A multi-center, randomized, controlled, single blinded, parallel-group study evaluating the clinical performance and safety of LiquiBand FIX8® versus control for hernia mesh fixation and peritoneal closure in groin hernia repair.

Clinical Evaluation of LiquiBand FIX8®

Clinical Investigational Plan

Protocol Number: LBF8-01

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Version / Date of Protocol	**Version 1.3 / 08Jan2021**

Sponsor Signatory

Brian Dowd, Director of Surgical Marketing
Advanced Medical Solutions (USA) Inc.

5/21/21
Date

CAUTION -- Investigational devices. Limited by United States law to investigational use.

INVESTIGATOR'S AGREEMENT

I have received and read the Report of Prior Investigations. I have read the LBF8-01 v1.3, (08Jan2021) protocol and agree to conduct the study as outlined. I agree to maintain the confidentiality of all information received or developed in connection with this protocol.

_____

Printed name of Investigator

_____

Signature of Investigator

_____

Date

CLINICAL INVESTIGATION SUMMARY

Study Title: A multi-center, randomized, controlled, single blinded, parallel-group study evaluating the clinical performance and safety of LiquiBand FIX8® versus control for hernia mesh fixation and peritoneal closure in groin hernia repair.

Investigational Device: LiquiBand FIX8® Hernia Mesh Fixation Device

Device Description: The device consists of:

a) n-butyl-2-cyanoacrylate adhesive monomer, in liquid form, supplied in a thin-walled, sealed glass vial; and,

b) a surgically invasive, laparoscopic 5mm diameter cannula, with a handle at the proximal end incorporating a loading chamber, filter, piston chamber and trigger. The distal tip of the device is open to allow the adhesive to be dispensed from it.

The device is designed to be used in conjunction with a 5 mm diameter laparoscopic port sleeve. Both the cyanoacrylate adhesive in the glass vial and the surgically invasive delivery device are supplied sterile, for single use only.

Indication for Use: The LiquiBand FIX8® device is intended for use in laparoscopic surgical repair of groin (femoral and inguinal) hernias, achieved through the fixation of prosthetic mesh to the abdominal wall and the approximation of peritoneum.

Design: Prospective, two-arm, randomized, single blinded, multi-center study.

Purpose: To demonstrate the efficacy and safety of LiquiBand FIX8® for groin hernia repair.

Objectives: Primary:

1. To compare the improvement in pain following groin hernia repair by LiquiBand FIX8® to control device as measured by Visual Analog Scale (VAS) at baseline (worst pain experienced within 1 month of screening visit) and at six months post hernia repair.

Secondary:

1. To evaluate the incidence of hernia recurrence in patients following laparoscopic (TEP and TAPP) hernia repair using LiquiBand FIX8® or control device at 6 months post hernia repair.
2. To compare the use of LiquiBand FIX8® to control device for mesh fixation at time of surgery.
3. To compare the use of LiquiBand FIX8® to control devices for the approximation of the peritoneum (TAPP repairs only) at time of surgery.

4. To evaluate the quality of life experienced by subjects following groin hernia repair by LiquiBand FIX8® or control as measured by the Carolinas Comfort Scale (CCS) at baseline (prior to surgery), and at 1 week, 2 weeks, 1 month, 3 months, 6 months, 9 months and 12 months following surgery.
5. To compare levels of pain experienced following laparoscopic (TEP and TAPP) groin hernia repair by LiquiBand FIX8® or control device, as measured by VAS at discharge, and at 1 week, 2 weeks, 1 month, 3 months, 6 months, 9 months and 12 months following surgery.
6. To evaluate the safety of LiquiBand FIX8® and control device for groin hernia repair by comparing incidence of all adverse events in patients post laparoscopic groin hernia repair.

Number of patients: 284 (142 per treatment arm)

Investigational centers: Up to 10 investigational centers will be recruited for this study, including the following institutions:

University of Kentucky

1. The Ohio State UniversityPrisma Health – Upstate
2. Overlake Medical CenterCleveland Clinic
3. Prisma Health – Upstate
4. Overlake Medical Center
5. Cleveland Clinic

Inclusion/Exclusion: Inclusion Criteria

Patients who meet all the following criteria at the time of enrollment may be included:

1. Is male or female, ≥22 years of age
2. Is willing and able to give written informed consent
3. Has a primary or recurrent groin hernia (unilateral or bilateral, inguinal or femoral)
4. Is currently scheduled and eligible for TAPP or TEP laparoscopic groin hernia repair (inguinal or femoral)
5. Hernia mesh to be used at the time of surgery is at least 4” x 6” in size and is one of the following;
   - **a.** 3D Max™ Mesh (Bard Inc.)
   - **b.** 3D Max™ Light (Bard Inc.)
   - **c.** Parietex™ 2D (order code starting with TEC) Flat Sheet Mesh (Medtronic)
   - **d.** Parietex™ 3D (order code starting with TET) Flat Sheet Mesh (Medtronic)
6. Is willing and able to comply with the protocol assessments at time of surgery and during the post surgical follow up period

Exclusion Criteria

Patients who meet any one of these criteria will be excluded from the investigation:

1. Has a hernia type not suitable for laparoscopic hernia repair as determined by the Investigator (i.e. strangulated)
2. Subject has a recurrent groin hernia previously repaired laparoscopically, has an anatomical defect or had prior surgical procedures that in the opinion of the Investigator prevents access to the pre-peritoneal space for TAPP or TEP laparoscopic hernia repair
3. Is pregnant or actively breastfeeding
4. Has a known sensitivity to cyanoacrylate or formaldehyde,D&C Violet No.2 dye or any component of LiquiBand FIX8® or control device
5. Has an active or potential infection at the surgical site or systemic sepsis
6. Hernia mesh to be used at surgery is less than 4”x6” in size, or not one of the types of mesh listed in Inclusion Criteria #5.
7. Cannot tolerate general anaesthesia
8. Has any significant or unstable medical or psychiatric condition that, in the opinion of the Investigator, would interfere with his/her ability to participate in the study.
9. Is currently enrolled in another clinical study or undergoing treatment with another investigational drug or device.

ENDPOINTS

Table 1: Primary and Secondary Efficacy and Safety Endpoints of the Investigational Study	
Primary Efficacy 1	Effectiveness of LiquiBand FIX8® will be assessed and compared to treatment with AbsorbaTack™ in subjects requiring laparoscopic (TEP and TAPP) hernia repair. Success will be determined by improvement in pain not inferior to control device as measured by a VAS value (0 = no pain to 10 = most pain imaginable) from baseline (worst pain experienced within 1 month of screening visit) to six months post hernia repair.
Secondary Efficacy 1	The incidence of hernia recurrence in patients following laparoscopic (TEP and TAPP) groin hernia repair by LiquiBand FIX8® or control (AbsorbaTack™) will be assessed by physical examination at 2 weeks, 3 months, and 6 months and evaluated following the 6 month timepoint. Suspected hernia recurrence will also be evaluated at any time following surgery and up to the 12 month follow up visit if reported by the subject. Suspected hernia recurrence will be confirmed by ultrasound imaging following physical examination.
Secondary Efficacy 2	LiquiBand FIX8® will be required to successfully fix hernia mesh in patients undergoing TEP and TAPP laparoscopic groin hernia repair, at a rate non-inferior to control device (AbsorbaTack™) in order to meet this end point. Successful mesh fixation would not require any additional fixation by alternate fixation device. Unsuccessful mesh fixation is defined as requiring the use of an alternative fixation device or additional procedure to achieve adequate fixation.
Secondary Efficacy 3	LiquiBand FIX8® will be required to successfully approximate the peritoneum in patients undergoing laparoscopic TAPP hernia repair, at a rate non-inferior to control devices in order to meet this end point. Successful peritoneal closure would not require any additional fixation by alternate fixation device or additional procedure. Unsuccessful peritoneal closure is defined as requiring the use of an alternative fixation device or additional procedure to achieve adequate fixation. Investigators in the study will be able to use AbsorbaTack™, sutures or staples for closure of the peritoneum.
Secondary Efficacy 4	Quality of Life will be assessed by completion of the Carolinas Comfort Scale (CCS) Questionnaire prior to surgery and at 1 week, 2 weeks, 1 month, 3 months, 6 months, 9 months and 12 months following laparoscopic (TEP and TAPP) groin hernia repair. CCS scores at each timepoint will be compared between the LiquiBand FIX8® and control (AbsorbaTack) treatment groups.
Secondary Efficacy 5	Evaluation of pain will be measured by VAS (0 = no pain to 10 = most pain imaginable) at baseline (pre-surgery), at discharge, and at 1 week, 2 weeks, 1 month, 3 months, 6 months, 9 months and 12 months post surgery.
Secondary Safety 1	The incidence of all adverse events whether or not determined to be related to the LiquiBand FIX8® device or control device (AbsorbaTack™) will be assessed intraoperatively, at discharge, and at each follow-up visit throughout the study, or for cause at any time in the follow up period.

SCHEDULE OF STUDY ASSESSMENTS

Table 2: Study design and schedule of assessments. (Shaded columns represent assessments performed in-clinic, non-shaded for remote visits).

	Pre-Surgery	Surgery	Discharge	Post-Surgery Visits							Unscheduled visit
Visit	1	2	3[3]	4	5	6	7	8	9	10	N/A
Day / Month	≤21 Days	Day 0	Day 0 or 1	Day 7	Day 14	Month 1	Month 3	Month 6	Month 9	Month 12	N/A
Visit Window (Days)				±3	-3 / +6	±7	±14	-21 / +14	-21 / +14	-21 / +14	N/A
Informed Consent	X										
Inclusion/ Exclusion	X										
Pregnancy Test (if applicable)		X[1]									
Medical History	X										
Analgesics usage	X	X[1]	X	X	X	X	X	X	X	X	X
Demographics	X										
Vital Signs (HR/BP/T/Ht/Wt)[4]	X	X[1]	X		X		X	X			X
Randomization[5]		X[2]									
Hernia Information (type & size)	X	X[2]									
Use of Investigational or control device		X[2]									
Number of Investigational or control device applications		X[2]									
Photograph following mesh fixation		X									
Photograph following peritoneal closure[6]		X									
Clinician evaluation of hernia repair & PE[7]					X		X	X			X
Subject Pain (0-10 VAS) Assessment	X		X	X	X	X	X	X	X	X	
Subject QOL Assessment	X			X	X	X	X	X	X	X	
AE Evaluation		X[2]	X	X	X	X	X	X	X	X	X

[1]Immediately prior to surgery
[2]During surgery
[3]At discharge post-surgery, either on same day as surgery or next day post-surgery according to standard of care
[4]Height only required at Pre-surgery visit. Unless Pre-surgery (Visit 1), Surgery (Visit 2) and Discharge (Visit 3) occur on the same date, weight should be obtained for each separate visit. Vital signs may be obtained remotely at Month 3 and 6 visits as volunteered by subjects using their own devices as available (e.g. thermometer, weight scales, smart wearable technology)
[5]Patient must be blinded to the randomized device
[6]Photograph following peritoneal closure only required for TAPP repairs

[7]Suspected hernia recurrence will be confirmed by ultrasound imaging following physical examination

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ABBREVIATIONS

ADE:	Adverse Device Effect
ADL:	Activities of Daily Living
AE:	Adverse Event
BO:	Bending Over
BP:	Blood Pressure
CB:	Couging or Deep Breathing
CCS:	Carolinas Comfort Scale
E:	Exercise
eCRF:	Electronic Case Report Form
EDC:	Electronic Data Capture System
FDA:	Food and Drug Administration
GCP:	Good Clinical Practice
HIPAA:	Health Insurance Portability and Accountability Act
HR:	Heart Rate
Ht:	Height
ICF:	Informed Consent Form
ICH:	International Conference on Harmonization
IDE:	Investigational Device Exemption
IRB:	Independent Review Board
LD:	Laying Down
OUS:	Outside USA
PE:	Physical Exam
PI:	Principal Investigator
QOL:	Quality of Life
S:	Stairs
SADE:	Serious Adverse Device Effect
SAE:	Serious Adverse Event
SU:	Sitting Up
T:	Temperature
TEP:	Totally Extraperitoneal
TAPP:	Transabdominal Preperitoneal
UADE:	Unanticipated Adverse Device Effect
VAS:	Visual Analog Scale
W:	Walking
Wt:	Weight

1 INTRODUCTION

1.1 Overview

Laparoscopic hernia mesh fixation has become more commonplace worldwide for abdominal herniorrhaphy since first demonstrated in the early 1990's [1] [2]. Mesh fixation by this technique typically requires the use of a mechanical fastener, such as suture or a screw-like tack to physically attach the mesh to the abdominal wall. While providing strong fixation, permanent metal fasteners have been associated with high instances of chronic pain and other complications. Absorbable fasteners have been more recently developed as alternatives to permanent devices, however chronic pain continues to be an issue due to the associated penetration of abdominal tissues [2]. Surgical adhesives have recently been promoted as an alternative to mechanical fasteners due to their strong adhesive properties, without tissue penetration. These adhesives have been used as alternatives to other penetrative wound closure methods such as sutures and staples in topical wound closure since the late 1990's [3]. Most commonly formulated from cyanoacrylate polymers, these adhesives rapidly polymerize in contact with moisture on the skin to bond opposing sides of a wound forming an effective and durable wound closure. The LiquiBand FIX8® device incorporates a similar cyanoacrylate adhesive formulation, packaged in a laparoscopic delivery instrument to provide internal mesh and peritoneal tissue fixation as opposed to topical wound closure. LiquiBand FIX8® obtained CE-marking for approval in the European Union in 2014 for inguinal hernia mesh fixation and is now approved for peritoneal closure in addition to other indications. In addition to the EU, LiquiBand FIX8® is approved for use in multiple other countries worldwide including Australia, Canada, Israel and the United Arab Emirates. Independent evaluations of the LiquiBand FIX8® device have found it to be safe and effective for hernia mesh fixation and peritoneal closure, and although the authors stated the low occurrence of complications, the limited scope of these studies did not include a detailed review of post-operative pain [4] [5] [6] [7] [8] [9] [11]. In this study, further evaluation of the clinical performance and safety of the LiquiBand FIX8® device is proposed, including the detailed assessment of any long term post operative pain and other complications experienced by study subjects.

1.2 Background

A detailed overview of pre-clinical and clinical evaluations of the LiquiBand FIX8® device and similar adhesive technologies can be found in the Report of Prior Investigations (provided separately to this document).

1.3 Description of Study Devices

1.3.1 Investigational Device (LiquiBand FIX8®)

The LiquiBand FIX8® device is a CE-Marked device approved for use in the laparoscopic surgical repair of inguinal hernia, achieved through the fixation of prosthetic mesh (including polypropylene, polyester or polypropylene/polyester combinations) to the abdominal wall (in inguinal and ventral incisional) and for tissue to tissue approximation of the peritoneum, in Europe and other OUS markets. For the IDE device IFU, refer to Appendix 9.2. An image of the device is shown in Figure 1 below. The device consists of:

1. n-butyl-2-cyanoacrylate adhesive monomer and D&C Violet #2 dye [10], in liquid form, supplied in a thin walled, sealed glass vial
2. a surgically invasive laparoscopic 5mm diameter cannula, with a handle at the proximal end incorporating a loading chamber, filter, piston chamber and trigger. The distal tip of the device is open to allow the adhesive to be dispensed from it.

