A Prospective Analysis of the Use of Gentrix® Surgical Matrix for Soft Tissue Reinforcement in Ventral Hernia Repair as Long Term Follow Up to T-GENVIH-002 study

Short Title: Gentrix Ventral Hernia Repair Long Term Follow Up study

Protocol Number: T-GENVIH-003

National Clinical Trial (NCT) Identified Number: 06034652

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Sponsor:
Integra LifeSciences Corporation
1100 Campus Drive, Princeton, New Jersey, 08540
USA
www.integralife.com

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A. ABBREVIATIONS

***The list below includes abbreviations utilized in this template. However, this list should be** customized for each protocol (i.e., abbreviations not used should be removed and new abbreviations used should be added to this list).*

AE	Adverse Event
ADE	Adverse Device Effect
ANCOVA	Analysis of Covariance
ASADE	Anticipated Serious Adverse Device Effect
CDC	Centers for Disease Control and Prevention
CIP	Clinical Investigational Plan
CFR	Code of Federal Regulations
CMP	Clinical Monitoring Plan
CONSORT	Consolidated Standards of Reporting Trials
CTA	Clinical Trial Agreement
CRF	Case Report Form
DD	Device Deficiency
EDC	Electronic Data Capture
EC	Ethics Committee
eCRF	Electronic Case Report Forms
FDA	Food and Drug Administration
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act
ICH	International Conference on Harmonization
IRB	Institutional Review Board
LOS	Length Of Hospital Stay
LSMEANS	Least-squares Means
LTFU	Long Term Follow Up
MedDRA	Medical Dictionary for Regulatory Activities
MIS	Minimally Invasive Surgery
NCT	National Clinical Trial
PI	Principal Investigator
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SOA	Schedule of Activities
SOC	System Organ Class
SOP	Standard Operating Procedure
SSI	Surgical Site Infection
SSO	Surgical Site Occurrence
SSOPI	Surgical Site Occurrences Requiring Procedural Intervention
US	United States
USADE	Unanticipated Serious Adverse Device Event

B. REVISION HISTORY

The table below is intended to capture changes of IRB/EC-approved versions of the protocol, including a description of the change and rationale. A Summary of Changes table for the current amendment is located in the Protocol Title Page. Procedures for amending this protocol can be found in the current SOPs.

Version	Date	Description of Change	Brief Rationale

C. AUTHORIZED SIGNATORIES FOR THE SPONSOR

Name, Position/Title	Signature
David Sheleheda Sr. Director, Global Clinical Operations	SignNow e-signature ID: 50aafb085e... 03-Aug-2023 13:27:48 UTC David Sheleheda (Signer)
D. Adam Young, PhD PMP Director of Medical Affairs, Tissue Technologies	SignNow e-signature ID: ca4e2febb8... 04-Aug-2023 12:58:42 UTC Adam Young (Signer)
Nicole Kotter Sr. Manager, Regulatory Affairs	SignNow e-signature ID: 1af883a482... 07-Aug-2023 16:27:26 UTC Nicole Kotter (Signer)
Karen Bartku Clinical Research Manager, Global Clinical Operations	SignNow e-signature ID: c8f4539756... 03-Aug-2023 13:46:47 UTC Karen Bartku (Signer)
Laurence Tong Lead Clinical Data Manager, Global Clinical Affairs	SignNow e-signature ID: cf015d6c9c... 04-Aug-2023 16:36:54 UTC Laurence Tong (Signer)
Weiwei Xu Sr. Biostatistician, Global Clinical Affairs	SignNow e-signature ID: 29a94f3dde... 03-Aug-2023 14:30:59 UTC Weiwei Xu (Signer)

D. STUDY INVESTIGATOR AND SITE MEDICAL STAFF

The list of the study investigator and other site medical staff along with their contact information can be found in the Trial Master File.

