedure.
- A medical or surgical procedure (e.g., ultrasound), although the condition that leads to the procedure may be an AE.
- Anticipated day-to-day fluctuations of pre-existing conditions present or detected at the start of the study that do not worsen.

17.6.2 Adverse Device Effect

Adverse event related to the use of the investigational medical device. This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation or any malfunction of the investigational medical device. This definition also includes any event resulting from use error or from intentional misuse of the investigational medical device.

17.7 Reporting of Adverse Events

Timely and complete reporting of AEs is essential. Monitoring and documentation of AEs allows for identification of treatment-related trends and for adherence to regulatory requirements.

17.7.1 Recording of Adverse Events

All AEs will be recorded from the time of device utilization during surgery through the final follow-up or early termination.

17.7.2 Grading of Adverse Events

All AEs will be graded using the following guidelines:

Grade refers to the severity of the AE. The Common Terminology Criteria for Adverse Events (CTCAE) Scale³⁴ displays Grades 1 through 5 with unique clinical descriptions of severity for each AE based on this general guideline:

-
- **Grade 1** – Mild: asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated.
 - **Grade 2** – Moderate: minimal, local or non-invasive intervention indicated; limiting age-appropriate instrumental ADL.¹
 - **Grade 3** – Severe: severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL.²
 - **Grade 4** – Life threatening or disabling: life-threatening consequences; urgent intervention indicated.
 - **Grade 5** – Fatal: Death related to AE.
-

¹Instrumental ADL refer to preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc.

²Self-care ADL refer to bathing, dressing, and undressing, feeding self, using the toilet, taking medications, and not bedridden.

17.8 Follow-up of Adverse Events

All AEs must be followed at a minimum through the final follow-up visit and until return to baseline, resolution or until the Investigator deems the event to be chronic, the patient stable, or the patient is lost to follow-up. All AEs must be followed in accordance with applicable regulatory requirements: 21 CFR 812 and/or ISO 14155-2020.

17.9 Relationship

The Investigator at each site will determine and document the relationship between the AE and study treatment (the Eximis CS medical device) and/or procedure. The following criteria, in addition to good clinical judgment, should be used as a guide for determining relationship:

Not Related: The event is clearly related to factors other than the study treatment and/or procedure(s), such as the patient's clinical state.

Possibly Related: The event follows a reasonable temporal sequence from the time of study treatment administration/procedure, and/or follows a known response pattern to study treatment/procedure(s) but could have been produced by other factors, such as the patient's clinical state or other therapeutic interventions.

Probably Related: The event follows a reasonable temporal sequence from the time of study treatment/procedure(s) and cannot be reasonably explained by other factors, such as the patient's clinical state or therapeutic interventions.

Definitely Related: The event follows a reasonable temporal sequence from the time of study treatment/procedure(s), and follows a known response pattern, and cannot be reasonably explained by other factors. In addition, the event occurs immediately following study treatment/procedure(s), improves on stopping the study treatment/procedure, and/or reappears on resumption of study treatment/procedure(s).

17.10 Serious Adverse Event/Unanticipated Adverse Device Effect

17.10.1 Definitions

SAEs are defined (21 CFR 812 and ISO 14155:2020) as those AEs meeting any of the following criteria:

1. Results in death
2. Led to serious deterioration in the health of the patient, that either resulted in
 - a life-threatening illness or injury, or
 - a permanent impairment of a body structure or a body function, or
 - in-patient or prolonged hospitalization, or
 - medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function.

NOTE: Planned hospitalization for a pre-existing condition or a planned procedure, without serious deterioration in health, is not considered a SAE.

UADEs are defined (21 CFR 812.3) as any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with a device, if that effect, problem or death was not previously identified in nature, severity, or degree of incidence in the CIP or IB, or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of patients.

NOTE: Anticipated adverse device effects are effects, which by nature, incidence, severity or outcome have been identified in the CIP and/or the IB.

17.10.2 SAE/UADE Reporting

In the interest of patient care and to allow the Sponsor to fulfill regulatory requirements, any SAE and/or UADE, regardless of causal relationship to study treatment or procedure(s), must be reported to the Sponsor within 24 hours of knowledge of the event.

