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# A Prospective, Multi-Center Evaluation of the ENSEAL X1 Large Jaw Tissue Sealer

## Protocol Number: ENG-17-001

| Document | Effective Date |
|---|---|
| Original | 03 AUG 2017 |
| Amendment 1 | 09 JAN 2018 |
| Amendment 2 | 24 MAY 2018 |
| Amendment 3 | 06 JUNE 2019 |

**Sponsor:** Ethicon Endo-Surgery, Inc.
4545 Creek Road
Cincinnati, Ohio 45242

**Regulatory Phase:** Post-Market Clinical Follow-Up (PMCF)

**Name of Finished Product:** ENSEAL® X1 Large Jaw Tissue Sealer

This is a dedicated bipolar electrosurgical instrument intended for use in open surgical procedures where ligation and division of vessels is desired.

[redacted]

**CONFIDENTIALITY STATEMENT**

**The information in this document contains trade secrets and commercial information that are privileged or confidential and may not be disclosed unless such disclosure is required by federal or state law or regulations. Subject to the foregoing, this information may be disclosed only to those persons involved in the study who have a need to know, but all such persons must be instructed not to further disseminate this information to others. These restrictions on disclosure will apply equally to all future information supplied to you which is indicated as privileged or confidential.**

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# PROTOCOL SIGNATURE PAGE

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[redacted]

This study will be performed in compliance with Good Clinical Practice (GCP), and in accordance with the Declaration of Helsinki, as well as any other applicable local and country regulatory requirements.

# INVESTIGATOR SIGNATURE PAGE

I have read, understood, and agree to:

- Ensure that the requirements for obtaining informed consent are met;
- Conduct the study in accordance with this protocol, including applicable local laws and regulations;
- Maintain the confidentiality of all information received or developed in connection with this protocol;
- Report all serious adverse events (SAEs) as soon as possible, but no later than 72 hours after becoming aware of the event;
- Adhere to the publication policy, as stated in the Clinical Study Agreement, for data collected during this study;
- Ensure that all associates, colleagues, and employees assisting in the conduct of the study are informed of their obligations in meeting the above commitments; and
- I will provide copies of the protocol and all pertinent information to all individuals responsible to me who assist in the conduct of this study. I will discuss this material with them to ensure they are fully informed regarding the conduct of the study.

I will ensure that the Institutional Review Board (IRB) / Ethics Committee (EC) review complies with governmental requirements and will be responsible for the initial and continuing review and approval of the clinical investigation. I also agree to promptly report to the IRB/EC all changes in the research activity and all unanticipated problems involving risks to human subjects or others. Additionally, I will not make any changes in the research without Sponsor and IRB/EC approval of an amended protocol, except where necessary to eliminate apparent immediate hazards to human subjects.

I agree to comply with all other requirements regarding the obligation of clinical Investigators and all other pertinent requirements of the Sponsor and government agencies.

_____ _____

Signature of Principal Investigator (PI) Date

_____

Printed Name of PI

# CLINICAL STUDY PROTOCOL SYNOPSIS

| | |
|---|---|
| **Regulatory Phase:** | Post-Market Clinical Follow-Up |
| **Indication:** | The ENSEAL® X1 Large Jaw Tissue Sealer instrument (ENSEAL X1) is a dedicated bipolar electrosurgical instrument intended for use in open surgical procedures where ligation and division of vessels is desired. It is a bipolar instrument for use with the Ethicon Generator G11 (GEN11). It is intended for use during open surgery to cut and seal vessels, cut, grasp, and dissect tissue during surgery. Indications for use include open general, gynecologic, urologic, thoracic, and vascular procedures. These procedures include hysterectomies, colectomies, Nissen fundoplication, adhesiolysis, oophorectomies, etc. The devices can be used on vessels (arteries, veins, pulmonary vasculature, lymphatics) up to and including 7 mm and tissue bundles. |
| **Objective(s):** | The primary objective of this study is to prospectively generate device-specific clinical data related to hemostasis in a post-market setting using the ENSEAL X1 per its instructions for use (IFU). Secondary objectives include proactive surveillance of safety and performance outcomes following use of the ENSEAL X1. |
| **Overview of Study Design:** | This prospective, single-arm, multi-center, evaluation will collect clinical data in a post-market setting. The three types of procedures studied will be colectomy, gynecological, and thoracic. Investigators will perform each procedure using the device in compliance with their standard surgical approach and the ENSEAL X1 IFU. There will be no blinding or planned interim analysis in this study.<br><br>Each site will utilize consecutive screening and enrollment in an effort to generate a random and representative patient population sample. Subjects will be consented and screened anytime between the time of scheduling the procedure and hospital admission (this period will vary per subject but may occur over several dates within an 8-week period prior to surgery). Subjects will be considered enrolled at the time of the first attempted vessel transection using the ENSEAL X1 device during their procedure for purposes of this study. The last study visit will be at the post-op follow-up visit at approximately 4 weeks; therefore, from the surgery date to study exit, the duration will be approximately four weeks and the total study participation can be up to 12 weeks. |
| **Number of Subjects:** | A total of 100 eligible subjects are planned to be enrolled in up to 8 sites with the following procedure targets (each site will utilize consecutive screening and enrollment):<br><br>• Minimum of 30 subjects enrolled for colectomy procedures (e.g., total colectomy, partial colectomy, hemicolectomy, proctocolectomy);<br>• Minimum of 30 subjects enrolled for gynecological procedures (e.g., hysterectomy);<br>• Minimum of 20 subjects enrolled for thoracic procedures (e.g., |

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| | esophagectomy); and<br>The remaining 20 subjects will be enrolled from any of the procedure groups (colectomy, gynecological, or thoracic). |
| **Criteria for Inclusion:** | Subjects satisfying the following criteria will be considered eligible for enrollment in this study:<br>1. Elective procedure (colectomy, gynecological, or thoracic) where at least one vessel is planned to be transected by the ENSEAL X1 device per its IFU;<br>2. Willingness to give consent and comply with all study-related evaluations and treatment schedule; and<br>3. At least 18 years of age. |
| **Criteria for Exclusion:** | Subjects meeting any of the following criteria will be considered not eligible for enrollment in this study:<br>1. Physical or psychological condition which would impair study participation; or<br>2. Enrollment in a concurrent clinical study. |
| **Test Product:** | ENSEAL X1 Large Jaw Tissue Sealer (Product Code: NSLX120L) and Ethicon Endo-Surgery Generator G11 |
| **Reference Therapy/Product:** | No comparator product is being used in this study. |
| **Duration of Treatment:** | Subjects will be exposed to the ENSEAL X1 device during the procedure they undergo and while the device is used as indicated in the IFU. |
| **Criteria for Evaluation:** | Primary performance endpoint:<br>• Percentage of vessels where hemostasis (≤ Grade 3) is achieved using the ENSEAL X1 and no additional hemostatic products (e.g., hemoclips, staples, sutures, fibrin sealants, other advanced energy) are needed to obtain hemostasis. Hemostasis grading scale:<br>o Grade 1: no bleeding at transection site;<br>o Grade 2: minor bleeding at transection site, no intervention needed;<br>o Grade 3: minor bleeding at transection site, mild intervention needed, use of monopolar device and/or touch-ups with ENSEAL X1;<br>o Grade 4: significant bleeding (e.g., pulsatile blood flow, venous pooling) requiring intervention such as extensive coagulation or ligation with additional hemostatic products (e.g., hemoclips, staples, sutures, fibrin sealants, other advanced energy products).<br>Secondary performance endpoints:<br>• Hemostasis grading assessment for each vessel transection; |