E. STATEMENT OF COMPLIANCE BY THE INVESTIGATOR

This clinical investigation will be conducted in compliance with the current ISO 14155 guidelines and applicable regulatory requirements, including the Medical Device Regulation (MDR) 2017/745 **[AND/OR]** United States (US) Code of Federal Regulations (CFR) applicable to clinical studies (45 CFR Part 46, 21 CFR Part 50, 21 CFR Part 56) and other applicable national and regional regulatory requirements whichever provides the greater protection of the individual.
This clinical investigation will not be initiated until approval has been obtained from the Ethics Committee(s) (and Regulatory Authority if applicable). Any additional requirements imposed by the Ethics Committee(s) (and Regulatory Authority if applicable) will be followed.
No deviation from the clinical investigation plan will be implemented without the prior review and approval of the Ethics Committee(s) except where it may be necessary to eliminate an immediate hazard to a subject. In such case, the deviation will be reported to the Ethics Committee(s) as soon as possible.

Investigator's Statement

By signing this document, I agree to conduct this clinical study in accordance with the design and specific provisions of this clinical investigation plan; modifications to the clinical investigation are only acceptable with a mutually agreed upon clinical investigation plan amendment as approved by the Sponsor and involved Ethics Committee(s).

I agree to await Ethics Committee approval of the clinical investigation plan and informed consent form before initiating the clinical investigation, to obtain consent from subjects prior to their enrolment, to collect and record data as required by the clinical investigation plan and associated case report forms, and to maintain documents related to the clinical investigation for the period of time required.

Confidential

This document contains confidential information belonging to Integra ® LifeSciences Corporation. Except as may be otherwise agreed to in writing, by accepting or reviewing these materials, I agree to hold such information in confidence and not to disclose it to others (except where required by applicable law), nor use it for unauthorized purposes.

Investigator Name

Investigator Signature Date

1 Protocol Summary

1.1 Protocol Synopsis

Title	A Prospective Analysis of the Use of Gentrix® Surgical Matrix for Soft Tissue Reinforcement in Ventral Hernia Repair as Long Term Follow Up (LTFU) to T-GENVIH-002 study
Short Title	Gentrix Ventral Hernia Repair LTFU study
Protocol Number	T-GENVIH-003
Study Description	The purpose of this study is to collect additional safety data and demonstrate the performance of Integra Gentrix® Surgical Matrix for reinforcement of ventral hernia repairs from a sub-population of participants in the T-GENVIH-002 study, specifically those with laparoscopic or robotic repair. Prospective data will be collected and assessed for later post-operative surgical site events and complications in the post-operative period from the last timepoint of data collection in T-GENVIH-002 to present.
Pre/Post-Market	Post-Market
Product(s)	Gentrix® Surgical Matrix - (6-layer), - Plus (8-layer), and -Thick **Refer to APPENDIX I at the end of the protocol for product-specific Stock Keeping Units (SKUs) to be included in this study.*
Indications for Use	Gentrix® Surgical Matrix is intended for implantation to reinforce soft tissue where weakness exists in patients requiring gastroenterological or plastic & reconstructive surgery. Reinforcement of soft tissue within gastroenterological and plastic & reconstructive surgery includes, but is not limited to, the following open or laparoscopic procedures: hernia (e.g., hiatal/ diaphragmatic) and body wall repair, colon and rectal prolapse repair, tissue repair, and esophageal repair. Gentrix® Surgical Matrix minimizes tissue attachment to the device in case of direct contact with viscera.
Study Design	Single-Arm, Prospective, Single-Center
Study Rationale	This study adds to the available data evaluating the safety and effectiveness of Gentrix® Surgical Matrix in ventral hernia repair, particularly in a real-world population and particularly in the sub-

	population of minimally invasive surgery (MIS) cases (i.e., laparoscopic and robotic) from the GENVIH-002 study.
Primary Objective	The primary objective of this study is to capture additional existing clinical performance data to confirm the continued performance of the Gentrix® Surgical Matrix over longer term.
Safety Objective	The safety objective is to capture existing Gentrix® Surgical Matrix Complication data in the longer term period post primary repair procedure, not previously reported in T-GENVIH-002 study. Gentrix® Surgical Matrix Complications are defined but not limited to: • Seroma • Abscess • Dehiscence • Hematoma • Wound necrosis • Ileus • Fistula • Delayed wound healing
Primary Endpoint	1. Incidence of clinically confirmed recurrence of the primary hernia to date, including not previously reported in T-GENVIH-002 study.
Secondary Endpoints	1. Incidence of self-reported recurrence (i.e., bulge) of the primary hernia to date, including not previously reported in T-GENVIH-003 study. 2. Incidence of Surgical Site Occurrences requiring Procedural Intervention (SSOPI) of the primary hernia repair to date, including not previously reported in T-GENVIH-002. 3. Incidence of Surgical Site Occurrences (SSOs) of the primary hernia repair to date (seroma, abscess, dehiscence, hematoma, wound necrosis, ileus, fistula, delayed wound healing), including not previously reported in T-GENVIH-002 study. 4. Incidence of Surgical Site Infections (SSIs) post primary hernia repair to date, including not previously reported in T-GENVIH-002 study.