Any SAE/UADE that occurs from utilization of the Eximis CS device during surgery through the final follow-up visit, regardless of relationship to the study treatment or procedures, must be reported within 24 hours of knowledge of the event, and the Sponsor/designee may request additional information from the Investigator to ensure the timely completion of accurate safety reports. Reporting of the event will occur by submitting a SAE/UADE Form to:

- Eximis Surgical, Inc.
- Email: ClinicalAffairs@EximisSurgical.com

Additionally, the SAE/UADE must be entered on the AE pages of the CRF. Follow-up reports relating to the subject's subsequent medical course after the SAE/UADE must be submitted to the Sponsor/designee and the reviewing IRB, according to the IRB reporting requirements, until either the event has subsided/resolved or until the subject's condition stabilizes and the likely overall clinical outcome has been ascertained (e.g., in the case of permanent impairment).

The Sponsor will be responsible for the following:

- Reporting SAE/UADEs to the regulatory authorities in accordance with applicable reporting regulatory guidelines
- Monitoring the safety of the study on an ongoing basis

The investigational site will be responsible for reporting all SAE/UADEs to the following:

- IRB, as required by local policy

17.10.3 Exclusions to SAE/UADE Reporting Requirements

The following are not considered SAEs/UADEs:

- Planned hospitalization.
- Anticipated day-to-day fluctuations of pre-existing conditions present or detected at the start of the study that do not worsen.

17.11 Safety Monitoring

It is the responsibility of the Investigators to oversee the safety of the study at his/her site.

The Sponsor representatives, including an engineer, will be present for device use during surgery to monitor device use and performance. In conjunction with the data safety monitor (DSM), the Sponsor/designee will review patient data, SAEs and UADEs to oversee the safety throughout the study.

17.11.1 Independent Data Safety Monitor

This trial will be monitored using an independent Data Safety Monitor (DSM), who is free of any conflict of interest, operating under a ratified charter. Qualifications for the DSM, at a minimum, shall include current experience with laparoscopic gynecological surgical procedures and management of the patient post-operatively and extensive research experience.

The DSM will review SAE/UADE reports on an ongoing basis. Additionally, the DSM will review listings summarizing the frequency and severity of UADEs and other relevant safety information as defined in the DSM charter. The DSM will determine if the observed AEs are acceptable for this patient population, and will make recommendations to the Sponsor regarding study continuation.

18 SAMPLE SIZE

This study is a human factors usability study. A sample size of $n=25$ procedures was chosen as it exceeds the minimum required by regulatory guidance for a human factor's usability study (Applying Human Factors and Usability Engineering to Medical Devices),³⁵ allows for the assessment of repeated use and collects additional data to further assess capture bag integrity.

19 DATA ANALYSIS METHODS

Continuous variables will be described using means, medians, and measures of dispersion, including standard deviation and ranges. Categorical variables will be summarized with frequencies and percentages.

19.1 Endpoints and Additional Measures

19.1.1 Primary Endpoint

1. The number of procedures where all critical tasks related to the Eximis CS are performed without serious use error.

19.1.2 Secondary Endpoints

1. Number of procedures successfully completed with use of the Eximis CS device.
2. Number of Capture Bags with breach of containment.
3. The number and severity of user adverse events caused by use error.
4. The number and severity of subject adverse events caused by use error.
5. All other adverse events.

19.1.3 Additional Measures (For Informal Evaluation)

1. Duration of the segmentation/extraction procedure (from insertion of the Eximis CS deployment instrument into the abdomen until removal of the Eximis CS Capture Bag from the abdomen).
2. Duration of the surgical procedure (from skin incision to skin closure).
3. Length of incision (mm) used for the Eximis CS device at procedure end (removal of Eximis CS Capture Bag).
4. Removed tissue weight (grams).
5. Number of extracted tissue segments per subject.
6. The size (mm) of the largest segment will be recorded defined as the segment with the largest cross-sectional area of the surface that is parallel with the incision opening.
7. Subject's pathology results of the extracted tissue and pathologist assessment of RF-energy impact to the tissue, if any, from use of the Eximis CS device.