The device is designed to be used in conjunction with a 5 mm diameter laparoscopic port sleeve. Both the cyanoacrylate adhesive in the glass vial and the surgically invasive delivery device are supplied sterile, for single use only.

Prior to the use of the device, surgeons should be fully proficient in minimally invasive/laparoscopic hernia repair surgical techniques.
LiquiBand FIX8® is supplied in outer packaging consistent with regulatory and safety requirements.

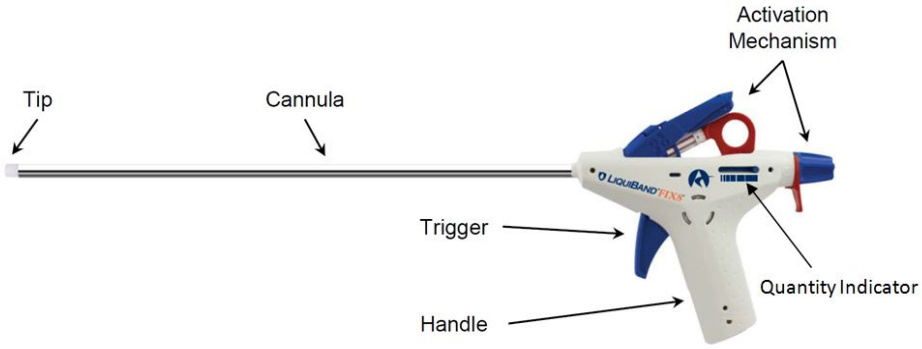


Figure 1: LiquiBand FIX8® Device

1.3.1.1 Principles of Operation & Mechanism of Action

Principle of Operation

The glass vial containing the liquid cyanoacrylate adhesive monomer comes preloaded into, and is subsequently broken in, a loading chamber in the handle of the delivery instrument. The adhesive is drawn through a filter into a piston chamber in the delivery instrument handle. After priming, each press of the trigger on the handle of the delivery instrument dispenses 12.5 mg of adhesive from the distal tip of the cannula. A single device contains sufficient adhesive for 40 or more individual applications of the adhesive. The gauge on the side of the delivery instrument gives an indication of the amount of adhesive delivered and the approximate amount remaining.

Mechanism of Action

When applied to the proximal surface of the hernia mesh, the liquid adhesive monomer permeates through the perforations in the mesh to the surface of the underlying tissue, where it polymerizes on contact with moisture on the tissue surface. This process of chemical polymerization fixes the mesh to the surface of the tissue at the site of adhesive

contact, maintaining the mesh in position while it is incorporated into the abdominal wall through the normal process of tissue fibrosis, becoming permanently implanted. Polymerization occurs as the adhesive comes into contact with moisture. The adhesive bond forms by the polymerization happening between the two overlapped sections of peritoneum tissue, and adhering the two surfaces together. The adhesive completes its polymerization reaction within approximately 10 seconds. Once completely polymerized, the adhesive becomes a solid plastic bonded to the tissue and mesh or tissue on tissue. This polymerized plastic has no residual adhesive property and will not bond with other materials or tissues, like instruments or organs.

1.3.1.2 Summary of Previous Clinical Experience

The LiquiBand FIX8® device was CE-marked on 13 June 2014 and since that time, Advanced Medical Solutions Ltd. has conducted Post Market Surveillance (PMS) as part of its obligation to Directive 93/42/EEC Annex II, clause 3 and EN ISO 13485:2016. The PMS process includes the documentation of customer complaints, customer feedback and compilation of any clinical evaluations. Since launch in 2014 until October 31, 2018, out of a total of 46,493 devices sold, 1272 units (2.73%) were associated with complaints of device malfunction and 19 units were associated with complaints of adhesive failure (0.04%). Investigation into the units associated with device malfunction found that these devices were unable to be activated due to a mechanical defect or malfunction, or were unable to deliver adhesive, which did not pose any risk to the patients. In each case of device malfunction, the investigator would be able to use a new device to complete the hernia repair, either LiquiBand FIX8® or another marketed fixation device. Investigation into the devices reported for adhesive failure found no issue with adhesive used in the same lot and reference numbers of devices and it is concluded that these reports were from improper use, or mechanical failure of the device as opposed to adhesive failure.

Along with pre-clinical testing, six(6) independent OUS clinical evaluations have been conducted evaluating the LiquiBand FIX8® device for hernia mesh fixation for groin hernia (inguinal and femoral), Spigelian hernia and Inguinal Disruption repair, with four (4) of the evaluations including peritoneal closure [4][5][6][7][9][11]. A combined total of 354 subjects were enrolled in these evaluations for a total of 415 hernia repairs (398 TAPP, 17 TEP) and the device was found to perform as intended with minimal post operative pain and complications (see section 4.0 below for a summary of these evaluations).

Additionally, the LiquiBand FIX8® device has been evaluated for use in other non-groin hernia repairs including; Incisional/Ventral, Parastomal, Umbilical, and Hiatal hernia repairs, with minimal complications observed from a total of 64 subjects [12][13][14]. In all evaluations, the Investigators reported that the device was safe and effective for use in abdominal hernia repair.

1.3.2 Control Device (AbsorbaTack™)

AbsorbaTack™ 5mm Absorbable Fixation Device (Medtronic/Covidien) is FDA-cleared for the fixation of prosthetic material, such as mesh, to soft tissue. The device consists of a laparoscopic delivery instrument that dispenses implantable tacks constructed of an absorbable synthetic polyester copolymer derived from lactic and glycolic acid and is dyed with D&C Violet No. 2.

The device is intended for fixation of prosthetic material to soft tissue in various minimally invasive and open surgical procedures such as hernia repair. For the device IFU, refer to Appendix 9.3.

1.4 Study Population

Subjects for this study will be recruited from patient populations at the Investigational sites already scheduled for laparoscopic (TEP or TAPP) groin hernia (inguinal or femoral) repair. Prospective subjects will be pre-screened prior to or at their pre-surgery visit to determine whether they may be eligible for participation based on the inclusion and exclusion criteria, and will then be recruited for participation. The Investigational sites participating in this study are hospitals and medical centers within the USA that specialize in minimally invasive surgery, including laparoscopic hernia repair. Inguinal hernias are the most common form of groin hernia and have a 9:1 male predominance, with a higher incidence among men over the age of 40 [15][16]. Additionally, white men have 2-times higher rate of incidence of inguinal hernia than black men [15]. Femoral hernias account for only 2% to 4% of all groin hernias and are more likely to occur in women than in men [17]. It is therefore expected that most subjects enrolled in this study are white males, 40 years and older. Recruitment will occur at up to 10 Investigational centers across the USA, each drawing from their own populations of patients scheduled for laparoscopic hernia repair.

1.5 Study Objective

The objective of this study is to compare the efficacy and safety of the LiquiBand FIX8® device to a tack-based control device (AbsorbaTack™) for the TEP (totally extraperitoneal) or TAPP (transabdominal preperitoneal) laparoscopic repair of groin (femoral or inguinal) hernia by mesh fixation and closure of the peritoneum (TAPP patients only).

2 PROTOCOL

2.1 Ethical Considerations and Regulatory Approval

This study will be conducted in accordance with ISO 14155:2011 Clinical Investigation of Medical Devices for Human Subjects-Good Clinical Practice, or the relevant parts of the ICH Guidelines for Good Clinical Practice, ethical principles that have their origins in the Declaration of Helsinki, and applicable regulatory requirements including 21 CFR 812 Investigational Device Exemptions and 21 CFR 50 Protection of Human Subjects. The study shall not begin until the required approval/favorable opinion from an Institutional Review Board (IRB) and/or regulatory authority has been obtained, if appropriate. Any additional requirements imposed by the IRB or regulatory authority shall be followed, if appropriate.

2.2 Study Design

This study is a multi-center, randomized, two-arm, single blinded, prospective trial in 284 patients (approximately 142 per treatment group) at up to 10 investigational sites in the USA.

This investigational study is intended to evaluate the performance and safety of the LiquiBand FIX8® device for TEP (totally extraperitoneal) or TAPP (transabdominal preperitoneal) laparoscopic repair of groin hernias (femoral and inguinal) and closure of the peritoneum (TAPP repairs only), compared to an existing marketed tack-based fixation device (AbsorbaTack™). This study will include three phases:

1. Pre-surgery (up to 21 days prior to and including day of surgery),
2. Surgery and discharge (Days 0 up to 1),

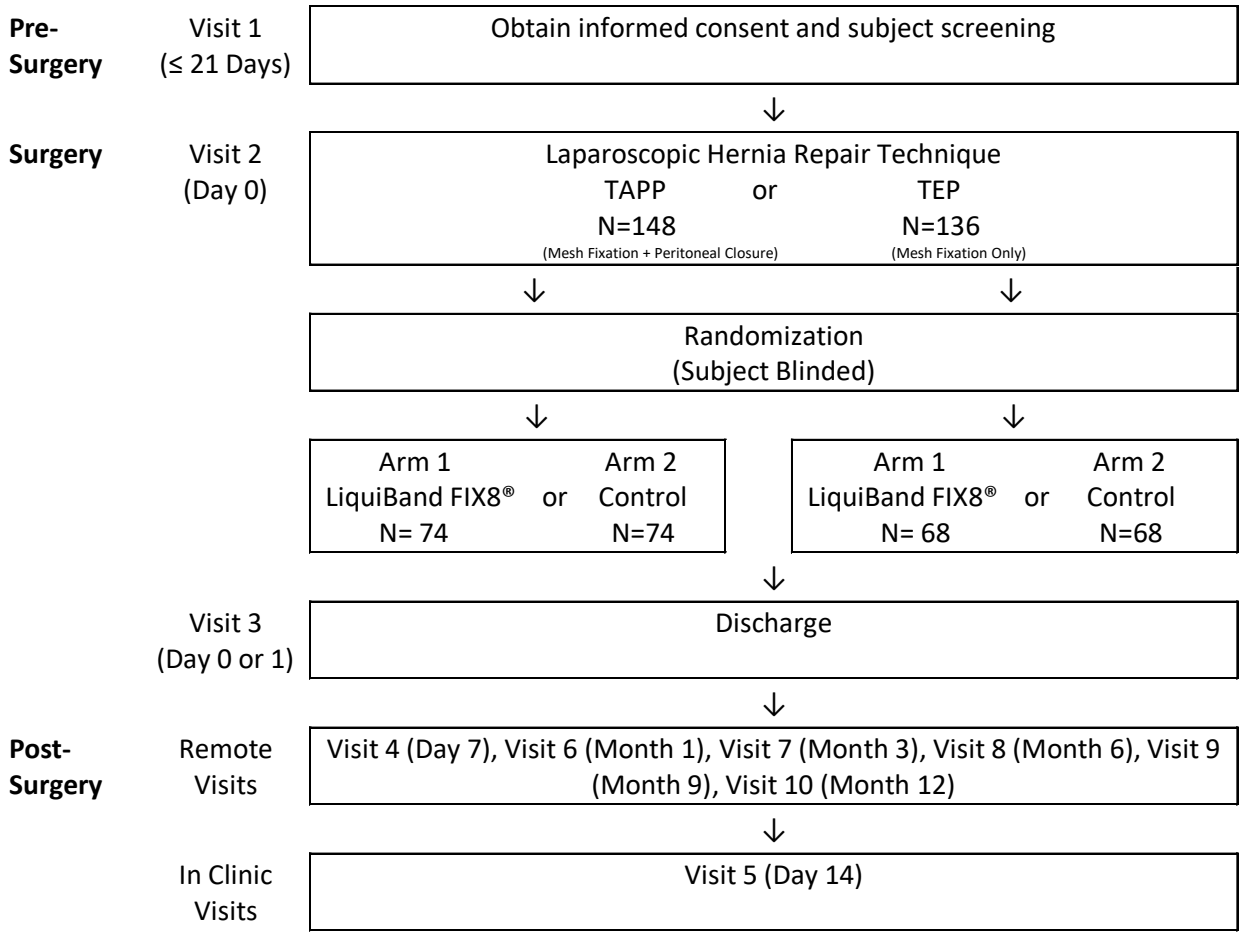
3. Post surgery (up to 12 months following surgery).

Patients already scheduled for laparoscopic (TEP or TAPP) groin hernia repair will be recruited and consented at Investigational sites at the pre-surgery visit and if meeting the inclusion and exclusion criteria will be randomized at time of surgery to either the Investigational LiquiBand FIX8® device, or to the control device (AbsorbaTack™) for their groin hernia repair. Subjects will be blinded to the device assignment and study staff will be instructed to maintain this blinding so as to not bias the subject's completion of assessments throughout the study.

The primary endpoint of reduction in pain will be evaluated at the 6 month visit and will measure the reduction of recorded VAS between baseline (worst pain experienced within 1 month of screening visit) and 6 month visits. The secondary endpoints of mesh fixation and peritoneal closure (TAPP repairs only) will be assessed at time of surgery.

Following discharge, study subjects will enter the follow up period consisting of in-clinic and remote visits to assess the secondary end points of pain, quality of life as well as incidence of hernia recurrence and adverse events. Subjects will exit the study following completion of the Month 12 visit, and subjects may be contacted to collect information up to 5 years following surgery. Refer to Figure 2 for the Study Design Diagram.

Figure 2: Study Design Diagram



Study Hypothesis

The study hypothesis is that the LiquiBand FIX8® device is non-inferior to a tack-based control device (AbsorbaTack™) for the laparoscopic (TEP and TAPP) repair of groin hernia. Non-inferiority will be demonstrated in a primary efficacy endpoint of improvement (decrease) of pain scores, measured by Visual Analog Scale (VAS), between baseline (worst pain experienced within 1 month of screening visit) and 6 months post-operatively.

2.3 Study Objectives and Endpoints

This study considers the primary efficacy endpoint as well as secondary efficacy and safety endpoints for which labeling claims based on hypothesis tests are desired (see listed in Table below).

The trial will be considered a success if the primary hypothesis is met for both the PP and ITT sets (details are provided in Table 3 below).

Below is the list of primary and secondary endpoints:

Table 3: Primary and secondary objectives and endpoints

	Objective	Endpoint
Primary 1	To compare the improvement in pain following groin hernia repair by LiquiBand FIX8® to control device as measured by Visual Analog Scale (VAS) at baseline (worst pain experienced within 1 month of screening visit) and at six months post hernia repair.	Effectiveness of LiquiBand FIX8® will be assessed and compared to treatment with AbsorbaTack™ in subjects requiring laparoscopic (TEP and TAPP) hernia repair. Success will be determined by improvement in pain not inferior to control device as measured by a VAS value (0 = no pain to 10 = most pain imaginable) from baseline (worst pain experienced within 1 month of screening visit) to six months post hernia repair.
Secondary 1	To evaluate the incidence of hernia recurrence in patients following laparoscopic (TEP and TAPP) hernia repair using LiquiBand FIX8® or control device.	The incidence of hernia recurrence in patients following laparoscopic (TEP and TAPP) groin hernia repair by LiquiBand FIX8® or control (AbsorbaTack™) will be assessed by physical examination at 2 weeks, 3 months, and 6 months. Suspected hernia recurrence will also be evaluated at any time following surgery and up to the 12 month follow up visit if reported by the subject. Suspected hernia recurrence will be confirmed by ultrasound imaging following physical examination.
Secondary 2	To compare the use of LiquiBand FIX8® to control device for mesh fixation at time of surgery.	LiquiBand FIX8® will be required to successfully fix hernia mesh in patients undergoing TEP and TAPP laparoscopic groin hernia repair, at a rate non-inferior to control device (AbsorbaTack™) in order to meet this end point. Successful mesh fixation would not require any additional fixation by alternate fixation device.