	5. Incidence of reoperation requirement of the primary hernia repair to date, including not previously reported in T-GENVIH-002 study.
Description of Study Intervention	A one-off subject interview with questionnaire will include a series of patients who underwent abdominal wall reconstruction for a ventral hernia repair with Integra Gentrix® Surgical Matrix to date, including not previously reported in the T-GENVIH-002 study.
Study Population	Patients from the sub-population of minimally invasive surgical approach (e.g., laparoscopic or robotic) of the T-GENVIH-002 study.
Inclusion Criteria	1. Patient was a subject in the T-GENVIH-002 study and underwent minimally invasive (i.e., laparoscopic or robotic) abdominal wall reconstruction for a primary hernia using Integra Gentrix® Surgical Matrix. 2. Subject has participated in the informed consent process and signed a study-specific informed consent document. 3. Subject is fluent in US English or US Spanish language. 4. Subject is willing to complete an e-consent and phone or in-office visit.
Exclusion Criteria	Not applicable.
Description of Sites/Facilities Enrolling Participants	One site located in the United States (US) will participate in this study.
Study Duration	Approximately three months.
Study Visits/Schedule of Study Activities	This prospective study specifically aims to collect data from the day of the primary hernia surgical repair procedure longer term post-operatively to date, including not previously reported in T-GENVIH-002 study.
Data Collection	Data will be collected via a phone visit and questionnaire administered by the study coordinator (or, in the alternative, an in-office visit and questionnaire administered by the study coordinator) and entered into an electronic data capture system by the site. The following data will be collected on the Long Term Follow Up (LTFU) of the primary hernia repair.

	Clinical Performance and Safety Evaluation: 1. SSOPI 2. SSO(s) 3. SSI(s) 4. Hernia Recurrence 5. Reoperation(s) 6. Adverse Event(s)
Statistical Methods & Analyses	Study outcomes will be summarized using descriptive statistics. Categorical variables will be summarized using frequencies and percentages. Continuous variables will be summarized using means, standard deviations, medians, quartiles, ranges, and numbers of observations. Statistical analysis will be based on data from all evaluable subjects meeting the eligibility criteria.

1.2 Schedule of Data Collection Activities

Table 1: Schedule of Data Collection Activities

***Prospective Data Collection**	**Screening**	**Subject Visit 1**
Eligibility/Consent	X	
Complete Case Report Form(s)	X	X
¥Adverse Events	X	X

*May occur on separate days
¥Primary hernia surgery

2 Introduction

2.1 Background

Ventral hernias are a type of abdominal hernias that can occur at any location along the vertical abdominal wall. Typically, these defects are acquired resulting from complications of a prior surgery, trauma, or natively weak points of the abdominal wall in some individuals. Obesity may contribute in large part to the weak points due to cyclic patterns of weight gain and loss. One in eight patients will develop an incisional hernia after abdominal surgery[1].

Ventral hernia repair is one of the most common surgical procedures performed in the United States. Every year there are approximately 350,000 repairs performed in the US with an estimated cost of $3.2 billion.[2] Different patient populations require different solutions in order to make a repair as cost-effective and risk-averse as possible.

Clinical evidence has shown that primary suture repair of a ventral hernia alone results in high recurrence rates (>50%), and that all incisional hernia repairs should be reinforced with surgical mesh.[3,4] Despite this consensus, due to the large variety of surgical meshes available currently, there is a lack of consensus on the ideal material for each repair. Ventral hernia treatment decisions are typically tied to patient operative risk, symptomatic concerns, and potential clinical complications of the repair.