19.2 Analysis Sets

There will be three analysis sets for this study.

1. The Initial User Analysis Set will include the initial procedure from each User (surgeon) enrolled in the trial (n=15).
2. The Repeat User Analysis Set will include the repeat procedures (n=10).
3. The Full Analysis Set will include all procedures (n=25).

All analysis groups will be used to assess safety and effectiveness of the device. The Primary Endpoint Analysis will be based on the Full Analysis Set (n=25). The Primary and Secondary Endpoints as well as the additional measures will be analyzed per the 3 Analysis Sets.

19.3 Patient Demographics and Baseline Characteristics

All demographic, baseline and medical history characteristics will be presented in by-patient listings and summary tables.

19.4 Eximis Capture Bag Integrity Testing

Capture bags will be tested for containment per a separate protocol. The pass/fail results for the Safety population will be included in the study report.

19.5 Adverse Event Reporting

Adverse Events experienced by the subject as a result of use error (primary endpoint) or non-use error (secondary endpoint) will be summarized by the Medical Dictionary for Regulatory Activities (MedDRA Version 22.0 or later) reporting the System Organ Class (SOC) and Preferred

Term (PT). Tables will describe the frequency and percentage of all AEs, SAEs, ADEs, and UADEs reported by participants in the Safety Population. Presentations will summarize AEs by maximum reported severity and relationship to device and procedure. AEs leading to study or procedure discontinuation will also be tabulated.

User and Subject Safety

The results of all 25 procedures will be used for analysis of safety. The frequency and severity of adverse events will be used to assess user and/or subject safety. The percentages of subjects experiencing the following will be presented:

1. Serious adverse events (SAEs)
2. Unanticipated adverse device effects (UADEs)
3. Any adverse event (AE)
4. Procedure related AEs/ADEs
5. Device-related AEs/ADEs

In addition to percent of subjects, the number of adverse events will also be provided.

19.6 Acceptance Criteria

The results must show that the Eximis CS can be used safely without serious use errors. All human factors data will be assessed qualitatively. Any user interface issues or error conditions must not constitute a serious risk to the patient or the user.

The objectives of the study, confirmation of device usability within an actual clinical setting, are met if the device usability observations meet the criteria described above and the benefits of use clearly outweigh any remaining risk.

19.7 Analysis of Results

For the human factors usability aspect of the study, observational data will be aggregated with the interview data and analyzed to determine the root cause of any close calls, use errors or problems that occur which have potential to result in serious harm. Additionally, RF-100 Controller internal data, which logs the sequence of events during use, and/or Eximis CS device assessment may be included to determine the root cause. The Controller internal data and/or device assessment does not contain any patient information.

Further data analysis will be performed that is consistent with the process defined in FDA Human Factors Engineering guidance and ISO 62366. Once root cause analysis is complete a determination will be made as to whether additional mitigation to reduce the risk of use error relating to serious harm is not required or not practicable. If determined not required or not practicable a justification for this determination will be reported. If mitigation is deemed necessary additional human factors testing may be necessary. It is expected, depending upon the type of mitigations, it may be possible to conduct testing in a preclinical setting.

The residual risk related to use will be analyzed in accordance with ISO 14971. Per ISO 14971 all risks must be considered when evaluating overall risk including the residual risk associated with usability of the medical device. To proceed with a regulatory submission for device commercialization, Eximis must be able to demonstrate that the probable benefit of the Eximis CS is outweighed by the residual risk, including use related risks.

20 STUDY MANAGEMENT

20.1 Investigator Responsibilities

20.1.1 Roles and Responsibilities of Key Study Personnel

Key Study Personnel are as follows:

- Lead Investigator: serves as the clinical subject matter expert with oversight of the overall study.
- Principal Investigator: study conduct and reporting requirements to the Sponsor and IRB at their institution.
- Research Coordinator: procedures with the subjects, maintain study records, data entry of study data, device accountability, contact with the Sponsor.

This is a multicenter study, the delegation of authority log at each investigational site will define the roles and responsibilities of study personnel.