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| | • Incidence of requirement (number of times and reason for use) for ENSEAL X1 touch-ups for Grade 3;<br>• Incidence of requirement (type, name of product, and number of times) for additional hemostatic products for Grade 4 interventions (e.g., hemoclips, staples, sutures, fibrin sealants, other advanced energy products) to obtain hemostasis on vessels;<br><br>Primary safety endpoint<br><br>• Safety will be assessed through summarization of all device-related adverse events (AEs). Adverse events will be assessed for seriousness, severity, action taken, and outcome.<br><br>Other key data collected:<br><br>• Surgical procedure conducted;<br>• Procedure duration;<br>• Hospital stay duration;<br>• Name and number of vessels that were transected;<br>• Incidence and location of cancer and occurrence of pre-surgical radiation/chemotherapy, if applicable (when and how many doses);<br>• Occurrence of vessel skeletonization;<br>• Presence of inflamed tissue or calcified tissues/vessels, if applicable;<br>• Volume of estimated intra-operative blood loss;<br>• Date(s) of chest tube placement and removal, if applicable;<br>• Daily volume and characteristics of chest tube(s) drainage, if applicable;<br>• Occurrence of ENSEAL X1 used for tissue cutting or dissection (description of tissue cut/dissected);<br>• Procedure-related AEs; and<br>• Device and Surgeon questionnaires. |
| **Statistical Analysis:** | **Analysis Sets**<br><br>The summary of all performance and safety endpoints will be performed on the set of subjects in whom the ENSEAL X1 device is utilized during the surgical procedure. The summary of all primary and secondary performance endpoints will be performed by procedure group (colectomy, gynecological, or thoracic). The summary of all safety endpoints will be performed by procedure group and on the entire pooled set of subjects.<br><br>**Sample Size Determination**<br><br>A sample size of 100 subjects is planned for enrollment in this study. No formal hypothesis is being tested in this study, thus the sample size was not statistically sized, but rather is considered sufficient for a descriptive summary of performance endpoints within each procedure group. It is expected that at least 2 vessels will be transected within each procedure, providing an expected minimum of at least 60 transections within colectomy and gynecological procedure groups and at least 40 |

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| | transections in the thoracic procedure group for a total of at least 200 transections.<br><br>From a safety perspective on the pooled analysis of 100 subjects and in consideration of rare AEs that may occur (e.g., bleeding requiring blood product transfusion), for an event that has an incidence rate of, for example, 2%, then in a sample of 100 subjects, the probability of observing at least 1 event is 86.7% under a binomial probability model. Thus, this sample size provides a high probability of observing rare events if they do occur, and provides reasonable assurance to conclude that the likelihood of such AEs is less than 3.7% if they do not occur based on the upper limit of an exact 95% confidence interval when 0 events out of 100 subjects are observed.<br><br>**Performance Analyses**<br><br>The number and percentage of vessels where hemostasis is achieved (≤ Grade 3) will be summarized and a 95% confidence interval will be estimated for each procedure group (colectomy, gynecological, or thoracic). Counts and percentages will be provided for type, size, and number of vessels transected, summary of grading scale distribution for all vessels transected, number of times ENSEAL X1 touch-ups were required, and incidence of requirement for additional measures to obtain hemostasis on vessels (other advanced energy devices or hemostatic products).<br><br>**Safety Analyses**<br><br>All device-related and procedure-related AEs reported during the study will be coded to the Medical Dictionary for Regulatory Activities (MedDRA). All AEs will be summarized by MedDRA system organ class and preferred term by procedure group and in total. Separate summaries will be provided for device-related and procedure-related AEs. Serious AEs will be summarized in a similar manner. |

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# PROTOCOL-SPECIFIC ACRONYMS AND ABBREVIATIONS

| Acronyms/Abbreviations | Terms |
|---|---|
| AE | Adverse event |
| CFR | Code of Federal Regulations |
| EC | Ethics committee |
| eCRF | Electronic case report form |
| EDC | Electronic Data Capture |
| EES | Ethicon Endo-Surgery, Inc. |
| ENSEAL X1 | ENSEAL® X1 Large Jaw Tissue Sealer |
| GEN11 | Ethicon Endo-Surgery Generator G11 |
| FDA | Food and Drug Administration |
| GCP | Good clinical practice |
| ICD | Informed consent document |
| IFU | Instructions for use |
| IRB | Institutional review board |
| MedDRA | Medical Dictionary for Regulatory Activities |
| OR | Operating room |
| PCF | Product complaint form |
| PHI | Protected health information |
| PI | Principal Investigator |
| PMCF | Post-market clinical follow-up |
| SAE | Serious adverse event |
| SAP | Statistical analysis plan |
| SOC | Standard of care |

# ETHICS

## Institutional Review Board/Ethics Committee

Participating investigators will ensure that this protocol, Informed Consent Document (ICD), ICD or protocol amendments, and if applicable, any other written information provided to the subjects that assist in the decision to participate are reviewed by an Institutional Review Board (IRB) or Ethics Committee (EC) that complies with governmental requirements. The approving IRB/EC will be responsible for the initial and continuing review and approval of this clinical investigation. Participating investigators will be required to promptly report to the IRB/EC as required by the IRB/EC's policies. Additionally, investigators will be required to refrain from making any changes in the clinical investigation plan without Sponsor and IRB/EC approval of an amended protocol, except where necessary to eliminate apparent immediate hazards to study subjects or others.

## Applicable Regulations

This study will be conducted in compliance with GCP and in accordance with the Declaration of Helsinki, as well as any other applicable local and country regulatory requirements.

## Subject Information and Consent

Regulations concerning the protection of subjects require that informed consent be obtained before a subject may participate in any clinical investigation. An IRB/EC approved informed consent must be sought from each subject and must be appropriately documented in the subject's medical record prior to initiating the study. It is the Investigator's responsibility to obtain written informed consent from the subject, the Investigator may delegate this responsibility if appropriately documented.

The informed consent process involves the following: giving a subject adequate information concerning the study, providing adequate time for the subject to consider all available options, responding to the subject's questions, ensuring that the subject has comprehended this information and finally, obtaining the subject's written consent to participate in this study. All subjects in this study should be completely informed about the purpose, risks, benefits, and other pertinent details of this study. The informed consent process is careful to avoid the perception of any coercion or undue influence on, or inducement of, the subject to participate, and does not waive or appear to waive the subject's legal rights. The ICD is presented in native, non-technical language that is understandable to the subject.

Prior to a subject's participation in this study, an ICD will be signed and dated by the subject and person who conducted the consent discussion. The subject will be provided a copy of the signed ICD. The ICD and any other written materials provided to the subject to assist in the decision to participate must be revised whenever new information becomes available that may be relevant to their willingness to participate or continue participation in this study. Revision to the ICD and other written materials will receive IRB/EC approval before implementation. Each subject will be required to sign any amended ICD (as required by the IRB/EC) and will receive a copy of the signed ICD.

## ADMINISTRATIVE REQUIREMENTS

This study is sponsored by Ethicon Endo-Surgery, Inc. (EES, Cincinnati, OH, USA) and will be conducted in up to eight surgery centers in the United States and/or European Union under a single protocol approved by each participating site's IRB/EC prior to implementation. The principal investigator at each study site is a surgeon qualified by education, experience, and training to perform the study procedure and to assume responsibility for the conduct of this study.