Permanent synthetic mesh has been the standard of care in the reinforcement of simple, clean hernias due to its minimal cost and history of low recurrence.[5,6] However, due to the inherent permanence, long-term complications such as product migration, contraction, erosion, and infection are common.[5-8] In the complex hernia setting, synthetic materials may not be ideal due to the increased risks of surgical site occurrences (SSOs) and resulting recurrences.[5-8] These complications can prove costly with each hernia recurrence and wound event estimated to cost an additional $44,000 and $85,000 respectively.[9,10] Specifically, a mesh infection can cost up to $140,000 and may require explantation of the mesh altogether.[10]

Biologically-derived materials, such as acellular dermal matrices, were developed for use in complex hernia repair to mitigate some of the risks seen with synthetic materials. However, long-term study of these materials demonstrated a 31.8% recurrence rate and 36.6% wound infection rate at 18.2 months follow-up.[11]

Approximately 74% of inpatient ventral hernia repairs are completed as open procedures. While this number is slightly lower for outpatient ventral hernia repairs (64%), this remains the predominant surgical approach[12] likely for more complex cases.

Currently available biologically derived mesh options for reinforced repairs include a class of non-dermal products including Gentrix® Surgical Matrix devices.

This post-market clinical study is being conducted to characterize the performance and safety of Gentrix® Surgical Matrix -(6-layer), -Plus (8-layer) and -Thick devices in the repair of ventral hernias in patients between 22 years and 80 years old (inclusive) at the time they underwent abdominal wall reconstruction utilizing Gentrix® Surgical Matrix as a reinforcement graft during the time period post primary hernia surgical repair to date, not previously reported in T-GENVIH-002, as a *longer term follow-up* of safety and performance data in the sub-population of minimally invasive surgical cases (i.e., laparoscopic and robotic).

2.2 Investigational Product Overview

Gentrix® Surgical Matrix is intended for implantation to reinforce soft tissue where weakness exists in patients requiring gastroenterological or plastic & reconstructive surgery.

Reinforcement of soft tissue within gastroenterological and plastic & reconstructive surgery includes, but is not limited to, the following open or laparoscopic procedures: hernia (e.g., hiatal/diaphragmatic) and body wall repair, colon and rectal prolapse repair, tissue repair, and esophageal repair. Gentrix® Surgical Matrix minimizes tissue attachment to the device in case of direct contact with viscera.

The Gentrix® Surgical Matrix Device configuration includes the Gentrix® Surgical Matrix (6-layer), Gentrix® Surgical Matrix Plus (8-layer), and the Gentrix® Surgical Matrix Thick.

2.2.1 Gentrix® Surgical Matrix (6-layer):

Gentrix® Surgical Matrix (6-layer) is composed of a porcine-derived extracellular matrix, also known as urinary bladder matrix. The device is supplied in a multilayer sheet configuration in sizes up to 10 cm x 15 cm and packaged in double peel-open pouches. The device is terminally sterilized using electron beam irradiation.

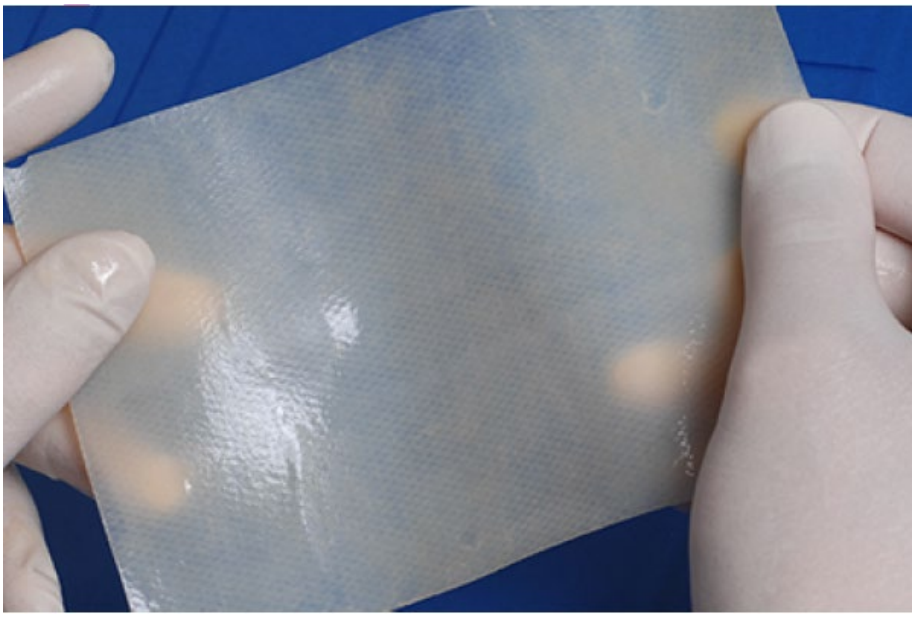

Figure 1: Gentrix® Surgical Matrix (6-layer)