		Unsuccessful mesh fixation is defined as requiring the use of an alternative fixation device or additional procedure to achieve adequate fixation.
Secondary 3	To compare the use of LiquiBand FIX8® to control devices for the approximation of the peritoneum (TAPP repairs only) at time of surgery.	LiquiBand FIX8® will be required to successfully approximate the peritoneum in patients undergoing laparoscopic TAPP hernia repair, at a rate non-inferior to control devices in order to meet this end point. Successful peritoneal closure would not require any additional fixation by alternate fixation device or additional procedure. Unsuccessful peritoneal closure is defined as requiring the use of an alternative fixation device or additional procedure to achieve adequate fixation.
Secondary 4	To evaluate the quality of life experienced by subjects following groin hernia repair by LiquiBand FIX8® or control as measured by the Carolinas Comfort Scale (CCS) at baseline (prior to surgery), and at 1 week, 2 weeks, 1 month, 3 months, 6 months, 9 months and 12 months following surgery.	Quality of Life will be assessed by completion of the Carolinas Comfort Scale (CCS) Questionnaire prior to surgery and at 1 week, 2 weeks, 1 month, 3 months, 6 months, 9 months and 12 months following laparoscopic (TEP and TAPP) groin hernia repair. CCS scores at each timepoint will be compared between the LiquiBand FIX8® and control (AbsorbaTack) treatment groups.
Secondary 5	To compare levels of pain experienced following laparoscopic (TEP and TAPP) groin hernia repair by LiquiBand FIX8® or control device, as measured by VAS at discharge, and at 1 week, 2 weeks, 1 month, 3 months, 6 months, 9 months and 12 months following surgery.	Evaluation of pain will be measured by VAS (0 = no pain to 10 = most pain imaginable) at baseline (pre-surgery), at discharge, and at 1 week, 2 weeks, 1 month, 3 months, 6 months, 9 months and 12 months post surgery.
Secondary 6	To evaluate the safety of LiquiBand FIX8® and control device for groin hernia repair by comparing incidence of adverse events in patients post laparoscopic groin hernia repair.	The incidence of all adverse events whether or not determined to be related to the LiquiBand FIX8® device or control device (AbsorbaTack™) will be assessed intraoperatively, at discharge, and at each follow-up visit throughout the study, or for cause at any time in the follow up period.

2.4 Study Period

The study is expected to begin in March 2019 and the study enrollment phase is expected to last approximately 18 months. With subject follow up of 12 months and 2 months of data analysis, the total study duration is expected to be approx. 32 months, and subjects may be contacted to collect information up to 5 years following surgery.

The clinical investigation of the study devices will not begin in any center until:

- Approval or no objection has been obtained from the FDA, as required by current national and/or local laws on the rights, safety, and welfare of human subjects.
- Approval has been obtained from the relevant IRB, including approval from national and/or local IRB as required by current national and/or local laws on the rights, safety, and welfare of human subjects.
- Liability coverage has been obtained by the sponsor, as required by current national and/or local laws on the rights, safety, and welfare of human subjects.
- Investigator agreement has been obtained from the investigator(s) in the center, as required by the Declaration of Helsinki and national/local laws on the rights, safety, and welfare of human subjects.

2.4.1 Duration of patient's participation in the study

Including the up to 21 days pre-surgery screening period, and 12 months of follow up visits, subject's individual participation in this study will be approx. 12-13 months, and subjects may be contacted to collect information up to 5 years following surgery. . Patient's participation in the study:

- Starts once the patient is determined eligible to participate and he/she has signed the consent form, after having received the appropriate information about the study.
- Ends if any of the following occurs:
  - Completion of all study visits
  - At any time, in the case of withdrawal of patient's consent or cooperation (i.e. the patient refuses to participate further in the study); in case the patient has been lost to follow-up, in case exclusion of the patient from the study is required for patient's safety according to the Investigator's judgment, in case of patient's death, or in case of withdrawal of approval from relevant IRB. The patient may also be withdrawn at any time at the decision of the study sponsor.

A Study Exit Form must be completed in order to document and justify the end of a patient's participation in the study.

2.5 Number of subjects under clinical study

284 patients (approximately 142 per treatment group) will be enrolled in this study. The Sponsor expects to enroll 100% of the patients across up to 10 investigational centers in the USA.

2.6 Eligibility Criteria

The patient population of this trial will consist of patients with primary or recurrent (except for prior laparoscopic repair), unilateral or bilateral groin hernia(s), scheduled for laparoscopic groin hernia repair and meet study eligibility criteria.

All study candidates must provide written informed consent before they undergo any study-related procedure.

2.6.1 Inclusion Criteria

Patients who meet all of these criteria at time of enrollment may be included in the investigation:

1. Is male or female, ≥22 years of age
2. Is willing and able to give written informed consent
3. Has a primary or recurrent groin hernia (unilateral or bilateral, inguinal or femoral)
4. Is currently scheduled and eligible for TAPP or TEP laparoscopic groin hernia repair (inguinal or femoral)
5. Hernia mesh to be used at the time of surgery is at least 4” x 6” in size and one of the following;
    a. 3D Max™ Mesh (Bard Inc.)
    b. 3D Max™ Light Mesh (Bard Inc.)
    c. Parietex™ 2D (order code starting with TEC) Flat Sheet Mesh (Medtronic)
    d. Parietex™ 3D (order code starting with TET) Flat Sheet Mesh (Medtronic)
6. Is willing and able to comply with the protocol assessments at time of surgery and during the post surgical follow up period

2.6.2 Exclusion Criteria

Patients who meet any one of these criteria will be excluded from the investigation:

1. Has a hernia type not suitable for laparoscopic hernia repair as determined by the Investigator (i.e. strangulated)
2. Subject has a recurrent groin hernia previously repaired laparoscopically, has an anatomical defect or had prior surgical procedures that in the opinion of the Investigator prevents access to the pre-peritoneal space for TAPP or TEP laparoscopic hernia repair
3. Is pregnant or actively breastfeeding
4. Has a known sensitivity to cyanoacrylate or formaldehyde, D&C Violet No.2 dye or any component of LiquiBand FIX8® or control device
5. Has an active or potential infection at the surgical site or systemic sepsis
6. Hernia mesh to be used at surgery is less than 4”x6” in size, or not one of the types of mesh listed in Inclusion Criteria #5.
7. Cannot tolerate general anesthesia
8. Has any significant or unstable medical or psychiatric condition that, in the opinion of the Investigator, would interfere with his/her ability to participate in the study.
9. Is currently enrolled in another clinical study or undergoing treatment with another investigational drug or device.

2.7 Study Procedures

All personnel performing surgical and/or follow-up assessments must be trained on Investigational device (LiquiBand FIX8®) usage and on this protocol (see section 5). Both the investigational (LiquiBand FIX8®) and control (AbsorbaTack™) devices must be used in accordance with their Instructions for Use (refer to appendix 9.2 and 9.3).

2.7.1 Summary of required clinical assessment and data collection

Refer to schedule of assessments above (Table 2) for a summary of all required clinical assessments and data collection.

2.7.2 Consent

The Principal Investigator(s) at each center will ensure that the patient is given full and adequate oral and written information about the nature, purpose, possible risk and benefit of the study along with alternative treatments, and the time and extent of the patient's involvement. Patients must also be notified that they are free to discontinue from the study at any time. The patient must be given the opportunity to ask questions and allowed time to consider the information provided. The informed consent process must be documented in patient's medical records. Prior to the first study assessment, all subjects must provide consent in writing by reviewing, signing, and dating an approved Informed Consent Form (ICF). The subject will receive a copy of the signed and dated form, and the original will be retained in the site study files. The ICF will contain all United States federally required elements, any state required elements, all ICH required elements, and Health Insurance Portability and Accountability Act (HIPAA) authorization information (as required). The process of obtaining informed consent will be in compliance with all federal regulations, ICH requirements, and local laws. If the ICF is amended during the study, the revised ICF should be signed by all new subjects; re-consent for ongoing subjects will be determined by the site's IRB.

Patients must sign the informed consent prior to the screening process detailed in Section 6.3.

2.7.3 Blinding

Randomization to either Investigational or control device will only occur at the surgery visit (Visit 2) and therefore the subjects will be blinded to their randomly assigned treatment device prior to surgery and during the follow up period following surgery. While it is not possible to blind investigators and staff members to the treatment device used, Investigators and staff members will not learn of randomized device until immediately prior to use of device, so as to maintain subject blinding prior to the hernia repair. Investigators and staff members will be asked to maintain subject blinding through the course of the follow up visits so as to not bias subject feedback on applicable study assessments. No device assignment information will be included on the source documentation to be completed by the study subjects (e.g. pain and quality of life assessments) and staff members, including the Investigator(s), will be instructed to not disclose this information during each study visit. Subjects will receive the same standard of care prior to, during and following surgery regardless of randomized device assignment, and therefore will not be able to individually determine what device they have been randomized to.

Randomization assignment will be revealed to subjects at conclusion of the study after all assessments and study visits are completed. A subject will be informed of their randomization assignment in the event they withdraw consent or are withdrawn from the study for any other reason.

2.7.4 Screening and Enrollment

2.7.4.1 Screening

Subjects for this study will be recruited from patient populations at the Investigational sites already scheduled for laparoscopic groin hernia repair. Prospective subjects will be pre-screened up to 21 days prior to or at their surgery visit (Day 0) to determine whether they may be eligible for participation based on the inclusion and exclusion criteria, and will then be recruited at this visit. Only following completion of informed consent, will any study-related procedures be performed.

Female subjects of child-bearing potential will be required to provide a negative urine pregnancy sample prior to surgery. Inclusion/exclusion criteria cannot be completely evaluated until surgery, as certain hernia characteristics, e.g. exact size and type cannot be accurately determined. Additionally, the Investigator may determine only at time of surgery that certain anatomical anomalies may exclude the subject from laparoscopic hernia repair or participation in this study.

Should the subject provide a positive pregnancy urine sample or be determined to not meet inclusion/exclusion criteria, they will not be randomized and will be considered screen-failed and should not be enrolled in the study.

2.7.5 Randomization

Subjects will be randomized to one of two treatment arms, LiquiBand FIX8® or Control (AbsorbaTack™) device at a 1:1 ratio based on randomly permutated blocks per site. Subjects will also be randomized according to laparoscopic technique used (TEP or TAPP hernia repair procedure), so that there is appropriate distribution between the Investigational and control devices as determined by the statistical plan (refer to section 3).

Randomization will occur immediately prior to use of either device for mesh fixation (TEP repairs) or mesh fixation and peritoneal closure (TAPP repairs only) and only after the Investigator has laparoscopically inspected the site of repair and determined the subject to be eligible for participation in the study.

Each site will determine the randomization assignment of each subject using the Electronic Data Capture (EDC) system. After the appropriate information is entered into the EDC, the randomization function will be activated and the assignment made (LiquiBand FIX8® or AbsorbaTack™). The randomization process is performed by the Investigator or delegated staff member. Once the randomized treatment group has been assigned, the study subject will be considered randomized.

The randomization process is detailed in Figure 3 below.

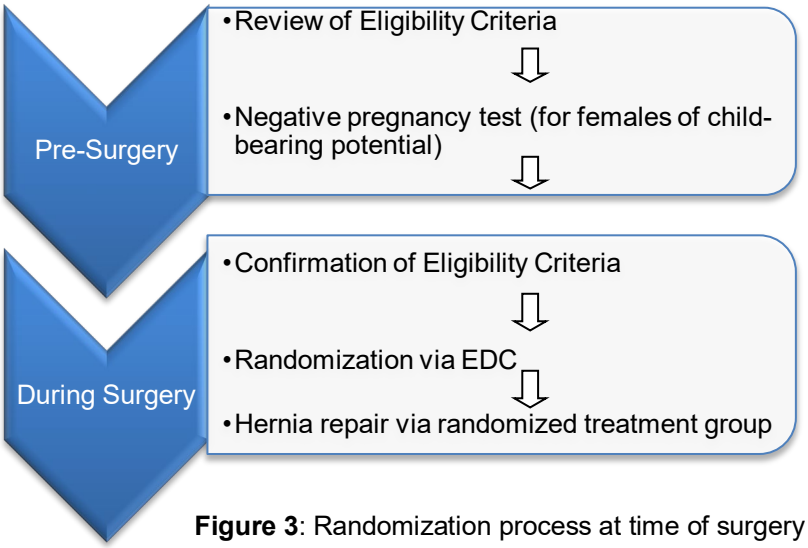


Figure 3: Randomization process at time of surgery (Day 0, Visit 2)

2.7.5.1 Enrollment

Subjects that sign the informed consent, meet all inclusion/exclusion criteria, pass screening, undergo randomization, and have a study device (treatment or control) inserted, are considered enrolled in this study.

2.7.5.1 Laparoscopic Hernia Repair Surgery

Pre-Surgery

All pre-surgical and surgical procedures up until mesh fixation and peritoneal closure (TAPP repairs only), will be performed as per Investigational site standard of care. Use of the Investigational device, LiquiBand FIX8®, is detailed below along with the Control device, AbsorbaTack™.

The following assessments will be performed prior to surgery:

- Medical History and Analgesic Medications. Medical history, and current analgesic medications (prescription and over the counter medications), and diseases will be assessed and recorded in the source documents. A review of body systems, including any past or present illnesses or dysfunction, substance abuse, and history of allergies are to be documented.
- Screening Eligibility. If screening and surgery is not performed on the same day, review of patient against inclusion/exclusion criteria is performed.
- Vital Signs. Blood pressure (Diastolic/Systolic, mmHg), pulse rate (heart rate beats per minute) and temperature (^{0}F or ^{0}C).
- Height (inch or cm) and Body weight (lb or kg).
- Physical Examination. This assessment will focus on reviewing the hernia to determine groin hernia type (primary or recurrent, and if known; direct or indirect, femoral or inguinal, unilateral or bilateral, multifocal (more than 1 hernia per side)) and size of the hernia (<3cm, ≥3cm), if known.
- Pregnancy Test. A urine pregnancy test will be performed pre-surgery for women of childbearing potential and for women who have had a bilateral tubal ligation and have not yet reached menopause. Pregnancy testing will not be performed for

women who have had a hysterectomy or bilateral oophorectomy, or are post-menopausal. Childbearing status for all women must be recorded in the source documents. A positive pregnancy test or actively breastfeeding will exclude the subject from randomization or continuation in the study.

- Subjects will be asked to rate the worst pain they experienced from their hernia within 1 month of the screening visit. Pain will be assessed by subject completion of a VAS (0=no pain to 10=worst pain imaginable).
- Quality of life will be assessed by subject completion of the Carolinas Comfort Scale (CCS) Questionnaire.

Product Application, LiquiBand FIX8®

Detailed directions for storage and use for LiquiBand FIX8® application are provided below and are also contained in the LiquiBand FIX8® IFU (see Appendix 9.2 below).