The Data Management and Biostatistics groups of the Sponsor will be responsible for the analysis of data from this protocol. An Electronic Data Capture (EDC) system will be utilized by study site personnel to transfer study data from source records (the first point of clinical data capture) onto common electronic case report forms (eCRFs). This system is a web-based, secure electronic software application ([redacted]

### Protocol Modifications

All protocol amendments must be issued by the Sponsor, signed and dated by the Investigator, and should not be implemented without prior IRB/EC approval, except where necessary to eliminate immediate hazards to the subjects or when the change(s) involves only logistical or administrative aspects of the study (e.g., change in monitor(s), change of telephone number(s)). The Investigator reports the protocol amendments to the IRB/EC as per their local requirements.

# 1.0 INTRODUCTION

The ENSEAL® X1 Large Jaw Tissue Sealer instrument (ENSEAL X1) is a dedicated bipolar electrosurgical instrument intended for use in open surgical procedures where ligation and division of vessels is desired. It is intended for use during open surgery to cut and seal vessels, cut, grasp, and dissect tissue during surgery. Indications for use include open general, gynecologic, urologic, thoracic, and vascular procedures.

Many of the benefits realized by the ENSEAL X1 are tied to the ergonomics of the device. The ENSEAL X1 has simplified the steps for use as compared to the ENSEAL® Super Jaw device. The device has separate seal and cut functionality, a 360° single hand rotation of the device shaft, a uniform compression system that reduces the potential for end effector damage, and steps for use that are intuitive for the user.

This study will specifically look at the use of ENSEAL X1 in colectomy, gynecological, and thoracic procedures.

# 2.0 STUDY OBJECTIVES

The primary objective of this study is to prospectively generate device-specific clinical data related to hemostasis in a post-market setting using the ENSEAL X1 per its IFU. Secondary objectives include proactive surveillance of safety and performance outcomes following use of the ENSEAL X1.

## 2.1 PRIMARY PERFORMANCE ENDPOINT

The primary performance endpoint in this study is the percentage of vessels where hemostasis (≤ Grade 3) is achieved using the ENSEAL X1 and no additional hemostatic products (e.g., hemoclips, staples, sutures, fibrin sealants, other advanced energy) are needed to obtain hemostasis. Hemostasis grading scale:

- Grade 1: no bleeding at transection site;
- Grade 2: minor bleeding at transection site, no intervention needed;
- Grade 3: minor bleeding at transection site, mild intervention needed, use of monopolar device and/or touch-ups with ENSEAL X1;
- Grade 4: significant bleeding (e.g., pulsatile blood flow, venous pooling) requiring intervention such as extensive coagulation or ligation with additional hemostatic products (e.g., hemoclips, staples, sutures, fibrin sealants, other advanced energy products).

## 2.2 SECONDARY PERFORMANCE ENDPOINTS

The secondary performance endpoints in this study are:

- Hemostasis grading assessment for each vessel transection;
- Incidence of requirement (number of times and reason for use) for ENSEAL X1 touch-ups for Grade 3; and
- Incidence of requirement (type, name of product, and number of times) for additional hemostatic products for Grade 4 interventions (e.g., hemoclips, staples, sutures, fibrin sealants, other advanced energy products) to obtain hemostasis on vessels.

### 2.3 PRIMARY SAFETY ENDPOINT

The primary safety endpoint in this study is the summarization of all device-related AEs. Adverse events will be assessed for seriousness, severity, action taken, and outcome.

### 2.4 ADDITIONAL KEY DATA COLLECTED

Additional key data collected in this study are:

- Surgical procedure conducted;
- Procedure duration;
- Hospital stay duration;
- Name and number of vessels that were transected;
- Incidence and location of cancer and occurrence of pre-surgical radiation/chemotherapy, if applicable (when and how many doses);
- Occurrence of vessel skeletonization;
- Presence of inflamed tissue or calcified tissues/vessels, if applicable;
- Volume of estimated intra-operative blood loss;
- Date(s) of chest tube placement and removal, if applicable;
- Daily volume and characteristics of chest tube(s) drainage, if applicable;
- Occurrence of ENSEAL X1 used for tissue cutting or dissection (description of tissue cut/dissected);
- Procedure-related AEs; and
- Device and Surgeon questionnaires.

## 3.0 INVESTIGATIONAL PLAN

### 3.1 OVERALL STUDY DESIGN AND PLAN - DESCRIPTION

This prospective, single-arm, multi-center, evaluation will collect clinical data in a post-market setting. The three types of procedures studied will be colectomy, gynecological, and thoracic. Investigators will perform each procedure using the device in compliance with their standard surgical approach and the ENSEAL X1 IFU. There will be no blinding or planned interim analysis in this study.

Each site will utilize consecutive screening and enrollment in an effort to generate a random and representative patient population sample. Subjects will be consented and screened anytime between the time of scheduling the procedure and hospital admission (this period will vary per subject but may occur over several dates within an 8-week period prior to surgery). Subjects will be considered enrolled at the time of the first attempted vessel transection using the ENSEAL X1 device during their procedure. Procedures will be performed per each institution's standard-of-care (SOC) that is specific for each procedure group (colectomy, gynecological, and thoracic). The last study visit will be at the post-op follow-up visit at approximately 4 weeks. Follow-up by phone for subjects is allowed when an on-site visit is not planned.

## 3.2 STUDY POPULATION

### 3.2.1 Enrollment

Subjects will be recruited from the existing patient population who plan to have an elective procedure from the proposed procedure groups (colectomy, gynecological, and thoracic). All eligible subjects (Sections 3.2.3 and 3.2.4) will be considered enrolled at the time of the first attempted vessel transection using the ENSEAL X1 device during their procedure. Up to 8 centers (United States and Europe) will be selected as study sites. Each participating investigator is expected to perform a minimum of two procedures using the ENSEAL X1 device. A total of 100 eligible subjects are planned to be enrolled with a minimum of 30 subjects enrolled for colectomy procedures (e.g., total colectomy, partial colectomy, hemicolectomy, proctocolectomy), a minimum of 30 subjects enrolled for gynecological procedures (e.g., hysterectomy), and a minimum of 20 subjects enrolled for thoracic procedures (e.g., esophagectomy). The remaining subjects will be enrolled from any of the three procedure groups and enrollment will be competitive between procedure groups and the remaining 20 subjects.

### 3.2.2 Screening Failures

All subjects signing consent who do not have at least one vessel transection attempted by ENSEAL X1 during their procedures will be recorded as screen failures. For subjects who are determined to be screen failures, only the relevant electronic eCRF pages (inclusion/exclusion criteria, demographics, AEs, subject completion/discontinuation) will be completed.

### 3.2.3 Inclusion Criteria

Subjects satisfying the following criteria will be considered eligible for enrollment in this study:

1. Elective procedure (colectomy, gynecological, or thoracic) where at least one vessel is planned to be transected by the ENSEAL X1 device per its IFU;
2. Willingness to give consent and comply with all study-related evaluations and treatment schedule; and
3. At least 18 years of age.

### 3.2.4 Exclusion Criteria

Subjects meeting the following criteria will be considered not eligible for enrollment in this study:

1. Physical or psychological condition which would impair study participation; or
2. Enrollment in a concurrent clinical study.

### 3.2.5 Removal of Subjects from Study

In accordance with the current revision of the Declaration of Helsinki and the CFRs, a subject has the right to withdraw from the study at any time for any reason without prejudice to his/her future medical care by the physician or the institution. Should a subject (or subject's legally authorized guardian/representative) decide to withdraw, 1) all data collected up to the point of withdrawal will be considered for analysis; and 2) all efforts will be made to collect and report the final visit observations as thoroughly and timely as possible. Participation may be terminated prior to completing the study for any of the reasons listed below (reasons that do not fit the categories below will be documented as "other").

**Adverse Event**

When the subject experiences an AE and the Investigator or Medical Monitor believes it is in the best interest of the subject to discontinue participation in the study, the subject will be withdrawn from the study.