20.1.2 Statement of Investigator

Each Investigator will provide to the Sponsor a current curriculum vitae and a signed Statement of Investigator prior to initiation of the study.

20.1.3 Financial Disclosure

Per 21 CFR 54 a Financial Disclosure Form shall be completed by each investigator as requested by the Sponsor.

20.1.4 Institutional Review Board

The Institution's IRB or other similarly functioning committee will review and approve the study protocol, protocol amendments, initial/revised ICF documents, and recruitment materials, if applicable. Upon IRB approval, documentation of that approval and the approved ICF documents will be sent to the Sponsor/designee before any subject is enrolled into this study.

20.1.5 Informed Consent

The Investigator is responsible for preparing the written informed consent documents for this study. The Sponsor will provide to the investigator an ICF template. The investigator may

rearrange or reword the contents of the templates or may add other elements or language, provided the meaning and content are not changed or deleted. The site-specific ICF will be reviewed/approved by the Sponsor/designee prior to submission to the IRB.

20.1.6 Record Retention

Investigational sites will maintain all records pertaining to this study for the longer of the following time periods:

- A minimum of 2 years following premarket approval (or applicable application); OR
- 2 years after the study was discontinued

Thirty (30) days before destroying any study-related records, investigational sites will provide written notice to the Sponsor.

Investigators must notify the Sponsor in the event they are leaving the institution.

20.2 Recording and Collecting of Data

The Investigator will maintain complete, accurate, legible, and easily retrievable documentation, including but not limited to, medical records, study progress notes, signed informed consent forms, device accountability logs, correspondence with the reviewing IRB, sponsor and study monitor, adverse event reports, and information regarding subject discontinuation or completion of the study.

The Investigator/institution will permit direct access to source data and documents in order for study-related monitoring, audits, IRB reviews, and regulatory inspections to be performed. The Investigator will obtain, as part of the informed consent process, permission for sponsor, authorized sponsor employees or representatives, study monitors or regulatory authorities to review, in confidence, records that identify patients in this trial.

Research records will be stored in a confidential manner so as to protect the confidentiality of subject information.

20.2.1 Source Documents

Source data is all information, original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of that trial. Source data are contained in source documents. Examples of these original documents and data records include hospital and clinic records, operative report, evaluation checklists, imaging scan, laboratory results, etc.

20.2.2 Case Report Forms

During the actual use of the Eximis CS System during the surgical procedure, observations related to task completion, close calls, use errors and post-procedure interview with the surgeon will be documented by an Eximis representative onto Human Factors Usability CRFs, which will serve as the source documentation for device use.

The patient data will be entered from the medical record onto either the source worksheets or directly into the EDC system. Any missing or questionable data will be queried and if it cannot be resolved, the rationale for missing data must be explained.

Completed subject CRFs will be reviewed and signed by the Investigator. The CRA will verify the data entered into the EDC system or paper CRF data in the event this is used with the patient's source data, evaluate the data for accuracy, consistency, and completeness, and will ensure that all forms with missing data and/or errors are ultimately addressed. Accurate and complete entry for a subject must be completed in a timely manner.

All data, human factors usability and subject data from the source documents, will be entered into the EDC system and the data in the EDC system will be considered the final data to support the de novo 510(k) premarket notification for the Eximis CS System.

Data Collection Forms to Be Completed by The Site:

1. **Screening and Eligibility Form:** This form includes demographics, inclusion/exclusion criteria, and the date informed consent was obtained, characterization of target tissue data, baseline standard of care laboratory results, medical surgical history, and gynecological exam results.
2. **Pathology Results and Study Termination:** This form includes the pathology results, pathologist assessment of impact of RF-energy to the tissue, if any, from use of the Eximis CS device, the reason for study termination and investigator's signature verifying the data is accurate.
3. **Follow-up Form:** The Follow-up form includes results from a gynecological exam.
4. **Adverse Event Form:** Adverse Event forms are to be completed when an adverse event/adverse device effect takes place from procedure through the final follow-up.