Priming the Device for Use

The device must be properly activated and primed to ensure that it operates correctly.

1. Remove the device from its packaging. Hold the device with the handle vertical and the distal tip of the cannula tilted downwards. Lift the blue lid firmly upward until a cracking sound of the glass ampoule breaking inside the lid is heard.
2. Wait for 5 seconds then, whilst the tip pointing downwards and handle held vertically slowly pull out red tab no. 2 (see Figure 4), observing that the adhesive is being drawn into the transparent barrel. This should take approximately 20 seconds. At the end of piston travel gently disengage the red tab and dispose of. ***Warning:*** A fast transfer stage could result in excessive air being drawn into the dispensing chamber.
3. Gently close the blue lid until it is completely aligned with the body and an audible click is heard.
4. Remove the red pull tab no. 4 (see Figure 4) and dispose of.
5. Rotate the blue knob clockwise approximately 320° until blue dispenser trigger alongside the handle is released. Care should be taken to avoid impeding the release of the trigger. The distal tip should be directed into the packing tray well no. 6 (see Figure 4) before the blue knob is rotated.
6. With the cannula tip placed into packing tray well no. 6, prime the device by actuating the trigger, approximately three times, until a droplet of adhesive freely emerges.
7. Wipe any excess adhesive from the tip of the cannula onto the inside of the packing tray or on a sterile wipe. The device is now ready for surgical use.

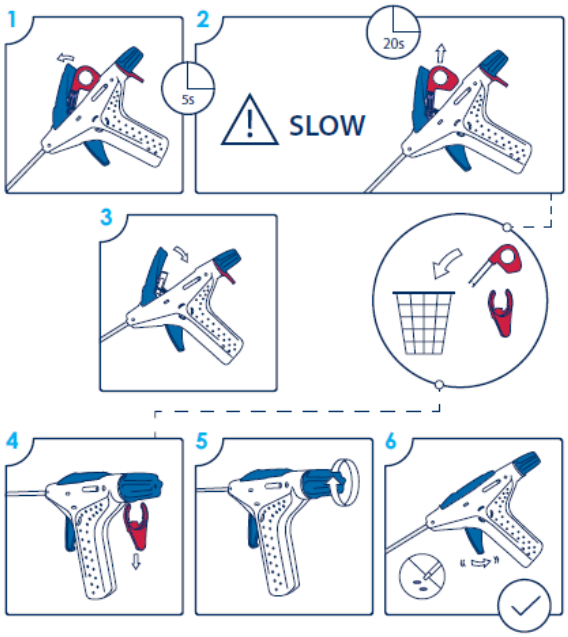


Figure 4: Diagram to demonstrate each priming step 1-6 for LiquiBand FIX8®

Using the device for hernia repair

- Do not use device for a hernia type or size not suitable for laparoscopic hernia repair (e.g. strangulated, incarcerated or too large for laparoscopic repair)
- Only use with hernia mesh greater than 4”x6” in size per hernia repair.
- Do not use with hernia mesh that is constructed from Polytetrafluoroethylene (PTFE), is non-porous, or made from absorbable, semi-absorbable or biological materials
- Note: Only the following mesh types are to be used in the investigational study; 3D Max™ or 3D Max™ Light Mesh (Bard Inc.), Parietex™ 2D (order code starting with TEC) Flat Sheet Mesh (Medtronic) and Parietex™ 3D (order code starting with TET) Flat Sheet Mesh (Medtronic).
- A suggested pressure for pneumoperitoneum is 15mmHg.
- A suggested orientation for the patient is that they are tilted into a head down position.
- Mesh fixation can be achieved by applying adhesive anchors in discrete locations across the mesh. As the adhesive is non-invasive and does not penetrate through the tissue, the adhesive can be applied at any location on the mesh.
- • The LiquiBand FIX8® device is designed to fix mesh to soft tissue for hernia repair. Whilst the adhesive will readily adhere to most tissues, the adhesive is not intended to be used over exposed bone as the safety and effectiveness has not been established to support this practice. To prepare the site for mesh fixation, excess moisture of the surgical field can be reduced by wiping with a sterile swab.
- To deploy a single adhesive anchor, hold the tip of the cannula against the mesh surface and depress trigger and release once. Adhesive should be visualized upon release of the trigger.
- Deploy a single anchor of adhesive as described above and hold device in place against the mesh for approximately up to 10 seconds until adhesive has polymerized or, as visualized by a change in opacity.

- This IDE only utilizes porous mesh. The adhesive can be applied to the proximal surface of the mesh, as the liquid adhesive monomer can permeate through the pores in the mesh to the surface of the underlying tissue. Ensure the mesh is positioned with minimal overlapping or folding so that adhesive can easily pass through the mesh pores

Using the device for peritoneal closure

- To reduce tension on the peritoneum, the intra-abdominal pressure should be decreased. A suggested pressure for pneumoperitoneum is 8mmHg.
- Gravity can also be used to reduce tension on the peritoneum by placing the patient into specific orientations. The patient can be levelled or put into a head up position.
- If the internal side of the lower peritoneal flap is notably fatty, it is possible to invert the lower peritoneal flap to avoid applying glue to the fatty areas.
- Excessive moisture may be removed from the peritoneum by use of a sterile swab. Position of the first adhesive anchor should be located in the area under least tension.
- Peritoneal closure can be achieved by dispensing a drop of adhesive to the upper peritoneal flap, before lifting and holding the lower peritoneal flap onto the adhesive until the adhesive is able to hold the lower peritoneal flap. Continue drop by drop until closure of the peritoneum is complete.
- Upon complete fixation of the peritoneum, the pneumoperitoneum should be evacuated and then re-inflated to check the continuity of the peritoneal closure.

Unintended application of LiquiBand FIX8® adhesive

The LiquiBand FIX8® device is designed to administer discrete volumes of adhesive directly to an intended target area (e.g. mesh and underlying tissues). Should adhesive be unintentionally applied to non-target tissues, adhesive may be partially removed once polymerized by gently peeling and removing polymerized adhesive from tissues using laparoscopic forceps. Investigators are requested to document all instances of unintended adhesive application and tissues affected on the Day of Surgery CRF.

Product Storage

This device should always be stored in its original packaging. Store only at temperatures between 5ºC (41ºF) and 25ºC (77ºF). Do not use the device after expiration dates shown on blister pack.

Product Application, AbsorbaTack™

Detailed directions for use for AbsorbaTack™ application are provided below and are also contained in the AbsorbaTack™ IFU (see Appendix 9.3 below).

The standard device may be inserted through a 5 mm or larger (with the use of a converter) cannula for use in minimally invasive procedures. The standard device may also be used in open procedures (study note: open repairs are not applicable for this study).

1. Grip the handle of the device and press the distal end of the shaft against the mesh at the location where fixation is desired.

2. If desired, the off hand may be used to apply counter pressure to the area immediately opposite the distal end of the device.

3. With the distal end of the shaft perpendicular to the area to be fixated, squeeze the trigger fully. The trigger should be squeezed to the full extent of its travel, and held in the fully squeezed position as the device is moved to the application site.

4. Release the trigger fully. The next tack reloads automatically, and the device is ready for the application of the next tack.

Using the AbsorbaTack™ device for peritoneal closure

Follow your standard of care practice for peritoneal closure using AbsorbaTack™. Sutures or staples may also be used for peritoneal closure, according to standard of care. Documentation of the type of device used for peritoneal closure is required on the Day of Surgery CRF.

Unintended application of AbsorbaTack™

The device is designed to deliver individual tacks to specific target areas (e.g. mesh and underlying tissues). Should tacks be administered to non-intended areas, Investigators are requested to document the location of these areas and any attempts to remove these tacks on the Day of Surgery CRF.

During Surgery

The following assessments will be performed during hernia repair surgery:

- Vital Signs. Blood pressure (Diastolic/Systolic, mmHg), pulse rate (heart rate beats per minute) and temperature (^{0}F or ^{0}C). Unless Pre-Surgery (Visit 1) and Surgery (Visit 2) occur on the same date, the subject's weight (lb/kg) should be captured for each visit.
- Confirmation of groin hernia type (primary or recurrent, direct or indirect, femoral or inguinal, unilateral or bilateral, multifocal (more than 1 hernia per side)) and size of the hernia (<3cm, ≥3cm).
- Hernia mesh fixation at time of surgery. Investigator confirmation (yes/no) at time of surgery of successful mesh fixation. Successful mesh fixation would not require any additional fixation by alternate fixation device. Unsuccessful mesh fixation may require the use of alternate fixation device to ensure adequate fixation. The use of an alternate fixation device for mesh fixation and peritoneal closure, if applicable, will be recorded on source worksheet, along and with the reason why.
- Approximation of the peritoneum at time of surgery (TAPP repairs only). Investigator confirmation (yes/no) at time of surgery of successful peritoneal closure. Successful peritoneal closure would not require any intervention by alternate fixation device. Unsuccessful peritoneal closure may require the use of alternate fixation device to ensure adequate closure.
- The anatomical locations and total number of glue anchors (LiquiBand FIX8®) or tacks (for control device(s)) used to fix mesh and to close peritoneum (for TAPP repairs only) will be captured. The total number of devices used per hernia repair will also be recorded.
- A digital photograph will be captured immediately following each mesh fixation (TEP and TAPP repairs) and peritoneal closures (TAPP repairs only). The digital photographs will not be labeled with any unique patient identifiers and only contain specific hernia repair identifiers including Subject ID, Left or Right side, Mesh Fixation or Peritoneal Closure & Date of surgery, e.g. Subject ID_Left_MF_05NOV2018.

- Assessment for adverse events will be conducted during and immediately following hernia repair for both treatment groups.

Post Surgery and Discharge

Post laparoscopic surgical procedures up until and including subject discharge will be conducted as per Investigational site standard of care. Vital Signs will be collected, including blood pressure (Diastolic/Systolic, mmHg), pulse rate (heart rate beats per minute) and temperature (^{0}F or ^{0}C). Unless Surgery (Visit 2) and Discharge (Visit3) occur on the same date, the subject's weight (lb/kg) should be captured for each visit.

Subjects will be assessed for adverse events prior to discharge. If hernia recurrence is suspected, an ultrasound will be performed to confirm the recurrence. Any analgesic medications or other pain management therapies taken post-surgery will be recorded. Additionally, subject pain will be assessed by subject completion of a VAS (0 = no pain to 10 = worst pain imaginable) and any adverse events will be evaluated at this time.

2.8 Follow-up study procedures (Day 7, Day 14, Month 1, Month 3, Month 6, Month 9, Month 12)

Patients will be followed by remote visit at Day 7, Month 1, Month 3, Month 6, Month 9, and Month 12 and by in-clinic visit at Day 14.

Remote visits can be conducted via telephone or via video conference at the discretion of the Investigational site and availability of video conferencing capabilities by the study subject, however the physical exam assessment at Month 3 and 6 should be conducted via video conference so that the Investigator can inspect the region of hernia repair.

2.8.1 Day 7 Remote Visit (7 ± 3 days post surgery)

- Pain will be assessed by completion of a VAS (0=no pain to 10=worst pain imaginable). Delegated study member will transcribe VAS recited from subject.
- Quality of life will be assessed through completion of the Carolinas Comfort Scale. A delegated study member will transcribe assessment answers recited from subject.
- Any change in analgesic medication usage or other pain management therapies will be captured on a Medication Log.
- If any Adverse Events occurred since the last visit, complete an Adverse Event Form.
- If any changes to existing Adverse Events have occurred since last visit, update Adverse Event Form.

2.8.2 Day 14 In Clinic Visit (14 -3/+6 days post surgery)

- Pain will be assessed by completion of a VAS (0=no pain to 10=worst pain imaginable).
- Quality of life will be assessed by completion of the Carolinas Comfort Scale (CCS) Questionnaire.
- The following vital signs will be captured: weight (kg/lb), blood pressure (Diastolic/Systolic, mmHg), pulse rate (heart rate beats per minute) and temperature (^{0}F or ^{0}C).

- Physical examination by Investigator and evaluation of hernia repair. If hernia recurrence is suspected, an ultrasound will be performed to confirm the recurrence.
- Any change in analgesic medication usage or other pain management therapies will be captured on a Medication Log.
- If any Adverse Events occurred since the last visit, complete an Adverse Event Form.
- If any changes to existing Adverse Events have occurred since last visit, update Adverse Event Form.

2.8.3 Month 1 Remote Visit (next calendar month ± 7 days post surgery)

- Pain will be assessed by completion of a VAS (0=no pain to 10=worst pain imaginable). Delegated study member will transcribe VAS recited from subject.
- Quality of life will be assessed through completion of the Carolinas Comfort Scale. A delegated study member will transcribe assessment answers recited from subject.
- Any change in analgesic medication usage or other pain management therapies will be captured on a Medication Log.
- If any Adverse Events occurred since the last visit, complete an Adverse Event Form.
- If any changes to existing Adverse Events have occurred since last visit, update Adverse Event Form.

2.8.4 Month 3 Remote Visit (3 calendar months ± 14 days post surgery)

- Pain will be assessed by completion of a VAS (0=no pain to 10=worst pain imaginable).
- Quality of life will be assessed by completion of the Carolinas Comfort Scale (CCS) Questionnaire.
- Vital signs may be obtained remotely by subject volunteering either of or a combination of the following assessments obtained by subject owned device (e.g. thermometer, weight scales, smart wearable technology); weight (kg/lb), blood pressure (Diastolic/Systolic, mmHg), pulse rate (heart rate beats per minute) and temperature (^{0}F or ^{0}C).
- Any change in analgesic medication usage or other pain management therapies will be captured on a Medication Log.
- Visual examination by Investigator and evaluation of hernia repair. Subjects may also be directed by the Investigator to perform a self-assessment for potential hernia recurrence by asking the following 3 questions; 1) Do you think your hernia has come back? 2) Do you feel or see a bulge? 3) Do you have physical pain or symptoms at the site? A yes response to any of those questions may be evaluated as a hernia recurrence or adverse event as applicable. If hernia recurrence is suspected, an ultrasound will be performed to confirm the recurrence.
- If any Adverse Events occurred since the last visit, complete an Adverse Event Form.
- If any changes to existing Adverse Events have occurred since last visit, update Adverse Event Form.

2.8.5 Month 6 Remote Visit (6 calendar months -21/+14 days post surgery)

- Pain will be assessed by completion of a VAS (0=no pain to 10=worst pain imaginable).
- Quality of life will be assessed by completion of the Carolinas Comfort Scale (CCS) Questionnaire.
- Vital signs may be obtained remotely by subject volunteering either of or a combination of the following assessments obtained by subject owned device (e.g. thermometer, weight scales, smart wearable technology); weight (kg/lb), blood pressure (Diastolic/Systolic, mmHg), pulse rate (heart rate beats per minute) and temperature (^{0}F or ^{0}C).
- Any change in analgesic medication usage or other pain management therapies will be captured on a Medication Log.
- Visual examination by Investigator and evaluation of hernia repair. Subjects may also be directed by the Investigator to perform a self-assessment for potential hernia recurrence by asking the following 3 questions; 1) Do you think your hernia has come back? 2) Do you feel or see a bulge? 3) Do you have physical pain or symptoms at the site? A yes response to any of those questions may be evaluated as a hernia recurrence or adverse event as applicable. If hernia recurrence is suspected, an ultrasound will be performed to confirm the recurrence.
- If any Adverse Events occurred since the last visit, complete an Adverse Event Form.
- If any changes to existing Adverse Events have occurred since last visit, update Adverse Event Form.