**Lost to follow-up**

When contact with the subject has been lost without completing a final contact assessment, and every attempt (3 times) to contact the subject has failed, the subject will be considered lost to follow-up. All attempts to contact the subject requesting his/her return for the final visit must be documented.

**Withdrawal of consent**

Any method of contact with the subject (or subject's legally authorized guardian/representative) in which he/she state they no longer want to participate in the study specific activities constitutes withdrawal of consent for participation in the study. When possible, the reason for withdrawal will be documented.

**Site Termination or Study Termination**

A study site or the entire study may be terminated. When this occurs, all subjects currently enrolled at the site will be withdrawn and documented as early terminations. Reasons for site or study termination may include, but are not limited to the following:

- Administrative concerns (e.g., inadequate subject enrollment, Investigator/institution non-compliance, change of business strategy, etc.);
- Safety Issues, including those due to non-compliance, which substantially affect the risk to benefit ratio of the study subjects at a site or for the study as a whole; or
- Regulatory Body Mandate(s).

The Investigator has the right to terminate the subject's participation at any time. Should this be necessary, procedures for termination will be provided by the Sponsor.

**Death**

- When possible, the cause of death will be documented.

**Other (which may include)**

- Investigator recommendation.

### 3.2.6 Subject Replacement in Study

Subjects who withdraw or are terminated early from the study will not be replaced.

## 3.3 STUDY PROCEDURES

### 3.3.1 Procedure Description

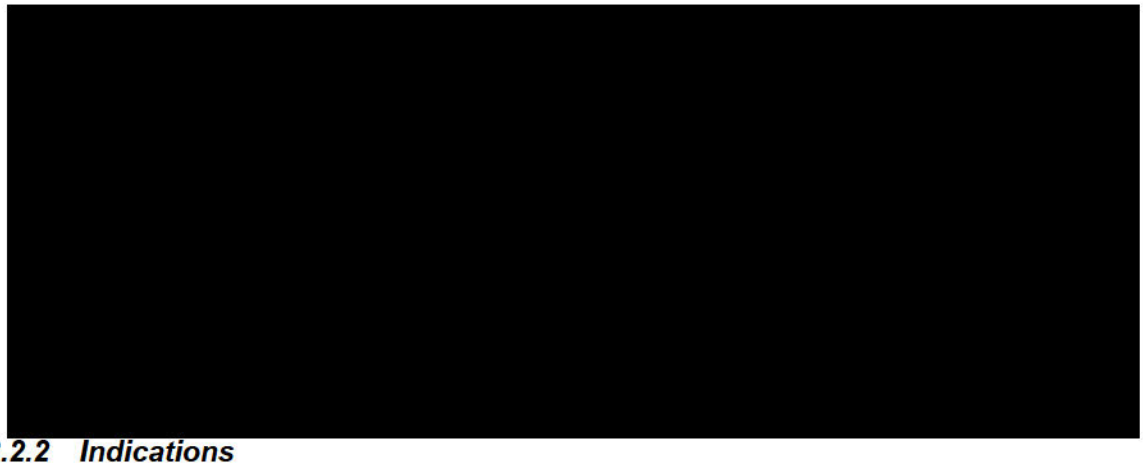
Elective colectomy, gynecological, or thoracic procedures (where ENSEAL X1 is indicated for use) will be performed per the institution's SOC.

### 3.3.2 Identity of Study Products

No investigational devices will be tested in this study. The ENSEAL X1 is a dedicated bipolar electrosurgical instrument.

#### 3.3.2.1 Device Description

The ENSEAL X1 instrument (Product Code NSLX120L) is a sterile, single patient use surgical instrument to coagulate and transect vessels up to and including 7 mm in diameter, tissue and/or vascular bundles. This device is for soft tissue only. The instrument consists of a grip housing assembly, a rotating shaft, a moveable jaw, and a knife. The instrument shaft can be rotated 360° to facilitate visualization and enable easy access to targeted tissue. The curved jaws are in a normally-opened position and can be partially or fully closed by squeezing the closing handle. The jaws are designed for grasping and holding targeted tissue when clamped. Bipolar energy is delivered when the SEAL button or MIN foot pedal is pressed. Pressing the CUT button advances the knife the length of the jaws to cut the targeted tissue. The power cord is permanently attached to the device and connects the instrument to the generator. The ENSEAL X1 instrument is designed for use exclusively with the GEN11 software version 2016-1 or later, packaged separately.



#### 3.3.2.2 Indications

The ENSEAL X1 is a dedicated bipolar electrosurgical instrument intended for use in open surgical procedures where ligation and division of vessels is desired. It is a bipolar instrument for use with the Ethicon Generator G11 (GEN11). It is intended for use during open surgery to cut and seal vessels, cut, grasp, and dissect tissue during surgery. Indications for use include open general, gynecologic, urologic, thoracic, and vascular procedures. These procedures include hysterectomies, colectomies, Nissen fundoplication, adhesiolysis, oophorectomies, etc. The devices can be used on vessels (arteries, veins, pulmonary vasculature, lymphatics) up to and including 7 mm and tissue bundles.

#### 3.3.2.3 Contraindications

The ENSEAL X1 has not been shown to be effective for tubal sterilization or tubal coagulation for sterilization procedures. Do not use this system for these procedures. The efficacy of the ENSEAL X1 for the indication of contraceptive tubal coagulation (permanent female sterilization) has not been evaluated and is unknown. The design of the ENSEAL tissue sealing device is significantly different from bipolar designs that are marketed for the indication of contraceptive tubal coagulation. The design differences may affect the efficacy of the procedure and failure rates may not be comparable. The instruments are not indicated for incising bone.

#### *3.3.2.4 Labeling of Study Products*

Both the ENSEAL X1 and the GEN11 have been cleared for distribution in the United States by the Food and Drug Administration (FDA) and are CE marked which allows for commercial distribution in the EU; therefore ENSEAL X1 has commercial labeling. The Sponsor requires no additional labeling in this study.

#### *3.3.2.5 Accountability of Study Products*

The ENSEAL X1 may be provided to the participating institutions. The GEN11 (including footswitches) will not be provided to any institution in the study. Each institution not provided with ENSEAL X1 will use devices acquired through normal procurement process. If institutions are provided ENSEAL X1, the devices will be tracked using shipping receipts and device accountability logs and all device returns will be managed by contacting EES. Devices provided for the study must be kept in a secure area and used only for treating subjects participating in the study, in accordance with the protocol. If applicable, the study device inventory must be available for periodic inspection/verification.

### 3.3.3 Prior and Concomitant Therapy

Study subjects may continue with his/her current medical care while in the study, including medications. In addition, following the surgical procedure, all medications administered due to a device-related or procedure-related AE will be collected for this study.

## 3.4 STUDY VARIABLES

Specific variables assessed in the study are provided in the following sections. Refer to Section 3.5 Schedule of Events for the time when the study variables will be collected throughout the course of the study.

### 3.4.1 Demographic and Baseline Characteristics

The following will be collected preoperatively:

- Age (years);
- Gender;
- Race;
- Ethnicity;
- Body weight (kg; no shoes);
- Body height (cm; no shoes);
- Review and collection of medical history and surgical history including the following:
    - For the gynecological procedure group, the gravidity and parity;
    - Surgical procedure to be conducted, including primary indication for surgery;
    - Smoking history; and
    - Incidence and location of cancer and occurrence of pre-surgical radiation/chemotherapy, if applicable (when and how many doses).