Data Collection Form to Be Completed by The User (Surgeon):

1. **User (Surgeon) Profile:** This form includes certifications, practice data, and procedure technique data.
2. **Post-procedure User Questionnaire:** This form includes general open-ended questions to capture usability aspects of device use.

Data Collection Forms to be Completed by the Sponsor:

1. **Usability Observation Forms:** This form includes records user performance and observations.
2. **Post-Procedure Debriefing User Interview Form:** This form contains the documentation of the sponsor's interview with the user.
3. **Equipment and extracted tissue specimen assessments**

Data Collection Forms to be Completed by the Site/Sponsor or designee

1. **Eximis CS System Device Training Record:** This form documents the surgeons and O.R. circulating nurses Eximis CS System device training.
2. **Surgical Procedure Source Worksheet:** The worksheet mimics the data entry collection and may serve as a source document to facilitate the collection of the surgical procedure information that may not be collected as standard clinical practice.

20.3 Clinical Investigation Plan Compliance

The Investigator is responsible for ensuring the study is conducted in accordance with the procedures and evaluations described in this protocol.

20.3.1 Deviations from the Clinical Investigation Plan

A protocol deviation is defined as any event where the investigator or site personnel deviate from the study protocol or study procedures for any reason.

It is the Investigator's responsibility to ensure that there are no protocol deviations throughout the duration of the study and that the study is conducted in full compliance with the protocol and all established procedures and conditions of the reviewing IRB. Protocol deviations that are due to unforeseen circumstances beyond the Investigator's reference, (e.g., if the patient did not arrive for their scheduled follow-up) are required to be reported on the protocol deviation form in order to ensure that all deviations from the standard subject population are adequately documented and reported.

The Investigator will inform the sponsor of all deviations and will inform the reviewing IRB of protocol deviations per IRB requirements. The occurrence of protocol deviations will be monitored by the Sponsor for evaluation of Investigator compliance to the protocol, GCP compliance, and regulatory requirements. In the event that an Investigator does not comply with the clinical study/Investigator agreement, and/or the protocol, the Investigator will be notified of their noncompliance, and the Sponsor will review the circumstances. Continued noncompliance may result in discontinued shipment of study devices and termination of the Investigator's and/or investigational site's participation in the study.

20.4 Sponsor Responsibilities

20.4.1 Amendments to the Clinical Investigation Plan

Any amendment to the CIP, as deemed appropriate by the Sponsor, will be implemented as the study progresses. Amendments will be submitted to the IRB for written approval before implementation.

20.4.2 General Responsibilities of Sponsors

As per ISO 14155 Section 8 and 21 CFR 812, the Sponsor is responsible for selecting qualified Investigators and providing them with the information they need to conduct the investigation properly, ensuring quality study conduct and proper monitoring of the investigation, ensuring required approvals are obtained and that significant new information about an investigation is promptly reported to reviewing IRB. Sponsor or designee will maintain essential study documentation.

The Sponsor/designee is responsible for trial registration on government clinical trial registries.

20.5 Joint Investigator/Sponsor Responsibilities

20.5.1 Training

The Sponsor will train applicable study team members to the device, protocol, and study procedures and will provide updated information as it becomes available during the course of the study, if applicable. The Investigator is responsible for ensuring that additional site personnel that were not trained by the Sponsor receive applicable documents and training.

20.5.2 Training Requirements

Each User, surgeon and circulating O.R. nurse will undergo validated device training by an Eximis Surgical, Inc. representative/designee to be completed prior to initial use of the device by each User.

The surgeon training will include a didactic PowerPoint® presentation, hands on training, a device demo video, review of the Eximis CS IFU and Eximis RF-100 Controller User Manual and a device use practicum in a benchtop model. The training will last approximately 1.5 hours. Surgeons will have access to the training materials at will. Refresher will be provided as requested by the User.

The training will take place at the institution in a location suitable to allow for use of the device in a benchtop model prior to use of the device in a human. Bovine tongue will be used as the tissue for training, if not available, pork loin or another cut of meat will be used.