2.8.6 Month 9 Remote Visit (9 calendar months -21/+14 days post surgery)

- Pain will be assessed by completion of a VAS (0=no pain to 10=worst pain imaginable). Delegated study member will transcribe VAS recited from subject.
- Quality of life will be assessed through completion of the Carolinas Comfort Scale. A delegated study member will transcribe assessment answers recited from subject.
- Any change in analgesic medication usage or other pain management therapies will be captured on a Medication Log.
- If any Adverse Events occurred since the last visit, complete an Adverse Event Form.
- If any changes to existing Adverse Events have occurred since last visit, update Adverse Event Form.

2.8.7 Month 12 Remote Visit (12 calendar months -21/+14 days) post surgery

- Pain will be assessed by completion of a VAS (0=no pain to 10=worst pain imaginable). A delegated study member will transcribe VAS recited from subject.
- Quality of life will be assessed through completion of the Carolinas Comfort Scale. A delegated study member will transcribe assessment answers recited from subject.
- Any change in analgesic medication usage or other pain management therapies will be captured on a Medication Log.
- Quality of life will be assessed by subject completion of the Carolinas Comfort Scale (CCS) Questionnaire.

- If any Adverse Events occurred since the last visit, complete an Adverse Event Form.
  If any changes to existing Adverse Events have occurred since last visit, update Adverse Event Form.

2.8.8 Unscheduled Follow-up

If the patient is seen due to a device or procedure related adverse event, the following procedures and assessments must be completed for each unscheduled or "extra" follow-up visit:

- The following vital signs will be captured: weight (kg/lb), blood pressure (Diastolic/Systolic, mmHg), pulse rate (heart rate beats per minute) and temperature (^{0}F or ^{0}C).
- Physical examination by Investigator and evaluation of hernia repair.
- Any change in analgesic medication usage will be captured on a Medication Log.
- If any Adverse Events occurred since the last visit, complete an Adverse Event Form.
- If any changes to existing Adverse Events have occurred since last visit, update Adverse Event Form.

2.8.9 Subject Compensation

Although subjects will not receive compensation for participation in this study, they may receive reimbursement to cover costs associated with transportation to the investigational site for completion of study-related visits.

2.8.10 Bilateral and Multifocal Groin Hernias

Bilateral groin hernia repairs will be included in this study and are defined as groin (inguinal/femoral) hernia(s) present on each side of the subject (left and right hemipelvis). Subjects with bilateral groin hernias will be randomized to the same treatment group for each of their hernias. Each side of a bilateral repair will be independently evaluated for the secondary objectives of mesh fixation and peritoneal closure (secondary objectives 2 and 3) and for hernia recurrence (secondary objective 1).

Multifocal groin hernias are defined as more than 1 groin (inguinal/femoral) hernia per side of the subject (left or right hemipelvis). Subjects with multifocal groin hernias will be randomized to the same treatment group for each of their hernias. As it is anticipated that multifocal hernias are repaired using 1 mesh as per a single hernia, they will be evaluated as a single grouping, per side (left and/or right) for the secondary objectives of mesh fixation and peritoneal closure (secondary objectives 2 and 3) and for hernia recurrence (secondary objective 1).

The type (inguinal/femoral, direct/indirect, primary/recurrent) and size (<3cm, ≥3cm) of each multifocal and/or bilateral hernia will be assessed at the pre-surgery (Visit 1) and Surgery (Visits 2) visits as applicable.

Pain and quality of life will be assessed per subject (primary objective 1 and secondary objectives 4 and 5) and not per individual hernia repair, as subjects are not expected to be able to determine the difference in pain or impact on QOL between each of their bilateral and/or multifocal hernias.

Adverse events (secondary objective 6) will be evaluated per subject, and also per hernia repair if the event can be attributed to an individual hernia repair.

2.8.11 Assessment of Hernia Recurrence

If a subject is suspected of hernia recurrence either at an in-clinic or remote follow up visit, an ultrasound will be required to confirm the recurrence following physical examination by the Investigator. Confirmed cases of hernia recurrence will receive treatment as per standard of care at the investigational site. Cases that are confirmed not to be hernia recurrence will be evaluated as potential adverse events and also treated as per standard of care as applicable.

2.8.12 Withdrawal / Death / Lost to follow-up

Every reasonable effort must be made to keep each patient in the study. In general, any patient who has their groin hernia repaired by use of LiquiBand FIX8® or Control device must be followed for the duration of the study, or death. However, a patient may withdraw from the study at any time without prejudice to his/her subsequent treatment. Also, the Investigator may discontinue a patient's participation in the study at any time should it be considered detrimental for the patient to continue. The well-being of the patient will always take precedence over the study.

Patients who are unable to be contacted at the time of scheduled visit should not immediately be considered lost to follow-up. Subjects can be considered lost to follow after not responding to a total of three attempts to contact them, including two telephone and one registered letter.

The patient will be withdrawn from the study:

- At any time in case of withdrawal of patient's consent or cooperation (i.e. the patient refuses to participate further in the study);
- At any time, at the discretion of the Investigator, withdrawal of the patient from the study is required for patient's safety;
- In case of patient's death;

All data available at the time of withdrawal (if any) will be used for analysis. There will be no further follow-up (per this study protocol) on the patient who has withdrawn. Patients who withdraw from the study will not be replaced.

All patient withdrawals from the study, including the reason must be documented in the patient's medical record and on a Study Exit Form.

In addition, an Adverse Event Form must be completed, where necessary.

Any death must be precisely documented on an Adverse Event Form. Refer to the guidelines for Handling and Reporting of Adverse Event for detailed instructions as described in Section 2.10.1.

2.8.13 Protocol Deviations

A protocol deviation is defined as an event where the Investigator or site study personnel did not conduct the trial according to the investigational plan, applicable laws or regulations, the Investigator Agreement or Clinical Trial Agreement.

Per regulations, Investigators are required to maintain accurate, complete and current records, including documentation of any deviations from the investigational plan including the date of and reason for the deviation. The deviations must also be reported to the Sponsor

Investigators are required to obtain prior approval from the Sponsor before initiating changes in or deviations from the investigational plan, except where necessary to protect the life or physical well-being of a patient in an emergency. Such approval will be documented in writing and maintained in the study files. Prior approval is generally not expected in situations where unforeseen circumstances are beyond the Investigator's control, (e.g., patient did not attend scheduled follow-up visit, etc.), however, is still considered a deviation.

Deviations shall be reported regardless of whether medically justifiable, pre-approved by the Sponsor, or taken to protect the patient in an emergency. Deviations to protect the life or physical wellbeing of the patient in an emergency must be reported to the Sponsor immediately. A notice shall be given to the sponsor no later than 5 working days after the emergency occurred and to the IRB according to their requirements. Patient specific deviations will be reported on a Protocol Deviation Form. Deviations that are not patient specific will be reported to the Sponsor in writing. Investigators will also adhere to procedures for reporting deviations to their IRB in accordance with their IRB.

2.9 Study Assessments

2.9.1 Quality of Life (QOL) Questionnaire

The QOL assessment to be used in this study is The Carolinas Comfort Scale (CCS), which is a 23-item, Likert-type questionnaire that measures severity of pain, sensation, and movement limitations from the mesh in the following eight categories: laying down (LD), bending over (BO), sitting up (SU), activities of daily living (ADL), coughing or deep breathing (CB), walking (W), stairs (S), and exercise (E). The CCS score is derived by adding the scores from each of the 23 items. The best possible score is 0 and the worst possible score is 115 [18]. A delegated study member will ask the subject to recite their score for each of the 23 items and will then transcribe their response on a printed version of the questionnaire.

2.9.2 Visual Analog Scale (VAS)

The VAS is a frequently used assessment for measuring subjective characteristics such as pain that cannot be directly measured by other means [19][20] . When responding to a pain VAS, subjects specify their level of pain by indicating a position along a continuous line between two end points, which in this study are 0 = no pain to 10 = worst pain possible. In this study, a VAS Pain Assessment Tool (Figure 5) will be used to quantify the level of pain experienced by a study subject. The subject will be given the scale and asked to rate their pain by sliding the ruler over the 0 – 10 scale, that includes caricatures depicting none, mild, moderate and severe pain (Figure 5A) as a reference. The ruler is then flipped over to reveal a corresponding millimetre (mm) value on a 0-10cm scale (Figure 5B) which will be captured by a delegated study member and used

as the subject's pain score for that visit, e.g. '2.4'.

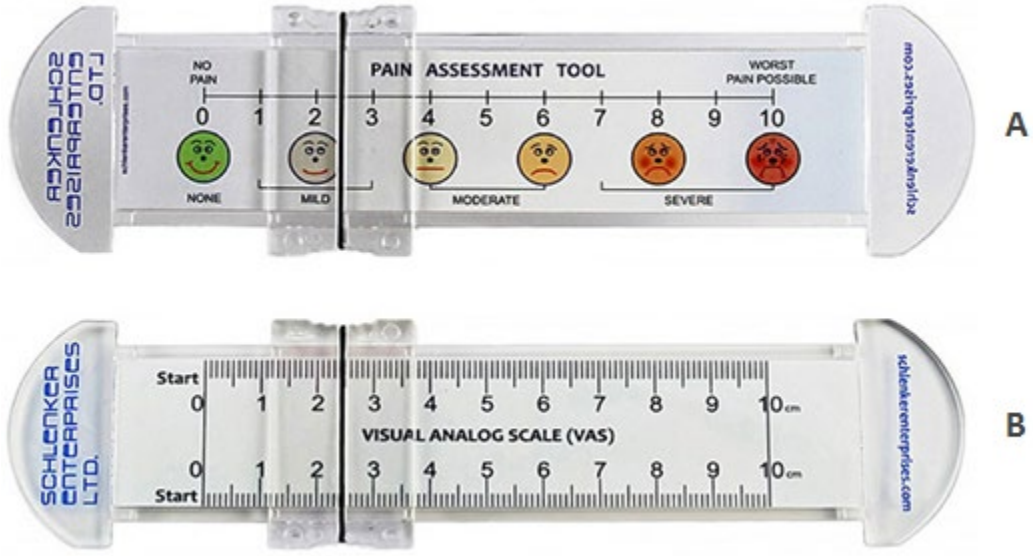


Figure 5: 0 – 10 VAS ruler assessment tool. Level of pain is selected by sliding ruler over 0 – 10 scale (0 = no pain and 10 = worst pain possible), with caricatures depicting none, mild, moderate and severe pain (A). The ruler is flipped over to reveal a 0-10cm scale, where the pain score in millimetres (mm) can be assessed (B).

2.10 Adverse Events: Guidelines, Definitions and Management

All Adverse Events (AEs) will be classified per the definitions of seriousness and relatedness to study device and/or procedure. Definitions are found in the Table below.

Table 4: Adverse Events Definitions	
Medical Device	As defined in in section 201(h) of the Federal Food Drug & Cosmetic (FD&C) Act, a medical device is "an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory which is: 1. recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them, 2. intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or 3. intended to affect the structure or any function of the body of man or other animals, and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of its primary intended purposes. The term "device" does not include software functions excluded pursuant to section 520(o).

Table 4: Adverse Events Definitions	
Adverse Event (AE)	Any untoward medical occurrence, unintended disease or injury or any untoward clinical signs (including an abnormal laboratory finding) in subjects, user or other persons. A clinical occurrence means that it affects or might affect a patient's normal function.
Adverse Device Effect (ADE)	Any Adverse Event related to the use of a Medical Device including those which might have occurred if: a) Suitable action had not been taken, or b) Intervention had not been made, or c) If circumstances had been less fortunate This includes any event resulting from insufficiencies or inadequacies in the instructions for use, the deployment, the implantation, the installation, the operation, or any malfunction of the Medical Device.
Adverse Event Severity	The severity of an adverse event will be graded according to the following criteria: • **Mild** - an adverse event that is easily tolerated by the subject causes minimal discomfort and does not interfere with everyday activities; • **Moderate** - an adverse event that is sufficiently discomforting to interfere with normal everyday activities; intervention may be needed; • **Severe** - inability to carry on normal activities and required professional medical attention
Adverse Event Relatedness	The Principal Investigator will determine the relationship of the adverse event to both the treatment device and to the study procedure using the following criteria: **Device Related** is an adverse event that is considered device related if it is a direct result of, or is affected by the use of the study device. Device relatedness will be further classified as: • **Definitely Related**: An adverse event that can be fully attributed to use of the study device (LiquiBand FIX8® or AbsorbaTack™). • **Possibly Related:** An adverse event that may be attributed to use of the study device (LiquiBand FIX8® or AbsorbaTack™). The event follows a reasonable temporal sequence related to treatment by the device, follows a known or suspected response pattern and a plausible alternative etiology cannot be identified. • **Unrelated to Device:** An event for which an alternative explanation is conclusively identified, e.g, concomitant medication(s), concomitant disease(s), and/or the relationship in time suggests that a causal relationship to device is highly unlikely. **Study Procedure Related** is an adverse event directly related to a study procedure which cannot be directly attributed to any particular device component.

Table 4: Adverse Events Definitions		
	• **Definitely Related**: An adverse event that can be fully attributed to the study procedure. • **Possibly Related:** An adverse event that may be attributed to the study procedure. • **Unrelated to Procedure:** An event for which an alternative explanation is conclusively identified, e.g, concomitant medication(s), concomitant disease(s), and/or the relationship in time suggests that a causal relationship to study procedure is highly unlikely.	
Serious Adverse Device Effect (SADE)	A Serious Adverse Device Effect is an Adverse Device Effect that has resulted in any of the consequences characteristic of a Serious Adverse Event.	
Serious Adverse Event (SAE)	Any Adverse Event that: a) led to death b) led to serious deterioration in the health of the subject that either resulted in: 1. a life-threatening illness or injury, or 2. a permanent impairment of a body structure or a body function, or 3. in-patient or prolonged hospitalization, or 4. medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function. 5. led to fetal distress, fetal death or a congential abnormality or birth defect 6. resulted in other serious outcomes (Important medical events) that require medical or surgical intervention. *NOTE: Planned hospitalization for a pre-existing condition, or a procedure required by investigatinal plan, without serious deterioation in health, is not considered a serious adverse event.*	
Unanticipated Adverse Device Effect (UADE)	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 investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.	
Device Deficiencies, Malfunctions and User Error*	Investigators are instructed to report all possible device deficiencies, malfunctions, misuse or use error observed during the course of the trial. These incidents will be evaluated and documented according to whether they occurred prior to or during use of the device as follows:	
	Prior to Use • Device damaged in packaging	During Use • Unable to deploy any anchors/tacks

Table 4: Adverse Events Definitions		
	• Issue with device packaging • Issue with device sterility • Issue with device quality/integrity • Other	• Unable to continue to deploy anchors/tacks after initial use • Unable to bond/hold tissues/mesh together • Dropped tack (AbsorbaTack™ only) • Device not used as intended • User error • Other

*If a Device Deficiency occurs, complete a Device Deficiency Form.