### 3.4.2 Surgical Variables

The following will be recorded preoperatively, intraoperatively, or postoperatively:

- Date/time of hospital admission;
- Procedure duration, defined as first incision to final closure;
- Did vessel skeletonization occur (Yes/No; if Yes, describe);
- Was there presence of inflamed tissue or calcified tissues/vessels, if applicable (Yes/No; if Yes, describe);
- Volume of estimated intra-operative blood loss;
- For each vessel transected with ENSEAL X1 (only the PI or sub-Investigator can use the device):
    - Name of each vessel;
    - Hemostasis grading scale assessment;
    - Tissue sticking – graded using a 4-point Likert scale (Appendix I);
    - For every Grade 3 vessel transection:
        - Touch-ups with a monopolar device, if applicable (Yes/No; if Yes, record number of touch-ups);
        - Touch-ups with ENSEAL X1 (Yes/No; if Yes, record number of touch-ups);
    - For every Grade 4 vessel transection intervention (additional hemostatic product was used to obtain hemostasis on vessels [e.g. hemoclips, staples, sutures, fibrin sealants, other advanced energy products]):
        - Type, name, and number of times used for each additional hemostatic product used;
- For the gynecological procedure group, if applicable:
    - Uterine size; and
    - Summary of histological diagnoses including fibroids (subserosal, intramural, submucosal), adenomyosis, endometriosis, endometrial abnormality, or other, specify;
- Chest tube data, if applicable:
    - Number of chest tubes placed;
    - Date(s) of chest tube placement and removal;
    - Daily volume and characteristics of chest tube(s) drainage;
- Occurrence of blood transfusion, if applicable (record the total required units of blood and rationale);
- Occurrence of ENSEAL X1 used for tissue cutting or dissection (Yes/No; if Yes, describe including description of tissue cut/dissected);
- Concomitant procedures, if applicable (defined as any medical or surgical procedure beyond activities associated with primary study procedure type). If a

concomitant procedure requires vessel transection by ENSEAL X1, each vessel transected will have the same information captured as stated above for vessel transections;

- Concomitant medication usage associated with AEs; and
- Date/time of hospital discharge.

### 3.4.3 Questionnaires

Data related to the following study variables will be obtained from the Device Procedure Questionnaire (Appendix II) after every completed procedure and the Surgeon Questionnaire (Appendix III) for every investigator after they have completed his/her second procedure.

**Device Procedure Questionnaire**

Investigators will be asked to answer a non-validated device questionnaire (Appendix II) related to his/her experience using the ENSEAL X1. The survey will be completed by the Investigators as soon as possible after each procedure, preferably on the same day. The survey responses will then be transcribed onto eCRFs.

**Surgeon Questionnaire**

Investigators will be asked to answer a non-validated surgeon questionnaire (Appendix III) related to his/her experience using the ENSEAL X1. The survey will be completed by the Investigators as soon as possible after they have completed his/her second procedure. The survey responses will then be transcribed onto eCRFs.

### 3.4.4 Safety Data Variables

All device-related and procedure-related AEs will be collected and captured as outlined in Section 5.0.

## 3.5 SCHEDULE OF EVENTS

**Table 1: Schedule of Events**

| Activity | Visit 1<br>Screening Visit | Visit 2<br>Procedure Through Discharge Visit | Visit 3<br>Post-procedure Follow Up Visit (28 ± 14 days)[a] |
|---|---|---|---|
| Informed consent | X | | |
| Demographics and vital signs[b] | X | | |
| Medical history[b] | X | X | |
| Surgical history[b] | X | X | |
| Background information (including smoking history[b]) | X | X | |
| Review of inclusion/exclusion criteria | X | X | |
| Surgical data captured for evaluation[b] | | X | |
| Collect surgeon reported questionnaire and device questionnaire[c] | | X | |
| Concomitant procedures conducted besides elective procedure | | X | X |
| Concomitant medications associated with captured AEs | | X | X |
| Assess for and record device-related and procedure-related AEs | | X | X |
| Unscheduled visits (if applicable) | | | X |
| Subject completion/discontinuation | | X | X |

[a] This can be either an office visit or telephone follow-up;
[b] See Section 3.4 for details of specific information collected;
[c] The device questionnaire will be collected after every procedure. The surgeon questionnaire will be completed after the investigator has completed his/her second procedure; and
AE = adverse events.

## 3.6 STUDY PROCEDURES

### 3.6.1 Visit 1 – Screening (may occur over visits within 8 weeks of Visit 2)

All subjects who satisfy inclusion/exclusion criteria will be approached for study participation in a consecutive manner.

Prospective subjects will be provided with the study information including the ICD. The subject must be given ample time to review and sign the ICD. Data will be collected as defined in Section 3.4.

### 3.6.2 Visit 2 – Procedure Through Discharge Visit

**Pre-procedure**

The following must be obtained prior to the surgical procedure:

- Updates to medical/surgical/smoking history;
- Confirm inclusion and exclusion criteria.

**Intra-operative and Post-operative**

Data collected during and after the procedure as defined in Section 3.4.

### 3.6.3 Visit 3 – Post-procedure Follow-up Visit

After the surgery, subjects will have a follow-up visit approximately 4 weeks later. This visit can be either an office visit or a telephone follow-up. Data to be collected is defined in Section 3.4.

### 3.6.4 Unscheduled Visit(s)

Any unscheduled visit between Visit 2 and Visit 3 will be documented including the reason for the visit.

## 4.0 DATA MANAGEMENT AND INTEGRITY

### 4.1 DATA COMPLETION AND RECORD KEEPING

#### 4.1.1 Source Documents

Source documents are documents on which information regarding subjects is first recorded, including printed, optical, or electronic documents. Investigator subject files or hospital records generally are the basis of source document information. This includes but is not limited to, original subject files; hospital/clinic records; original recordings /tracing; digital images from automated instruments (e.g., cameras); radiographs; device accountability records; photographic negatives; and records kept at the investigation site, at the laboratories and at other departments involved in the clinical investigation. Source document worksheets may also be used to facilitate data collection and entry into eCRFs.

Source documents must be retained by the Investigator as part of the subject's study record. The information in the source documents is used to complete the eCRFs. All information captured on the eCRFs should be completely and accurately supported in source documentation. Any additional information relevant to the study should be included in the source documents. Any deviations from the study protocol or procedures should be recorded in the source documents. The Investigator will retain originals of all source documents, subject consent forms, and study data per site policy.

#### 4.1.2 Electronic Data Capture

An electronic database capture (EDC) system will be utilized by study site personnel to transfer study data from source records (medical records and/or source document worksheets) onto common eCRFs. This system is a web-based, secure electronic software application [redacted] The EDC system will be used to facilitate the collection of all study data at the site. Designated site personnel will be responsible for entering subject data into the EDC system. All external and Sponsor internal users will be trained on the EDC application at a level dependent on their planned function. An EDC digital User Manual will be available under the help menu within the [redacted] to assist in the collection and entry of source data into the electronic casebook.

A 24/7/365 Help Desk Support line [redacted] staffed by the outsourced vendor will also be available to respond to site and monitor questions.

### 4.1.3 Data Collection

Each EDC eCRF will be completed by the PI or PI's designee. Every effort should be made to respond to all monitoring and/or data management questions on each eCRF as completion of the data is required by the protocol. A unique ID number will identify each subject and will be visible on each eCRF. At no time should the subject name appear on the eCRFs.

All data should be recorded accurately and completely. The PI is responsible for reviewing and approving each completed eCRF. Assurance of overall review and approval will be documented by the PI electronically signing each subject's electronic casebook.

### 4.1.4 Data Correction

Required data corrections to eCRFs will be prompted via automated electronic edit checks and/or queries manually created by Sponsor reviewers. The change(s), individual making the change(s), and time the change(s) was made to the eCRFs will be automatically captured in the audit trail [redacted].