2.2.2 Gentrix® Surgical Matrix Plus (8-layer):

Gentrix® Surgical Matrix Plus (8-Layer) is composed of porcine-derived extracellular matrix, also known as urinary bladder matrix. The device is supplied in a multilayer sheet configuration in sizes up to 10 cm x 15 cm and packaged in double peel-open pouches. The device is terminally sterilized using electron beam irradiation.

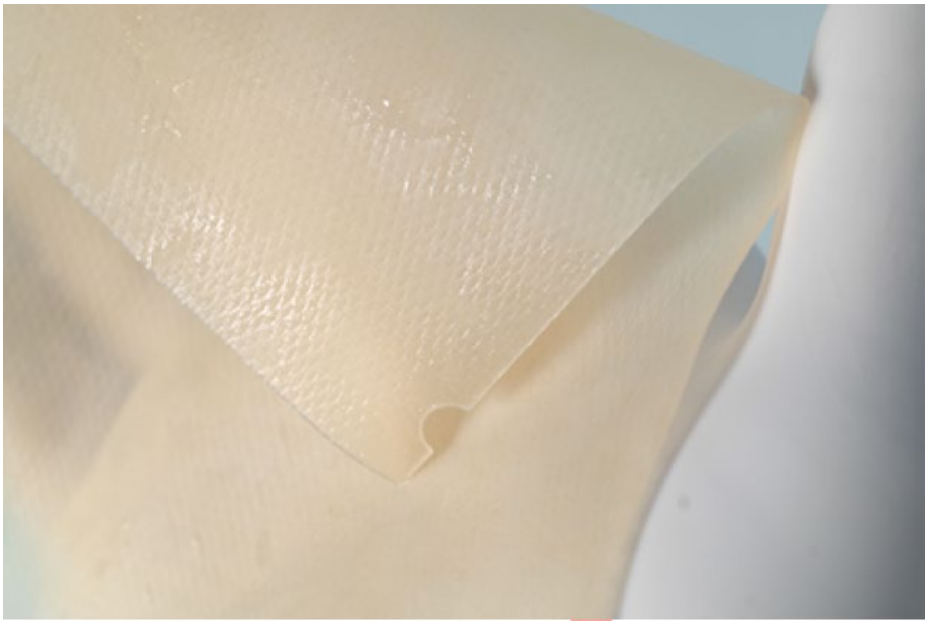

Figure 2 : Gentrix® Surgical Matrix Plus (8-layer)

2.2.3 Gentrix® Surgical Matrix Thick:

Gentrix® Surgical Matrix Thick is composed of a porcine-derived extracellular matrix, also known as urinary bladder matrix. The device is supplied in a multi-layer sheet configuration in sizes up to 30 cm x 40 cm and packaged in double peel-open pouches. The device is terminally sterilized using electron beam irradiation. Animal studies have shown device resorption in approximately 240 days.