2.10.1 Handling and Reporting of Adverse Events

2.10.1.1 Adverse Event Reporting

All Adverse Events will be reported for each subject from the time of LiquiBand® FIX8 or control (AbsorbaTack™) device attempt to fix mesh and close peritoneum (TAPP repair only) through to the end of the study within a timely manner. Adverse Events will be recorded on an Adverse Event Form and reported to the Sponsor or designee through the EDC system within 10 working days of learning of the event. Adequate information must be supplied to the Sponsor or designee including seriousness, severity and whether the Adverse Event is related to use of the device.

Adverse events must be updated with additional information related to the subject's subsequent medical course until the event has resolved, or the subject's study participation is complete, or, in the case of permanent impairment, until the event stabilizes and the overall clinical outcome has been ascertained.

All reported adverse events will be reviewed and coded using MedDRA coding software.

2.10.1.2 Expedited Reporting of Serious Adverse Events

All Serious Adverse Events (Serious Adverse Device Effects both Anticipated or Unanticipated), including any Device Deficiency that could have led to a SADE, **must be reported to the Sponsor or designee within 24 hours of knowledge of the event.** It is the responsibility of each Investigator to report all Serious Adverse Events and/or Serious Adverse Device Effects and Device Deficiencies that could have led to a Serious Adverse Device Effect to their IRB, according to Institutional Review Board requirements.

2.10.1.3 Reporting Unanticipated Adverse Device Effects

It is the responsibility of the Investigator to report the occurrence of any UADE to the sponsor and IRB as soon as possible, but in no later than 24 hours of the Investigator's knowledge of the event. Reporting to the IRB will only take place after sponsor review of the event and confirmation that it is a UADE. It is the Sponsor's responsibility to investigate any reporting of an UADE, and to report the results of the evaluation to FDA, all reviewing IRBs, and participating investigators within 10 working days after the sponsor first receives notice of the effect.

It is the Sponsors responsibility to determine whether an unanticipated adverse device effects presents an unreasonable risk to subjects and to terminate all or parts of investigations presenting that risk as soon as possible. Termination shall occur not later than 5 working days after the sponsor makes this determination and not later than 15 working days after the sponsor first received notice of the effect.

2.10.1.4 Notification of Adverse Events

The sponsor is responsible for reporting AEs, SAEs and Device Deficiencies to regulatory authorities in line with applicable regulatory requirements and for reviewing the risk analysis, determining the need for corrective or preventative action and informing Investigators and regulatory authorities accordingly.

2.10.1.5 Clinical Events Committee (CEC)

A CEC will be utilized for this study. The purpose of the CEC is to enable consistent, accurate and objective Adverse Event assessment and reporting during the clinical investigation. The primary role of the CEC will be to determine the relationship between the event and the study devices and to determine if the event is accurately reported according to the Adverse Event definitions in the protocol.

The CEC will meet regularly throughout the study to adjudicate events in an ongoing and timely fashion. All adjudication decisions will be made by the CEC in an independent fashion based upon review of all available medical evidence associated with an event. The events, as adjudicated by the CEC, will be utilized in relevant study reports.

2.11 Data Collection and Monitoring

2.11.1 Data Collection

All required data for this study will be collected on standardized electronic CRFs utilizing an electronic data capture (EDC) system. Instructions and training for use of the EDC system and proper completion of the form will be provided to the clinical sites.

The Investigator (or designated investigational site staff) will assure primary data collection based on source-documented medical chart reviews and study assessments. The study CRFs should be completed within 10 working days of the data availability. All applicable sections of the study CRFs must be filled out completely and accurately. Any corrections to the study CRFs in the EDC system will include an electronic audit trail with changes clearly attributed and dated. All completed study CRFs must be reviewed and signed by the Investigator. Investigator review and sign off should be completed within 10 working days after the last applicable procedure/assessment has been concluded for each subject.

Data will be collected on source documents as described below and transferred on to the study CRFs.

2.11.2 Source Documentation

Auditors, Monitors, IRB, the study Sponsor, and regulatory authorities may have access to the medical records related to this study. Original or certified copies of records of all relevant clinical findings, observations, and other activities throughout the clinical investigation must be maintained in the medical file of each enrolled subject. At a minimum, the following must be included in each subject's file:

- Sufficient medical history and current physical condition, including any medication(s) the subject is taking at the time of the procedure to assess the subject's eligibility;
- The medical file should reveal the subject's participation in this study, including documentation of written informed consent;
- Dated report of the investigational procedure including medication, material usage, and complications, if applicable;
- Dated reports of the discharge and follow-up assessments;
- Any adverse event(s), the resultant action or treatment, and outcome, if applicable; and
- In the case of withdrawal of subject consent, reason and subject status at time of withdrawal.

The investigator will permit study-related monitoring, audits, IRB review and regulatory authority inspections by allowing direct access to the source data.

In case of electronic source data verification, access will be allowed or certified and dated print-outs will be made available during the monitoring visit. Print-outs should not be limited to the study data only, but should include all available data related to the identified subject(s).

2.11.3 Monitoring Procedures

2.11.3.1 General Monitoring Procedures

Monitoring will be performed according to specific predefined monitoring Standard Operating Procedures (SOPs) and a study specific Monitoring Plan to ensure that the Investigator and his/her study team conduct the clinical investigation in accordance with the signed Clinical Trial Agreement and Investigator Agreement, the Clinical Investigational Plan, any conditions imposed by the IRB, the Declaration of Helsinki, 21 CFR Parts 50 and 812, Good Clinical Practice according to ICH E6, and any other applicable regulations, to ensure adequate protection of the rights and safety of subjects and the quality and integrity of the resulting data. Monitoring visits will be documented using monitoring visit reports.

2.11.4 Monitor Selection

The Sponsor's designated monitor(s), as stated in the investigational plan, will monitor the clinical investigation in accordance with all applicable US regulations. The Monitor(s) will be qualified by training and experience and possesses the appropriate skills necessary to properly monitor the investigational study.

2.11.5 General Duties of Monitor

The Monitor must ensure that the investigation is conducted in accordance with:

a. The signed Clinical Trial Agreement and Investigator Agreement;
b. The Clinical Investigational Plan;
c. Any conditions imposed by the IRB;
d. The requirements of 21 CFR 812 and applicable US regulations, as appropriate.

2.11.6 Monitoring Reports to the Sponsor

The Monitor will provide timely reports to the Sponsor regarding:

a. Any noncompliance with any item listed in the General Duties of Monitor section above; and
b. Any previously unreported Serious Adverse Events or Device Effects.

If a clinical Monitor becomes aware that an Investigator is not complying with the requirements mentioned above, the Sponsor will be notified by the Monitor. The Sponsor will evaluate the non-compliance and if necessary, immediately either secure compliance or discontinue shipments of the investigational device to the Investigator and terminate the Investigator's participation in continued enrollment in the investigation.

2.11.7 Study Initiation

Prior to initiating any clinical use of the investigational device, the Monitor or the Sponsor must establish that the site is qualified and trained to conduct the study and ensure that:

a. The Investigator understands the investigational status of the LiquiBand FIX8® device;
b. The Investigator understands and accepts the obligation in conducting the clinical investigation;
c. The Investigator, Sub-Investigator(s) and delegated study staff have completed all applicable study training;
d. The Investigative site has sufficient controls for storage of the Investigational device;
e. The Investigator and research staff have sufficient time and access to a sufficient number of subjects to conduct the clinical investigation;
f. A signed Investigator Agreement is on file; and
g. The IRB approval is on file and all conditions imposed by the IRB have been met.

2.11.8 Study Conduct

During the course of the investigation, the Monitor will:

a. Conduct periodic discussions with the Investigator or delegated research staff to ensure that the study is being conducted in accordance with the Investigational Plan, any conditions imposed by the IRB, and applicable regulations as appropriate;
b. Review study CRFs and records to ensure they are complete, accurate and legible;
c. Ensure study-related activities are performed only by delegated study members as identified on the site delegation log;
d. Review medical records for any unreported Adverse Events or Adverse Device Effects; and
e. Ensure the Investigator has properly disposed of or returned all investigational devices to the Sponsor as directed unless this action would jeopardize the rights, safety or welfare of the subjects, and has recorded disposition on the Device Accountability Log

2.11.9 Monitor Records

The Monitor will prepare and maintain records of each periodic visit. These records will include:

a. Date, Purpose of visit, Investigator name and address, and names of other staff members present at each meeting;
b. A summary of the findings of the visit; and

c. A statement of any action taken by the Monitor.

2.12 Investigational Device Management

2.12.1.1 Device Accountability

The Sponsor will only distribute the investigational device, LiquiBand FIX8®, to qualified investigators and sites that are part of the clinical investigation. The Sponsor will maintain complete, current and accurate records pertaining to the distribution of the investigational devices and follow record keeping requirements in accordance with applicable regulations.

All LiquiBand FIX8® investigational devices must be stored in a secure storage area to which only the Investigator and/or designated study staff will have access. The Investigator is responsible for device accountability at the study site. The Investigator may assign the responsibility for the device accountability to an appropriate study staff member, but remains the final responsible person. The Investigator must ensure that the devices are used only in accordance with the investigational plan. The Investigator is responsible for maintenance of adequate records of the receipt, disposition (administration to each subject as well as any device component that is opened but not used). Used devices (excluding malfunctioning devices) may be disposed of according to site disposal practices.

Use of the investigational device outside of the investigational plan is strictly forbidden and may constitute grounds for removal of the investigator/site from the study.

2.12.1.2 Device Return

All LiquiBand FIX8® investigational devices suspected in malfunction, device failure, device complaint, user error, or other issues, must be returned to the Sponsor immediately according to the Sponsor's returned goods process and observations recorded and reported. Any contaminated investigational devices suspected as being faulty or deficient in function that have been used in a patient with a history of a high risk blood bourne disease, for example, human immunodeficiency virus (HIV), Hepatitis B Virus (HBV) and Hepatitis C virus (HCV), do not need to be returned and can be disposed of at the site according to their local policy. All unused investigational devices must also be returned to the Sponsor according to the Sponsor's returned goods process and recorded. The investigational site will seek sponsor approval prior to disposal or return shipment of any device.

3 STATISTICAL CONSIDERATIONS

3.1 Statistical Hypotheses

A detailed statistical analysis plan will be finalized prior to locking the database to expand upon the statistical methods presented below.

Primary Endpoint: Effectiveness of LiquiBand FIX8® will be assessed and compared to treatment with AbsorbaTack™ in subjects requiring laparoscopic (TEP and TAPP) hernia repair. Success will be determined by improvement in pain not inferior to control device as measured by a VAS value (0 = no pain to 10 = most pain imaginable) from baseline (worst pain experienced within 1 month of screening visit) to six months post hernia repair.

The statistical hypothesis is:
H_0: $\delta_T - \delta_C \geq 0.9$[21, 22]

H_1: $\delta_T - \delta_C < 0.9$ [21, 22],
where δ is the change from baseline (worst pain experienced within 1 month of screening visit) to 6-month on VAS for the appropriate treatment group.

Secondary Endpoints: To assess efficacy and safety outcomes following TAPP or TEP laparoscopic groin hernia (femoral and inguinal) repair by LiquiBand FIX8® compared to AbsorbaTack™ by evaluating the following:

- Recurrence rate in subjects following laparoscopic (TEP and TAPP) groin hernia repair by LiquiBand FIX8® or control (AbsorbaTack™) at 2 weeks, 3 months, 6 months, and 12 months.
  The statistical hypothesis for the recurrence rate at 6 months is:
  H_0: $q_T - q_C \geq 10\%$[25]
  H_1: $q_T - q_C < 10\%$[25],
  where q is the recurrence rate at 6 months for the appropriate treatment group.
- Rate of successful hernia mesh fixation in subjects undergoing TEP and TAPP laparoscopic groin hernia repair.
  The statistical hypothesis is:
  H_0: $p_C - p_T \geq 10\%$
  H_1: $p_C - p_T < 10\%$,
  where p is the rate of successful hernia mesh fixation at time of surgery for the appropriate treatment group.
- Rate of successful peritoneal closure in subjects undergoing laparoscopic TAPP hernia repair.
  The statistical hypothesis is:
  H_0: $\pi_C - \pi_T \geq 15\%$
  H_1: $\pi_C - \pi_T < 15\%$,
  where π is the rate of peritoneal closure at time of surgery for the appropriate treatment group.

- Quality of Life assessed by the Carolinas Comfort Scale (CCS) Questionnaire prior to surgery and at 7 days, 14 days, 1 month, 3 months, 6 months, 9 months and 12 months following laparoscopic (TEP and TAPP) groin hernia repair.

3.2 Sample Size Determination

For the primary efficacy endpoint on change from baseline (worst pain experienced within 1 month of screening visit) to 6-month on VAS, two sample t-test was used to calculate the sample size using PASS 15 power analysis and sample size software (NCSS LLC, UT USA). The mean change was assumed to be the same, and standard deviation was assumed to be the same at 2.4 for both the LiquiBand FIX8® and AbsorbaTack™ for TAPP and TEP laparoscopic groin hernia (femoral and inguinal) repair. The non-inferiority margin was set to 0.9 (as supported by the following references; [21] [22]), alpha at 0.025, and the target statistical power at 80%. Under these assumptions, a total sample size of 226 subjects (113 per group) is required for the study. With an attrition rate of about 20%, a total of 284 subjects will be enrolled.

3.3 Population for Analysis

The following subject populations will be created:

- Intent-to-Treat (ITT): All enrolled subjects. ITT analysis will be per randomized group irrespective of the treatment actually received.
- Per Protocol (PP): All ITT subjects excluding those with major protocol violations. PP analysis will be per actual treatment group which is the same as the treatment initially randomized.
- As the PP analysis is more conservative for non-inferiority hypothesis, all hypotheses will be tested with the PP population. ITT analysis will also be performed for all hypotheses, as the primary analysis for the primary endpoint, and the supportive analysis for secondary endpoints with non-inferiority hypothesis.

3.4 Statistical Analysis

3.4.1 General Approach

The primary efficacy endpoint will be tested for non-inferiority of treatment to control with a predefined non-inferiority margin of 0.9 on the VAS scale. Confounding factors for the pain score including analgesic use or other pain management therapies will be measured at screening and all follow up visits, and compared between treatment arms to ensure proper balance within each site. The study will be claimed successful if both PP and ITT analyses on the primary efficacy endpoint showed significance at 0.025. Once the hypothesis tests succeed for both analysis sets on the primary efficacy endpoint, key secondary endpoints will be compared between treatments sequentially in a non-inferiority manner. The following sequential analysis approach will be taken:

- Primary non-inferiority on the PP set; if significant at one-sided alpha=0.025, and
- Primary non-inferiority on the ITT set; if significant at one-sided alpha=0.025, then proceed to key secondary endpoints detailed in Section 3.1.
- Secondary non-inferiority on the PP set on Hernia Recurrence rate in subjects following laparoscopic (TEP and TAPP) groin hernia repair by LiquiBand FIX8® or control (AbsorbaTack™) at 6 months, at one-sided alpha=0.025.
- Secondary non-inferiority on the PP set on Rate of successful hernia mesh fixation in subjects undergoing TEP and TAPP laparoscopic groin hernia repair; if significant at one-sided alpha=0.025, then
- Secondary non-inferiority on the PP set on Rate of successful peritoneal closure in subjects undergoing laparoscopic TAPP hernia repair; if significant at one-sided alpha=0.025, then

The family-wise type I error will therefore be controlled at 0.025.