### 4.1.5 Data Privacy

The collection, use, and disclosure of all personal data, including subject health and medical information, are to be maintained in compliance with applicable personal data protection and security laws and regulations that govern protected health information and the informed consent given by each study subject. When collecting and processing such personal data, appropriate measures are to be taken to maintain the confidentiality of subject health and medical information and to prevent access by unauthorized persons.

### 4.1.6 Record Retention, Inspection, and Custody

The PI must maintain all documentation related to the study until notified by the Sponsor. The PI will allow representatives of the Sponsor or other government regulatory agencies to inspect all study records, eCRFs, and corresponding portions of the subject's office and/or hospital medical records at regular intervals during the study. These inspections are to verify adherence to the protocol, integrity of the data being captured on the eCRFs, and compliance with applicable regulations.

Subject study records will be maintained in a confidential manner. Study reports will not identify subjects by name. These reports may be submitted to regulatory authorities.

If custody of the records is transferred, notice of such a transfer should be given to the Sponsor no later than 10 working days before the transfer occurs.

## 4.2 MEDICAL DICTIONARY CODING

Medical dictionary coding of medical history and verbatim AEs captured on eCRFs will be performed using a coding thesaurus algorithm. The Medical Dictionary for Regulatory Activities (MedDRA) will be used after data entry and query resolution, via auto-encoding and interactive coding processes.

## 4.3 DATA QUALITY ASSURANCE

Steps to be taken to assure the accuracy and reliability of data include the selection of qualified investigators and appropriate sites, review of protocol procedures with the Investigator and associated personnel prior to the study, and periodic monitoring visits by the Sponsor. The Sponsor will review eCRFs for accuracy and completeness during onsite monitoring visits; any discrepancies will be resolved with the Investigator or designees, as appropriate.

### 4.3.1 Site Personnel Training

Prior to screening subjects for this study, the PI, Sub-Investigator(s), Study Coordinator, and other designated staff (as applicable) will be trained on study execution, data collection, and procedures specific to this clinical protocol.

### 4.3.2 Monitoring

This study will be monitored by the Sponsor or its representative to ensure:

- The rights and well-being of the subjects are protected;
- The reported study data is accurate, complete, and verifiable from source documents; and
- The conduct of the study is in compliance with the currently approved protocol/amendment(s), applicable GCPs, and with applicable local/regional regulatory requirements.

The extent and nature of monitoring will be predetermined and agreed to by the Sponsor and investigators. Monitors will comply with established written standard operating procedures as well as procedures specified by the Sponsor for monitoring this study as characterized in the monitoring plan for this study.

### 4.3.3 Quality Assurance

The extent and nature of quality assurance audits will be predetermined and based on considerations such as the regulatory classification, objective, and complexity of the study. Any audits performed will comply with established written standard operating procedures and the audit plan for this study.

## 4.4 PROTOCOL DEVIATIONS

A deviation (any activity conducted outside the parameters established by the protocol) can be identified from a number of sources. Potential sources for identification of deviations include, but are not limited to: a member of the Investigator's staff, a Sponsor representative during monitoring visits, or a member of the data management or statistical groups when entering or analyzing data. Regardless of the source, it is crucial to document the deviation. The PI will report protocol deviations to the IRB/EC as required by the IRB/EC procedures.

## 4.5 STATISTICAL METHODS PLANNED IN THE PROTOCOL AND DETERMINATION OF SAMPLE SIZE

The Sponsor will be responsible for the analysis of data from this protocol. A detailed Statistical Analysis Plan (SAP) will be written and approved prior to final database lock. The SAP will describe all planned analyses based on the statistical design of this study and the subsequent data collected. A brief overview of key statistical analyses is provided below.

### 4.5.1 Study Design

Study design is described in Section 3.1.

### 4.5.2 Treatment Assignment

This is a single-arm study where all enrolled subjects will have the ENSEAL X1 device utilized for transection of a least one vessel.

### 4.5.3 Interval Windows

Interval windows for the purpose of analysis in this study will not be defined outside of those already specified in the protocol for visit scheduling as the collection of data for the

primary and secondary performance endpoints occurs intra-operatively. The final visit occurs approximately 4 weeks after surgery, thus no interval windows need to be defined given the absence of long-term follow-up in this study. The Schedule of Events specifies a window of 14 days around the scheduling of the 4-week follow-up visit, and any information entered in the eCRFs at this visit will correspond to the 4-week visit. There will be no assigning of observations to time points outside of the visit to which they are recorded in the eCRFs.

### 4.5.4 Primary and Secondary Endpoints and Associated Hypotheses

All study endpoints are described in Section 2.1 through Section 2.4. No formal hypotheses are specified for this study. The study endpoints are representative of endpoints that are currently reported in the available literature for similar energy devices and this will allow for comparisons with the results from this study. There also will be a stratification of vessel sealing based on medical history, named vessel type, and vessel condition.

### 4.5.5 Levels of Significance

No hypotheses are specified for this study and no p-values are being calculated, therefore no level of significance is specified. All estimation of endpoints will be performed using 95% confidence intervals.

### 4.5.6 Analysis Sets

The summary of all performance and safety endpoints will be performed on the set of subjects in whom the ENSEAL X1 device is utilized during the surgical procedure. The summary of all primary and secondary performance endpoints will be performed by procedure group (colectomy, gynecological, or thoracic). The summary of all safety endpoints will be performed by procedure group and on the entire pooled set of subjects.

### 4.5.7 Sample Size Justification

A sample size of 100 subjects is planned for enrollment in this study. No formal hypothesis is being tested in this study, thus the sample size was not statistically sized, but rather is considered sufficient for a descriptive summary of performance endpoints within each procedure group. It is expected that at least 2 vessels will be transected within each procedure, providing an expected minimum of at least 60 transections within colectomy and gynecological procedure groups and at least 40 transections in the thoracic procedure group for a total of at least 200 transections.

From a safety perspective on the pooled analysis of 100 subjects and in consideration of rare AEs that may occur (e.g., bleeding requiring blood product transfusion), for an event that has an incidence rate of, for example, 2%, then in a sample of 100 subjects, the probability of observing at least 1 event is 86.7% under a binomial probability model. Thus, this sample size provides a high probability of observing rare events if they do occur, and provides reasonable assurance to conclude that the likelihood of such AEs is less than 3.7% if they do not occur based on the upper limit of an exact 95% confidence interval when 0 events out of 100 subjects are observed.

### 4.5.8 Data Monitoring Committee

There are no plans to utilize a data monitoring committee during this study.

### 4.5.9 Analyses to be Conducted

#### *4.5.9.1 General Conventions*

Categorical variables will be summarized descriptively by frequencies and associated percentages. Continuous variables will be summarized descriptively by number of subjects, mean, standard deviation, median, minimum, and maximum. Confidence intervals will also be provided for procedure-related variables.

#### *4.5.9.2 Disposition of Study Subjects*

Subject disposition will be summarized in total and by procedure group using counts and percentages. The number and percentage of subjects completed and discontinued will be tabulated along with the specific reasons for discontinuation.

#### *4.5.9.3 Demographic, Baseline, and Surgical Characteristics*

Summary statistics of subject demographics (age, gender, and race) will be presented in total and by procedure group. Surgical characteristics including, at minimum, number of chest tubes placed, estimated blood loss, requirement for blood transfusion, and procedure duration will be summarized by procedure group and in total.