The operating room circulating nurse, who will be involved in setting up the equipment and connecting cables during use of the Eximis CS device, will undergo training by an Eximis representative per the training plan which has previously been validated. The training will include a device demo video, a didactic PowerPoint® presentation, hands on demonstration, practicum use of the Eximis RF-100 Controller and review of the Eximis CS IFU and Eximis CS RF-100 Controller User Manual. The training will be completed prior to initial use of the device by the surgeon and will last approximately 30 minutes. Circulating nurses will have access to the training materials at will. Refresher will be provided as requested by the User.

20.5.3 Compliance

The study will be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, United States 21 CFR, 812, ISO14155:2020 and any regional or national regulations, as appropriate. The study will not begin until the required approvals/favorable opinion from the local IRB and the regulatory authority have been obtained.

20.6 Data Monitoring

The Sponsor will ensure that study monitors have adequate education and experience for the roles. The study data will be monitored to ensure data accuracy, the identification, documentation, and analysis of adverse events, compliance with the protocol, and ethical requirements are in place for conducting research to protect the safety and well-being of all subjects.

20.6.1 Access to Information for Monitoring and Auditing

Monitoring: The CRA/monitor must have direct access to the subject's source documentation in order to verify the data recorded in the CRF/EDC. The CRA is responsible for routine review of the CRFs at regular intervals throughout the study and to verify adherence to the protocol, as well as the completeness, consistency, and accuracy of the data being recorded. The investigator agrees to cooperate with the monitor to ensure that any problems detected in the course of these monitoring visits are resolved. This study will be source data verified by a qualified CRA as per the criteria outlined in the study monitoring plan. The monitor will also verify that the site and Sponsor study files contain all of the required essential documents as outlined in ISO14155:2020, Annex E.

Auditing: In the event that an Investigator is contacted by a regulatory agency in relation to this study, the Investigator will notify the Sponsor immediately. The Investigator or designee must be available to respond to reasonable requests and audit queries made by authorized regulatory representatives during the audit process. The Investigator must provide the Sponsor with copies of all correspondence that may affect the review of the current study or their qualification as an Investigator in clinical studies conducted by the Sponsor. The Sponsor will provide any needed assistance to regulatory audits or correspondence.

20.6.2 Termination of the Study

For reasonable cause, either the Investigator or the Sponsor may terminate the Investigator's participation in this study, provided a written notice is submitted within the time period provided for in the Clinical Trial Agreement (CTA). In addition, the Sponsor may terminate the study at any time upon immediate notice for any reason, including but not limited to, the Sponsor's belief that termination is necessary for the safety of subjects.

20.6.3 Financing

The Sponsor will compensate the Investigational sites according to the terms of a CTA between the Sponsor, the Investigator, and the Investigational Site that will list the anticipated cost and expenses relating to the conduct of this study. However, the Sponsor will not compensate the Investigator for evaluation of subjects in a manner other than specified in the protocol.

The Investigator is not financially attached to private enterprises, foundations, etc., that may have interests in this clinical study.

20.6.4 Publication Policy

The Sponsor recognizes the importance of communication of medical study data. The Sponsor encourages the publication of such data in reputable scientific journals and the presentation of such data at scientific seminars and conferences. Any proposed publication or presentation of the data generated from the study must be conducted in accordance with the terms of the Clinical Trial Agreement (CTA). Because this will be a multi-center trial, all Investigators agree not to publish individual site data without prior approval from the Sponsor, as negotiated in the CTA.

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22 INVESTIGATOR'S SIGNATURE

Study Title: Human Factors Actual-Use Confirmatory Validation Study of the
Eximis CS (Contained Segmentation) System ("Contain" Study)

Study Number: CIP2020-001

Version/Date: Version 6.0 / 23 Sept 2021

I have read the clinical investigation plan and I agree that it contains all necessary details for my staff and I to conduct this study as described. I will conduct this study in compliance with the clinical investigation plan, Good Clinical Practices, and all applicable regulations. I will make a reasonable effort to complete the study within the time designated.

I will provide all study personnel under my supervision with copies of the clinical investigation plan and grant access to all information provided by Eximis Surgical. I will discuss this material with all study personnel under my supervision to ensure that they are fully informed about the study.

Investigator Name (printed)

Signature

Date