Summary statistics will consist of the number and percentage of responses in each category for discrete variables, and the mean, median, standard deviation (SD), minimum, and maximum for continuous variables. One-sided statistical tests will use a significance level of $\alpha = 0.025$, and two-sided tests will use a significance level of $\alpha = 0.05$.

3.4.2 Analysis of the Primary Efficacy Endpoint

To test change from baseline (worst pain experienced within 1 month of screening visit) to 6-month on VAS between LiquiBand FIX8® and AbsorbaTack™, a general linear model (ANCOVA) will be run using SAS Proc GLM, with the treatment arm and laparoscopic repair technique (TAPP or TEP) as covariates. (SAS Institute Inc. NC USA). A p-value of < 0.025 will be considered evidence that LiquiBand FIX8® is not inferior to the AbsorbaTack™. 95% confidence interval will be calculated for the difference on changes from baseline (screening visit) to 6-month visit on VAS between LiquiBand FIX8® and

AbsorbaTack™. This endpoint will be assessed when the enrollment is completed, i.e., when 148 subjects have been enrolled in the TAPP cohort, and there are at least 226 evaluable subjects with 6-month data for change from baseline to 6-month on VAS. Tipping point analysis will also be performed to evaluate the impact of missing data.

3.4.3 Poolability Analysis of the Primary Efficacy Endpoint

All investigational sites will follow the requirements of a common protocol and standardized data collection procedures and CRFs. The primary efficacy endpoint will be presented separately for each site using descriptive statistics. Poolability of the primary efficacy endpoint across investigational sites will be evaluated using a regression model with fixed effects for treatment, site, and treatment by site interaction. Sites enrolling less than 5 subjects will be combined to form one-quasi site. If the quasi-site exceeds the maximum enrollment allowed per investigational site, centers will be combined based on geographical proximity to form multiple quasi-sites until at least 5 subjects are included in each quasi-site. If the p-value for the interaction effect is <0.15, additional exploratory analyses will be performed to understand any variations in outcomes by site.

3.4.4 Analysis of the Secondary Endpoints

The following safety and clinical outcomes will be evaluated.

The safety and clinical outcomes assessments include:
1. Hernia recurrence up to 12 months following surgery.
2. Hernia mesh fixation at time of surgery.
3. Approximation of the peritoneum at time of surgery (TAPP repairs only).
4. Quality of Life following groin hernia repair as measured by Carolinas Comfort Scale at baseline and at 7 days, 14 days, 1 month, 3 months, 6 months, 9 months and 12 months following laparoscopic (TEP and TAPP) groin hernia repair.
5. Subject pain following groin hernia repair as reported by VAS at screening, discharge and at 7 days, 14 days, 1 month, 3 months, 6 months, 9 months and 12 months following surgery.
6. Rate of device and procedure-related adverse events reported throughout the duration of the study.

To test the secondary endpoints #1, 2, and 3, a binomial non-inferiority test will be run using SAS Proc Freq with the Farrington-Manning method on the PP set. A p-value of < 0.025 from the binomial non-inferiority test will be considered evidence that LiquiBand FIX8® is not inferior to AbsorbaTack™. Confidence interval on the difference of the rates will be reported and non-inferiority is indicated if the upper limit of the confidence interval is less than the non-inferiority margin. ITT analyses will be performed for the three secondary endpoints with hypothesis statements as supporting sensitivity analyses.

3.4.5 Handling of Missing Data

All attempts will be made to limit the amount of missing data. Unless otherwise specified, no attempt will be made to impute missing data. If a data point is missing, that data point will not contribute to that portion of the analysis. The number of evaluable observations will be reported in analysis so that extent of missing data can be assessed.

3.4.6 Safety Analysis

Safety endpoints are included in the secondary objectives are covered in Section 3.4.4

3.4.7 Baseline Descriptive Statistics

Demographics will be summarized using descriptive statistics and will be broken out by the subgroups listed in Section 3.4.9.

3.4.8 Planned Interim Analysis

There will be no interim analysis planned in this study. Applicable data will be submitted to the FDA and IRBs as part of the Annual Progress reports. Data does need to be summarized and hypotheses are not assessed for these Annual Progress reports.

3.4.9 Sub-Group Analysis

Analyses for the primary endpoints will be summarized and analyzed by the following strata, as appropriate:

- Size of hernia (<3cm or ≥3cm)
- Sex of subject (M or F)
- Age of subject (in years)
- Femoral or Inguinal groin hernia
- Direct or indirect groin hernia
- Primary or recurrent groin hernia
- Unilateral or bilateral groin hernia
- TEP or TAPP hernia repair procedure
- Comparison of 6 month visit assessments obtained either in-clinic or obtained remotely due to COVID-19 pandemic visit restrictions.
- Multi-focal vs single Unilateral Groin Hernias

3.4.10 Tabulation of Individual Participant Data

Data listings will be provided which contain all CRF data by measure and time point. All listings will be sorted for presentation in order of treatment group, site number, subject number, and date of procedure or event.

4 RISK ANALYSIS

As with any medical procedure or implantable device, the study device carries potential risks and potential benefits. In addition to the known potential risks described below, the device may pose additional potential risks, the nature of which are unknown.

The potential benefits from using LiquiBand FIX8® for mesh fixation and peritoneal closure (TAPP repairs only) for groin hernia repair compared to tack-fixation devices such as the control device (AbsorbaTack™) include the following:

- A more secure fixation of mesh due to being able to fix mesh over areas considered too sensitive for tack-based fixation such as over nerves and blood vessels. In a single center evaluation of 200 subjects or 247 TAPP hernia repairs (181 Inguinal, 18 Femoral, 4 Spigelian, 44 Inguinal Disruption), Wilson P. 2018 [8] [11], reported that the use of adhesive from LiquiBand FIX8® provided better mesh fixation than conventional tacking.
- Less incidence of chronic pain following hernia repair, as has been reported from the use of tack-based fixation devices due to the potential for disrupting sensitive

underlying tissues such as nerves [2]. Of the six (6) independent Outside USA (OUS) clinical evaluations conducted evaluating the LiquiBand FIX8® device for hernia mesh fixation in laparoscopic groin hernia repair, only 2 instances of chronic pain out of a total 415 repairs (incidence of 0.48%) were reported [4] [5] [7] [6] [8] [9] [11].

- Less incidence of complications such as hematoma, seroma and hernia recurrence following groin hernia repair, as has been reported from the use of mechanical fixation devices [19][12][2]. Of the six (6) independent OUS clinical evaluations conducted evaluating the LiquiBand FIX8® device for hernia mesh fixation in laparoscopic groin hernia repair; only 26 complications were reported out of a total of 415 repairs (incidence of 6.27%), including 9 hematomas, 9 seromas and 2 cases of recurrence (incidence of 2.17%, 2.17% and 0.48% respectively).
- Less incidence of complications such as bowel obstruction or entrapment, as has been reported following use of mechanical fixation devices for peritoneal closure [24]. Of the four (4) independent OUS clinical evaluations conducted evaluating the LiquiBand FIX8® device for both hernia mesh fixation and peritoneal closure, zero (0) complications related to peritoneal closure were reported [5] [6] [7] [8] [11].
- Potential earlier return to normal physical activities, as has been reported from the use of mechanical fixation devices [12]. In a single center evaluation of 247 TAPP groin hernia repairs, Wilson P. 2018, noted there may be a faster return to normal activity compared to previous experience using mechanical fastener devices [8] [11].

4.1 Description of Increased Risks to Subjects

The known potential risks to which subjects will be exposed by the investigation include:

- Risks related to the laparoscopic hernia repair procedure including use of anesthesia and use of the control device (AbsorbaTack™);
- Risks related to the investigational (LiquiBand FIX8®) device;
- Risks related to study conduct.

4.1.1 Risks related to the laparoscopic hernia repair surgery

Potential risks related to the laparoscopic groin hernia repair procedure may include but are not limited to:

- Wound Infection
- Port site bleeding
- Port site hernia
- Chronic pain
- Injury to nerves
- Injury to vessels
- Injury to organs
- Seromas
- Hematomas
- Hernia recurrence
- Death
- Deep Vein Thrombosis
- Pulmonary Embolism
- Urinary tract complications
- Peritonitis
- Bowel Obstruction or entrapment
- Mesh infection
- Mesh in-growth
- Reaction to mesh
- Adhesion
- Urinary Retention
- Minor Surgical Emphysema
- Port Site Infection
- Lateral Port Site Hemorrhage

- Bladder Perforation
- Intraperitoneal Bleeding
- Sub Hepatic Abscess
- Post-Operative Ileus
- Chest Infection
- Mesh Migration
- Mesh Erosion
- Re-Operation

4.1.2 Risks related to use of LiquiBand FIX8® device:

Potential risks specific to the use of LiquiBand FIX8® for laparoscopic hernia repair procedure include but are not limited to:

- Toxic reaction
- Allergic reaction
- Thermal tissue injury

4.1.3 Risks related to the study conduct

The risk increase for patients participating in the study might be related to the new technology featured in the device (in the US market) and to procedures required in the study. However it is expected that study participation may also benefit the patients due to the close scrutiny of their device function and rigorous identification of adverse events.

The procedures and methods for data collection required by the protocol do not differ significantly from routine hernia repair surgery and follow-up practices in patients with groin hernia(s).

Use of the device not in conformance with this investigational plan and/or with the Instructions for Use could introduce other issues.

4.2 Risk Minimization

Several factors minimize the risk to subjects enrolled in the study:

- To protect the welfare of subjects, IRB approval of the investigation will be obtained for each site prior to the first implant at that site.
- Investigators selected to participate will have experience in laparoscopic hernia repair and following patients with groin hernia(s) and will be trained in the implantation and use of the LiquiBand FIX8® device prior to study participation. Trained and experienced clinical personnel representing Advanced Medical Solutions (USA) Inc. will be made available to provide training and for troubleshooting.
- Each Investigator will sign an Investigator's Agreement stating his/her responsibility to conduct this study according to this investigational plan, to adhere to the records and reporting requirements, and to supervise use of the investigational device.
- Only patients fulfilling the inclusion/exclusion requirements will be enrolled.
- Through careful design and testing, Advanced Medical Solutions (USA) Inc. has attempted to minimize the risk to patients. Tests included: bench testing of device performance, design validation and animal testing. The LiquiBand FIX8® device has also been evaluated in European clinical studies.
- Advanced Medical Solutions (USA) Inc. has attempted to reduce the risk of random component failure through selection, screening, and qualification of vendors in

accordance with medical device industry practice, and by carrying out quality control testing prior to product release.

5 SELECTION AND TRAINING OF STUDY SITES AND INVESTIGATORS

5.1 Investigator and Site Selection

The Sponsor will select Investigators who are qualified by training and experience to perform clinical research and to participate in the clinical investigation. Sites will be selected based upon an assessment of the qualifications of the Investigator, research staff and the facilities at each site.

Investigators selected to participate in this study:

- Must be experienced in follow up of patients with laparoscopic groin hernia repair
- Must be willing to accept the responsibilities of Investigator including supervising testing and use of the investigational and control device
- Must allow the Sponsor's designated Monitors and representatives to review the records pertaining to this study, source documentation and patient informed consents
- Must allow Quality Assurance visits (FDA, IRB or Sponsor audits)

A pre-investigation visit will be conducted at each study site to assure that the Investigator and the study staff understand the obligations for using and managing the investigational and control device, following the investigational plan, obtaining informed consent, adhering to Regulatory Authorities and IRB regulations, and conducting clinical research.

Prior to initiating any clinical use of the investigational device, the Sponsor will establish that the site is qualified to conduct the study and ensure that:

a. The Investigator understands the investigational status of the LiquiBand FIX8® device;
b. The Investigator understands and accepts the obligation in conducting the clinical investigation;
c. The Investigator and research staff have sufficient time and access to a sufficient number of subjects to conduct the clinical investigation;
d. A signed Investigator Agreement is on file;
e. The IRB approval is on file and all conditions imposed by the IRB have been met; and
f. The Investigator and research staff are adequately trained.

5.2 Training

All Investigators/trial personnel are required to attend study specific training sessions, which may be conducted at an Investigator's meeting, a site initiation visit, or other appropriate training sessions. Remote over-the-phone or web-based training may take place as necessary. Training of Investigators/study personnel will include, but is not limited to, the Clinical Investigational Plan, subject recruitment, enrollment (including review of inclusion and exclusion criteria), subject retention, investigational device usage, adverse event reporting, investigational plan requirements, case report form completion, trial personnel responsibilities and good clinical practices (GCP). A training record will be completed to document all study related trial personnel training.

The specific training requirements for all Investigators will include review of multimedia training aides and hands-on emulation of LiquiBand FIX8® use.

6 ETHICAL AND REGULATORY CONSIDERATIONS

6.1 IRB and Institutions

The Investigator will assure that an appropriately constituted IRB complies with the requirements of 21 CFR part 56 or applicable regulations. Prior to initiation of the study, the Investigator will forward copies of the Clinical Investigational Plan, Report of Prior Investigations, subject Informed Consent Form, any other written materials that will be provided to the study subjects, and any other applicable documents to the IRB for its review and approval. A copy of the written IRB approval must be provided to the Sponsor (or designee) and should include the following:

1. A statement of IRB approval for the proposed study at the institution;
2. The date the study was approved and the duration of approval (if applicable);
3. Identification of the approved documents including version dates and/or other references. At a minimum, the following documents should be listed:
    i. Clinical Investigational Plan
    ii. Subject Informed Consent Form
    iii. Report of Prior Investigations
    iv. Any additional written materials to be provided to the subject
4. A listing of any conditions attached to the approval (if applicable);

Any amendments to the Clinical Investigational Plan, as well as possible associated information and consent form changes, will be submitted to the IRB and written approval obtained prior to implementation. Adverse Event reports and Protocol Deviations will be submitted as required by the Sponsor, the IRB, and any applicable regulations.

6.2 Regulatory Approval

The Sponsor is responsible for notifying the Food and Drug Administration (FDA) according to regulatory requirements. Investigators may not commence enrollment of subjects until they have met any local IRB and institution management requirements and have received confirmation from the Sponsor that the appropriate regulatory approvals have been obtained.

The Sponsor is responsible for maintaining records of study investigational sites, site Principal Investigators, the name, address and chairperson of all IRB that have been asked to review the Clinical Investigational Plan, any action taken by reviewing IRB, and for updating this information to FDA in accordance with 21 CFR Part 812 and to other relevant Regulatory Authorities as applicable.

6.3 Informed Consent

The subjects will provide informed consent for the study prior to enrollment, as described Section 2.7.2. The background of the proposed study and the benefits and risks of the procedures and study must be explained to the subject in the Informed Consent Form. The subject must agree to participate and sign the current IRB approved study Informed Consent Form prior to enrollment.

Information should be given in a language and at a level of complexity understandable to the subject in both oral and written form by the Investigator or assigned designee. Subjects should not be coerced, persuaded, or unduly influenced to participate or remain in the trial. A subject must be given ample time and opportunity to inquire about details of the trial and all questions about the trial should be answered to the satisfaction of the subject. The informed consent process should be documented in each subject's medical record. The subject must receive a signed copy of the Informed Consent Form.