#### *4.5.9.4 Primary and Secondary Endpoint Analyses*

The number and percentage of vessels where hemostasis is achieved (≤ Grade 3) will be summarized and a 95% confidence interval will be estimated for each procedure group (colectomy, gynecological, or thoracic). Counts and percentages will be provided for type, size, and number of vessels transected, summary of grading scale distribution for all vessels transected, number of times ENSEAL X1 touch-ups were required, and incidence of requirement for additional measures to obtain hemostasis on vessels (other advanced energy devices or hemostatic products).

All device-related and procedure-related AEs reported during the study will be coded to MedDRA. All AEs will be summarized by MedDRA system organ class and preferred term by procedure group and in total. Separate summaries will be provided for device-related and procedure-related AEs. Serious AEs will be summarized in a similar manner.

#### *4.5.9.5 Plans for Interim Analyses*

No interim analyses for the purpose of stopping early are planned for this study.

#### *4.5.9.6 Handling of Missing Data*

All summaries will be performed only on subjects undergoing the scheduled procedure and only observed data will be summarized. There will be no imputation of data for early terminated subjects or for missing data within the database.

#### *4.5.9.7 Subgroup Analyses*

Subgroup analyses are planned to be performed for the subgroup of subjects who have a medical history of treatment for cancer (e.g. chemotherapy or radiation) and may be performed for additional groups pending the distributions of baseline demographic or clinical characteristics. These analyses will be exploratory and summary statistics for the procedure-related parameters will be provided for each subgroup.

# 5.0 ADVERSE EVENTS

## 5.1 DEFINITIONS

### 5.1.1 Adverse Event

An AE is defined as any untoward medical occurrence. An untoward medical occurrence includes any new, undesirable medical experience or worsening of a pre-existing condition, which occurs throughout the duration of the clinical study.

In this study, an AE is defined as any undesirable clinical occurrence in a subject that may be attributable to the study procedures or the ENSEAL X1 device. Only AEs attributable to the study procedures or the ENSEAL X1 device are to be recorded in the eCRF and reported to the Sponsor.

### 5.1.2 Serious Adverse Event

It is the Investigator's responsibility to determine the "seriousness" of a reportable AE.

A SAE is defined as an AE (as defined in Section 5.1.1) that results in any of the following:

- Death;
- A life-threatening illness or injury;
- A permanent impairment of a body structure or a body function;
- Required in-patient hospitalization or prolongation of existing hospitalization;
- Resulted in medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function;
- Led to a fetal distress, fetal death, or a congenital abnormality or birth defect.

Note: "Death" should not be reported as an AE. The cause of death should be reported as the AE. The only exception is "Sudden Death" when the cause is unknown.

Note: Planned hospitalization for a pre-existing condition, or a procedure required by the protocol, without serious deterioration in health, is not considered a SAE.

### 5.1.3 Severity of Adverse Events

It is the Investigator's responsibility to assess the severity of an AE. A change in severity may constitute a new reportable AE.

The following guideline should be used to determine the severity of each AE:

- **MILD:** A type of AE that is usually transient and may require only minimal treatment or therapeutic intervention. The event does not generally interfere with usual activities of daily living.
- **MODERATE:** A type of AE that is usually alleviated with additional specific therapeutic intervention. The event interferes with usual activities of daily living, causing discomfort but poses no significant or permanent risk of harm to the research participant.
- **SEVERE**: A type of AE that interrupts usual activities of daily living, or significantly affects clinical status, or may require intensive therapeutic intervention.

### 5.1.4 Relationship of Adverse Events

It is the Investigator's responsibility to assess the relationship of a reportable AE (as defined in Section 5.1.1). Only AEs attributable (relationship of unlikely, possible, probable, causal relationship) to the study procedures or the ENSEAL X1 device are to be

recorded in the eCRF and reported to the Sponsor.

The following guidelines should be used in determining the relationship of an AE in the study:

- **Not related** – Relationship to the procedures or device can be excluded when:
  - The event is not a known side effect of the product category the device belongs to or of similar devices and procedures;
  - The event has no temporal relationship with the use of the device or the procedures;
  - The event does not follow a known response pattern to the device (if the response pattern is previously known) and is biologically implausible;
  - The discontinuation of the device application or the reduction of the level activation/exposure (when clinically feasible) and reintroduction of its use (or increase of the level of activation/exposure), does not impact on the event;
  - The event involves a body-site or an organ not expected to be affected by the device or the procedure;
  - The event can be attributed to another cause (e.g. an underlying or concurrent illness/clinical condition, an effect of another device, drug, treatment, or other risk factors);
  - Harms to the subject are not clearly due to use error; or
  - To establish the non-relatedness, not all the criteria listed above might be met at the same time, depending on the type of device/procedure and the event.
- **Unlikely** – The relationship with the use of the device seems not relevant and/or the event can be reasonably explained by another cause, but additional information may be obtained.
- **Possible** – The relationship with the use of the device is weak but cannot be ruled out completely. Alternative causes are also possible (e.g. an underlying or concurrent illness/condition and/or an effect of another device, drug, or treatment). Cases where relatedness cannot be assessed or no information has been obtained should also be classified as possible.
- **Probable** – The relationship with the use of the device seems relevant and/or the event cannot reasonably be explained by another cause, but additional information may be obtained.
- **Causal relationship** – The event is associated with the device or with procedures beyond reasonable doubt when:
  - The event is a known side effect of the product category the device belongs to or of similar devices and procedures;
  - The event has a temporal relationship with the device uses/application or procedures;
  - The event involves a body-site or organ that:
    - The device or procedures are applied to;

- The device or procedures have an effect on;

- The event follows a known response pattern to the medical device (if the response pattern is previously known);
- The discontinuation of medical device application (or reduction of the level of activation/exposure) and reintroduction of its use (or increase of the level of activation/exposure), impact on the event (when clinically feasible);
- Other possible causes (e.g. an underlying or concurrent illness/clinical condition and/or an effect of another device, drug, or treatment) have been adequately ruled out;
- Harm to the subject is due to error in use; or
- To establish the relatedness, not all the criteria listed above might be met at the same time, depending on the type of device/procedure and the event.

### 5.1.5 Pre-existing Condition vs. Adverse Event

A pre-existing condition is defined as a medical condition that is present before the performance of the study procedure. Pre-existing conditions are to be reported as part of the subject's medical history. Worsening of a pre-existing condition while on study may be considered an AE.

## 5.2 REPORTING PROCEDURES FOR ADVERSE EVENTS

### 5.2.1 Recording Adverse Events

The Investigator will record all AEs (both AEs and SAEs) considered attributable (relationship of unlikely, possible, probable, causal relationship) to the study procedure or the ENSEAL X1 in the source documents and eCRF.

Standard medical terminology should be used when recording AEs. In addition, the following information should be recorded:

- Onset date;
- Resolution date or date of death;
- Severity of the event;
- Indication of whether the event is serious;
- Relationship of AE to the device used in the study;
- Relationship of AE to the study procedure;
- Action taken;
- Event status; and
- Was the event anticipated or not.

Data related to SAEs will be collected until the event resolution, or until the event is considered stable, or until all attempts to determine the resolution of the event are exhausted. All SAEs that are unresolved at study completion (or at the last visit completed for early withdrawal subjects) will be recorded as ongoing at study end.

### 5.2.2 Reporting Adverse Events

The Investigator is required to report AEs to the Sponsor experienced by subjects who provided informed consent to the Sponsor within two weeks from when they became aware of the event. All AEs must be reported on the AE eCRF and be documented throughout the clinical investigation.

### 5.2.3 Reporting Serious Adverse Events

Any AE that the Investigator determines to be a SAE must be reported by the study site within 72 hours of becoming aware of the event to the Sponsor by completing the SAE eCRF. A notification containing the pertinent data will be automatically generated by the EDC system and forwarded to the Sponsor. Supporting SAE documentation should be de-identified and emailed to the Clinical Study Lead.