Failure to obtain informed consent prior to use of an investigational device must be reported to the Sponsor and the reviewing IRB within 5 working days after the use occurs. The Sponsor shall be responsible for reporting use of the investigational device without obtaining informed consent to FDA within 5 working days of the Sponsor's knowledge of such use.

The Investigator shall inform the subjects of any new significant findings occurring during the clinical investigation, including the need for additional medical care that may be required, that may be relevant to the subject and his/her willingness to continue participation in the study. The consent form should be updated or amended whenever such new information becomes available and updated consent shall be recorded.

6.4 Termination of the Study

The Sponsor reserves the right to terminate the study, or parts of the study, but intends only to exercise this right for valid scientific or administrative reasons and reasons related to protection of subjects.

The Sponsor may inactivate study participation at a specific investigational site if there has been no subject enrollment at the site. The site may be replaced with another active site.

The Sponsor reserves the right to suspend or terminate the enrollment of additional subjects at an active investigational site at any time during the study. Specific instances that may precipitate terminating further enrollment at a study site may include, but is not limited to, the following:

- Unsatisfactory subject enrollment
- Failure to comply with Clinical Investigational Plan
- Failure to obtain appropriate informed consent
- Inaccurate and/or incomplete data recording on a recurrent basis
- Failure to report SAEs in timely manner
- Loss of (or unaccounted for) investigational product inventory
- Protocol deviations without justification or failure to implement corrective actions
- In the event of a UADE that poses risk to the study patients
- Upon fulfilment of a study arm

Notification of study suspension or termination will occur no later than five (5) working days after the sponsor makes the determination. In the event of study suspension or termination, the Sponsor will send a report outlining the circumstances to the IRB and Investigator. A suspended or terminated study may not be reinitiated without approval of the reviewing IRB.

The Investigator should notify the IRB in writing as soon as possible but no later than within 10 days if the premature termination is related to safety or compliance issues. The same procedure will be applied to the Food and Drug Administration.

6.5 Auditing

As a quality assurance measure, the site may be audited during the course of the ongoing clinical trial as well as following completion of the trial. The purpose of an audit is to provide an independent evaluation separate from routine monitoring or quality control functions of trial conduct, investigational plan, and GCP compliance. The audit may be conducted by the Sponsor (or designee) or by an external agency or regulatory authority.

6.6 Subject Privacy and Confidentiality

Sponsor will keep all data related to patient identification in strict confidence. Patient identity will not be revealed in any of the reports or publications resulting from this study. U.S. Federal Regulations require Sponsor to maintain records regarding the identity of patients who have received an implantable device that is subject to U.S. device tracking requirements. To comply with these regulations, the Investigator must complete the Patient Registration Form provided in each package and return the completed form as instructed.

Patients will be identified on all Case Report Forms (CRFs) by a unique numeric reference (site number, patient number). No identification will be made using the patient name. Each center will maintain as part of the investigation file a separate list identifying all patients screened and enrolled.

The Sponsor affirms and upholds the principle of subject confidentiality. The Investigator agrees that representatives of Sponsor, appropriate contract research organizations working on behalf of the sponsor to conduct this study and regulatory authorities may inspect included subjects' records to verify trial data.

This clinical trial will be registered and information and data will be available on http://www.ClinicalTrials.gov, as required by U.S. law. This web site will not include identifiable individual patient information.

The HIPAA Privacy Rule establishes the conditions under which protected health information may be used or disclosed by covered entities for research purposes. Research is defined in the Privacy Rule as, "a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge." see 45 CFR 164.501. A covered entity may always use or disclose for research purposes health information which has been de-identified (in accordance with 45 CFR 164.502(d), and 164.514(a)-(c) of the Rule) without regard to the appropriate provisions. The Privacy Rule protects the privacy of individually identifiable health information, while at the same time ensuring that researchers continue to have access to medical information necessary to conduct vital research. This study operates under the Common Rule (45 CFR Part 46, Subpart A) and/or the Food and Drug Administration's (FDA) human subject protection regulations (21 CFR Parts 50 and 56).

6.7 Roles and Responsibilities

6.7.1 Investigator's responsibilities

Before participating in the study, all Investigators must agree to respect and fulfill the terms of this Investigational Plan and sign and date an Investigator Agreement (separately provided to this document) as well as certification and disclosure of financial interest.

The Principal Investigator at each clinical site will have the following responsibilities:

- Obtaining IRB approval
- Obtaining informed consent from patients
- Enrolling of patients, performing medical procedures
- Adhering to the Clinical Investigational Plan, signed agreement with the sponsor, applicable FDA regulations and any conditions of approval imposed by an IRB or FDA
- Supervise the use of the investigational device (LiquiBand FIX8®) and ensure the device is to be used only on subjects under the investigator's supervision and shall not supply an investigational device to any person not authorized to receive it.
- Following patients through the end of the study
- Completing CRFs on time, completely, and accurately
- Reporting Adverse Events in a timely manner
- Supplying the sponsor with his/her updated curriculum vitae and that of the co-Investigators as applicable
- Maintaining records and providing reports according to regulations (21 CFR 812.140(a)
- Sharing all relevant study-related information with co-Investigators
- Filing and archiving study documentation as per regulations in force
- Disclosure to the sponsor sufficient accurate financial information through completion and accurate certification or disclosure statements required under 21CFR54. The investigator and Sub-Investigator(s) shall promptly update this information if any relevant changes occur during the course of the investigation and for 1 year following completion of the study.
- Disposing of device: Upon completion or termination of a clinical investigation or the investigator's part of an investigation, or at the sponsor's request, an investigator shall return to the sponsor any remaining supply of the device.

6.7.2 Sponsor’s responsibilities

The sponsor of this study is responsible for the following:

- Selection of the clinical Investigators qualified by training and experience
- Obtaining approval to begin the study
- Development of Clinical Investigation Plan (CIP), CRFs and any other study related documents
- Obtaining study agreements with Investigators/hospitals,
- If applicable, selecting and obtaining agreements with clinical research organizations (CROs), and other involved parties
- Selection of monitors qualified by training and experience
- Development and/or approval of an adequate Informed Consent Form
- Ensuring training on the study protocol, procedures and use of the Investigational device (LiquiBand FIX8®)
- Ensuring that appropriate information is given to the clinical Investigators, including copies of the Investigational Plan and the Report of Prior Investigations of the device
- Database management, and maintenance
- All communications with regulatory bodies
- Informing Investigator of his/her responsibilities
- Maintaining records and providing reports according to regulations

- Ensuring that the Adverse Event reports are reported by the clinical Investigators and are forwarded to the relevant authorities, where required
- Ensure Unanticipated Adverse Device Effects are evaluated immediately, and responsible for termination and resumption of terminated studies in accordance with 812.46(b)(2)
- Control of investigational device
- Securing compliance of investigational sites

7 RECORDS AND REPORTS

All records and reports related to this investigation are subject to inspection and must be retained together in an organized, retrievable manner for two (2) years after either the date the investigation is terminated or the date that the records are no longer required to support regulatory approval of the device, whichever is longer.

7.1 Investigator

The Investigator is responsible for the retention, and in some cases, preparation of the records and reports cited below:

a. All site-specific correspondence that pertains to the investigation

b. Records of receipt, use, or disposition of the devices that includes the quantity, dates of its receipt, batch number and names of all persons who received, used, disposed, or returned each device and the number and reason for any return of the device(s) to Sponsor or disposal to ensure accountability for all investigational devices

c. Patient records, including but not limited to:

   i. Screening forms of all patients screened for the study, whether included or excluded;

   ii. Signed and dated Informed Consent Form for each enrolled patient and, for any use of a device by the investigator without informed consent, any written concurrence of a licensed physician and a brief description of the circumstances justifying the failure to obtain informed consent;

   iii. All relevant source documentation such as preoperative medical history, information on the condition of the subject during the investigation, the results of all applicable diagnostic tests;

   iv. Observations of Adverse Device Effects, whether anticipated or unanticipated; and

   v. All Case Report Forms which include a record of exposure of each subject to the investigational device.

d. A copy of the Investigational Plan and Protocol, with documentation showing the date of and reason for each deviation from the protocol

e. A copy of all the signed and dated Investigator Agreements and the curriculum vitae and financial disclosure statement of each Investigator at the center

f. If the investigator was involved in an investigation or other research that was terminated, an explanation of the circumstances that led to termination

g. IRB approval documentation and correspondence

h. The Investigator is responsible for the complete and accurate preparation and timely submission of the reports cited in Table 5 (or per local Authority Guidelines).

Table 5: Investigator Reporting Responsibilities		
Type of Report	**Report Prepared For**	**Reporting Time Frame**
All Adverse Events (AEs)	Sponsor	Within 10 working days of data availability.
All Serious Adverse Events (SAEs)	Sponsor	Must be reported to the Sponsor or designee within 24 hours of first knowledge of the event.
All Unanticipated Adverse Device Effects (UADEs)	Sponsor and IRB	ASAP, but to the Sponsor no later than 24 hours after Investigator is first aware of the event. To IRB according to local guidelines.
Withdrawal of IRB Approval or other action on part of the IRB that affects the study	Sponsor	Within 5 working days of IRB decision.
Study Progress Reports	Sponsor and IRB	At intervals dictated by the IRB, but no less than yearly.
Emergency Deviations from study protocol to protect life or physical well-being of a subject	Sponsor and IRB	ASAP, but to Sponsor no later than 5 working days after the deviation occurs. To IRB according to local guidelines.
Inappropriate Informed Consent	Sponsor and IRB	To Sponsor within 5 working days after the deviation occurs. To IRB according to local guidelines.
Final Report	Sponsor and IRB	To Sponsor within 3 months after termination or completion of study or Investigator's participation. To IRB according to local guidelines.
Other	As Required	Upon request by the IRB to provide accurate, complete, and current information about any aspect of the study.

7.2 Sponsor

Sponsor will maintain the following accurate, complete and current records and reports relating to the investigation:

a. All correspondence and reports pertaining to the investigation with another sponsor, a monitor, an investigator, an IRB or FDA
b. Records of shipment and disposition of devices, including records of devices returned to the Sponsor and the reasons and methods of disposal of any device(s). Records of shipment shall include the name and address of the consignee, type and quantity of device, date of shipment, and batch number
c. Signed and dated Investigator Agreements , financial disclosure statements and curriculum vitae of each participating Investigator
d. Records concerning Adverse Device Effects (whether anticipated or unanticipated) and complaints
e. The Investigational Plan, including all amendments or modifications, and reports of prior investigations
f. Pre-study visit report(s)
g. Monitoring report(s)
h. Copies of IRB approvals and correspondence
i. Sponsor is responsible for the complete and accurate preparation and timely submission of the reports cited in Table 6.

Table 6: Sponsor Reporting Responsibilities

Type of Report	Report Prepared For	Reporting Time Frame
Serious Adverse Events (SAEs)	FDA, Participating Investigators	Annual
Unanticipated Adverse Device Effect	FDA, all IRBs and Participating Investigators	Sponsor will report any unanticipated adverse device effect within 10 working days of being notified of the event
Withdrawal of IRB approval	FDA, all IRBs, and Participating Investigators	Report will be made within 5 working days of notification.
Withdrawal of Regulatory approval	All IRBs and Principal Investigators	Report will be made within 5 working days of notification.
Current Investigator List	FDA	Sponsor will submit a current list of the names and addresses of all participating Investigators at 6-month intervals. The first such list 6 months after FDA approval.
Progress Report	FDA, all IRBs and Principal Investigators	A progress report will be submitted at least yearly.

Table 6: Sponsor Reporting Responsibilities		
Recall and Device Disposition	FDA, all IRBs	Notification will be made within 30 working days of Sponsor decision to request that an investigator return, repair or otherwise dispose of any units of the deviceand will include the reasons for the request.
Final Report	FDA, all IRBs, and Participating Investigators	Sponsor will notify the FDA within 30 working days of the completion or termination of the investigation. A final report will be submitted within 6 months after termination or completion.
Failure to Obtain Informed Consent	FDA	Sponsor will submit, within 5 working days of receipt of the report from the Investigator, a copy of the report of the use of the device without informed consent.
Other Required Reports	IRBs or FDA	Sponsor will, upon request by a reviewing IRB or any applicable regulatory agency; provide current information about any aspect of the investigation.

8 PUBLICATION POLICY

8.1 General

The Sponsor and the Investigators are committed to the publication and widespread dissemination of the results of the study in the scientific community. This study represents a joint effort between Sponsor and Investigators, and as such, the parties agree that the recommendation of any party concerning manuscript or text shall be taken into consideration in the preparation of final scientific documents for publication or presentation. The responsibility for the publication of the scientific manuscripts and abstracts from the study data ultimately rests with the Sponsor and the study Principal Investigators.

The Investigators shall have the right to publish, present, or use any data or results arising out of the performance of the study for their own instruction, research, or publication purposes, subject to the limitations described below. The Investigators will provide the Sponsor with a copy of any proposed publication or the full text of any other intended disclosure to the Sponsor at least 90 days in advance of the date of submission for publication or disclosure or at least 90 days prior to submission of an abstract. Within said 90 day period, the Sponsor shall: a) review such proposed publication for any inventions, patentable subject matter or Confidential Information; b) identify with specificity the text or graphics in the proposed publication which contain such Confidential Information so that the proposed publication may be edited appropriately to remove reference to the Confidential Information prior to publication as determined solely by the Sponsor. If the proposed publication contains inventions or patentable subject matter, the Sponsor may request additional time (not to exceed 90 days from the expiration of the initial 90 day review period, to enable the Sponsor to file a patent application for such Sponsor inventions.

Investigators shall not independently publish the results of this clinical study before a multi-center results paper is published. The Sponsor and Investigators agree that if the multi-center study data is not submitted for publication within twelve (12) months after conclusion, abandonment, or termination of the study at all sites, the Institution or Principal Investigator may publish the results from the Institution's site individually in accordance with above policy.

All clinical data or any other information gathered during or after this Study related to the Study, people involved or materials involved, will be considered confidential. Confidential information will be treated as and remain confidential as specified in the Clinical Trial Agreement.

8.2 Papers and Authorship

8.2.1 Primary Study Outcomes Paper

The primary outcomes will be communicated first in the primary outcomes publication. First author: Principal US Study Investigator. Co-authors: other participating Investigators (number of authors depending Journal Authorship policy).

8.2.2 Other Non-Primary Outcomes Papers-abstracts

The agreement of the Sponsor is mandatory before any submission prior to the publication of the first primary results paper or abstracts. The Sponsor will approve or deny based on reasons such as potential for bias, potential impact on study results, and independence of other ideas. In general, authorship to be determined by who presented the publication concept, and appropriateness and timing related to primary outcomes paper.

The publication policy described below applies for all publications not related to primary study outcomes.

For abstracts/sub-studies using the entire dataset, publication will be reviewed on a case by case basis. Authorship will be lead author being primary idea contributor, last author is US Study Principal Investigator.

For center-specific abstracts/sub-studies using exclusively center data: In the case where site Sub-Investigators participating in the study and belonging to the same center wish to publish, the principal Investigator of the center is solely responsible to designate the names and order of the authorship.

9 APPENDIX

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9.2 LiquiBand FIX8® IDE IFU

9.3 AbsorbaTack™ IFU