The Investigator will be required to assess if the SAE is considered anticipated (Appendix IV) and if the event involved a product complaint. The report of an SAE by a study site does not constitute an admission that study personnel or the user facility (hospital/clinic) caused or contributed to the event. The study site is also responsible for submitting to the reviewing IRB/EC per their IRB/EC procedures.

## 5.3 SAFETY MONITORING

If any serious and unexpected AEs occur during the study, all PIs will be notified by the Sponsor within 10 days of learning of the event.

# 6.0 PRODUCT COMPLAINTS

A product complaint is any written, electronic, or oral communication that alleges deficiencies related to the identity, labeling, quality, durability, reliability, safety, effectiveness, or performance of a device after it is released for distribution. A product complaint may or may not be associated with an AE/SAE.

## 6.1 REPORTING PRODUCT COMPLAINTS FOR MARKETED DEVICES

All product complaints related to devices in the procedure shall be documented throughout the clinical investigation. Product complaints related to an Ethicon-manufactured ENSEAL X1 must be reported to the Sponsor in a timely manner and no later than 24 hours after becoming aware of the event. When a sponsor representative becomes aware of a product complaint, the Product Complaint Team must be notified within 24 hours after becoming aware of the event. The Product Complaint Form must be emailed to the Sponsor Customer Complaint team at the following email address:

[redacted]

The sites will report Product Complaints by completing the Product Complaint Form (PCF). If a product complaint is related to an AE, the site must complete an AE eCRF as well. The site will indicate on the PCF if this complaint is related to an AE and provide the description. One copy of the processed form should be kept on-site and the device should be retained. Sponsor representatives will organize collection of the device for evaluation as needed.

# APPENDIX I – VESSEL SEALING ASSESSMENT

**Table 1 | Tissue Sticking**

| Score | Description |
|---|---|
| 1 | No sticking |
| 2 | Slight sticking requiring activation of study device to release tissue |
| 3 | Tissue sticking requiring counter-tension to **gently** grasp and remove tissue |
| 4 | Tissue sticking requiring counter-tension and **extensive force** to remove tissue or such that tissue is damaged or torn during removal process |

**Comments:**

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# APPENDIX II – DEVICE PROCEDURE QUESTIONNAIRE

## DEVICE PROCEDURE QUESTIONNAIRE

ENSEAL® X1 Large Jaw Tissue Sealer

Surgeon's (Printed) Name: _____

Procedure Date: _____ Subject #: _____

1. Was the transection of the vessels by the ENSEAL® X1 device performed with just one hand or were two hands needed at any time to complete it:

   ☐ One hand ☐ Two hands

   If two hands were used, please describe:

   _____

   _____

2. Did the ENSEAL® X1 device have to be removed and then put back into the surgical field during the transection of the vessels for repositioning or adjustment:

   ☐ Yes ☐ No

   If yes, please describe and list how many times this was done:

   _____

   _____

3. Was there a need to change hand positions to activate the ENSEAL® X1 device during the transection of the vessels:

   ☐ Yes ☐ No

   If yes, please explain:

   _____

   _____

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# APPENDIX III – SURGEON QUESTIONNAIRE

## SURGEON QUESTIONNAIRE

**ENSEAL® X1 Large Jaw Tissue Sealer (ENSEAL® X1)**

**Surgeon's (Printed) Name:** _____

**Glove Size:** _____ **Procedure Date:** _____

1. The ENSEAL® X1 device was better balanced compared to previous advanced bipolar device use:

   ☐ Strongly disagree ☐ Slightly disagree ☐ Neutral ☐ Slightly agree ☐ Strongly agree

   Comments:_____

   _____

2. You experienced less hand fatigue using the ENSEAL® X1 device compared to previous advanced bipolar device use:

   ☐ Strongly disagree ☐ Slightly disagree ☐ Neutral ☐ Slightly agree ☐Strongly agree

   Comments:_____

   _____

3. The buttons were easily distinguishable on the ENSEAL® X1 device:

   ☐ Strongly disagree ☐ Slightly disagree ☐ Neutral ☐ Slightly agree ☐Strongly agree

   Comments:_____

   _____

4. The firing (sealing/cutting) of the ENSEAL® X1 device was easier compared to previous advanced bipolar device use:

   ☐ Strongly disagree ☐ Slightly disagree ☐ Neutral ☐ Slightly agree ☐Strongly agree

   Comments:_____

   _____

5. Transection of vessels with the ENSEAL® X1 device could be performed with just one hand compared to previous advanced bipolar device use:

☐ Strongly disagree ☐ Slightly disagree ☐ Neutral ☐ Slightly agree ☐Strongly agree

Comments:_____

_____

6. Were there any differences in the general ease of use and dissecting and sealing capabilities of the ENSEAL® X1 device compared to previous advanced bipolar device use:

☐ Yes ☐ No

If yes, please describe and list the previous device used:

_____

_____

7. Were there any noticeable differences in terms of thermal spread of the ENSEAL® X1 device compared to previous advanced bipolar device use:

☐ Yes ☐ No

If yes, please describe and list the previous device used:

_____

_____

# APPENDIX IV – ANTICIPATED ADVERSE EVENTS

**Associated with General Anesthesia, Thoracic Surgery, Colectomy Surgery, and Gynecological Surgery**

Abscess
Acute respiratory distress syndrome
Adhesions
Air/gas embolism
Altered mental status
Anaphylaxis
Anastomotic leak
Anemia
Angina
Atelectasis
Bacteremia
Bladder injury
Bleeding
Bowel/bladder urgency or incontinence
Bowel obstruction
Bradycardia
Broncho pleural fistula
Cardiac arrhythmia
Central line infection
Cerebrovascular accident/stroke
Chylothorax
Congestive heart failure
Constipation
Deep venous thrombosis
Dehydration
Dementia
Diaphragmatic injury
Diarrhea
Discharge of feces through drain
Disseminated intravascular coagulation (DIC)
Dizziness
Dysphagia
Dyspareunia
Electrolyte imbalance
Empyema
Esophageal injury
Evisceration
Fever, pyrexia
Fistula
Headache
Hematuria
Hemorrhage
Hemothorax
Hernia
Hypernatremia
Hyperphosphatemia
Hypertension
Hypotension, shock
Hypoxia
Ileus
Incisional hernia
Infection/SSI/abscess
Infertility
Intercostal nerve injury
Ischemia
Jaundice
Leak
Lethargy
Leukocytosis
Liver failure
Mesenteric infarct
Mesenteric ischemia
Myocardial infarction
Nausea
Nerve injury
Nutrient deficiency
Obtundation, depressed levels of consciousness
Oliguria
Pain (increased/severe/chronic)
Peritonitis
Pneumonia
Pneumothorax
Premature menopause
Prolonged air leak
Pulmonary air leak
Pulmonary embolism
Renal failure
Respiratory failure
Respiratory insufficiency
Sepsis
Sexual dysfunction (or erectile/ejaculatory dysfunction)
Somnolence
Stricture
Systemic inflammatory response syndrome
Tachycardia
Thoracic duct injury
Thromboembolic event
Tightness of the chest
Thrombocytopenia
Thromboembolic event
Thrombosis
Transient ischemic attack
Tightness of the chest, angina
Tinnitus
Urinary retention
Urinary tract infection
Ureteric injury
Vaginal cuff dehiscence
Vascular injury
Volume depletion, hypovolemia
Vomiting
Wheezing
Wound dehiscence
Wound infection