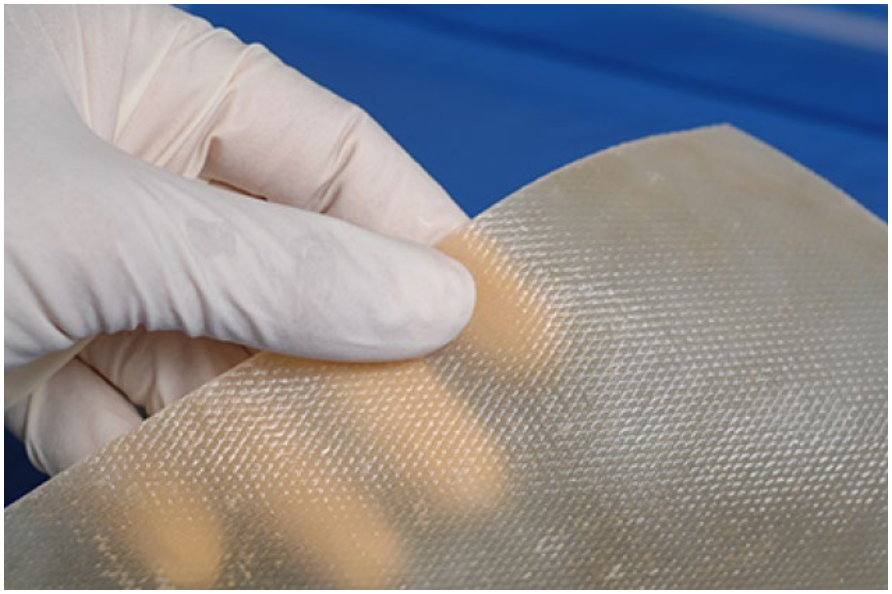

Figure 3 : Gentrix® Surgical Matrix Thick

2.2.1 Study Device Intended Purpose

The Gentrix® Surgical Matrix devices were used within label in this prospective study. There were no specific medical or surgical procedures involved in the use of the study devices, other than the standard of care. A full description of the medical and surgical procedures related to the Gentrix® Surgical Matrix devices is available in the Instructions for Use (IFU).

2.2.2 Study Device Contraindication

Patients with known sensitivity or allergy to porcine materials.

2.2.3 Required Training and Experience

Previously trained on the use of the devices, the investigator must have used the devices within label in this study. Integra LifeSciences Corporation did not train, nor dictate, the surgery

technique(s). The investigator must meet certain expectations per Sponsor Standard Operating Procedures (SOPs).

2.2.4 Device Accountability

No device accountability will be performed for the purposes of this study given the study is noninterventional.

2.2.5 Device Traceability

No device traceability will be performed for the purposes of this study given the study is noninterventional.

2.3 Study & Design Rationale

This is a single-arm, single-center, prospective study to collect in routine use additional safety data and demonstrate the performance of Integra Gentrix® Surgical Matrix for reinforcement of minimally invasive (i.e., laparoscopic and robotic) ventral hernia repairs as a LTFU of the T-GENVIH-002 study. Routine use data to date – longer term, not previously reported -- will be collected prospectively at one site. This study adds to the available data evaluating the safety and effectiveness of Gentrix® Surgical Matrix in ventral hernia repair, particularly in a real-world population, and particularly in the sub-population described.

3 Objectives and Endpoints

3.1 Primary Objective

The primary objective of this study is to capture existing clinical performance data to confirm the continued performance of the Gentrix® Surgical Matrix as a long term follow up (LTFU) to T-GENVIH-002 study for minimally invasive surgical approach (laparoscopic and robotic) sub-population of cases post primary hernia surgical repair to date, not previously reported in the T-GENVIH-002 study.

Existing clinical data support the safety and performance of the Gentrix® Surgical Matrix. There are currently no safety concerns with these products. This clinical investigation will confirm the safety and performance of the Gentrix® Surgical Matrix particularly in MIS cases and identify any unknown or not previously reported side-effects.

3.2 Safety Objective

The safety objective of this study is to capture existing Gentrix Surgical Matrix Complication data in the later post-operative period to date, not previously reported in the T-GENVIH-002 study.

Gentrix® Surgical Matrix Complications are defined but not limited to:

- Seroma
- Abscess
- Dehiscence
- Hematoma
- Wound necrosis
- Ileus
- Fistula
- Delayed wound healing

3.3 Primary Endpoint

The primary endpoint of this prospective study is to determine the incidence of clinically confirmed recurrence of the primary hernia to date, including not previously reported in T-GENVIH-002 study.

3.4 Secondary Endpoints

1. Incidence of self-reported recurrence (i.e., bulge) of the primary hernia to date, including not previously reported in T-GENVIH-003 study.
2. Incidence of Surgical Site Occurrences requiring procedural intervention (SSOPI) of the primary hernia repair to date, not previously reported in T-GENVIH-002.
3. Incidence of Surgical Site Occurrences (SSOs) of the primary hernia repair to date (seroma, abscess, dehiscence, hematoma, wound necrosis, ileus, fistula, delayed wound healing), including not previously reported in T-GENVIH-002 study.
4. Incidence of Surgical Site Infections (SSIs) post primary hernia repair to date, including not previously reported in GENVIH-002 study.
5. Incidence of reoperation requirement of the primary hernia repair to date, including not previously reported in GENVIH-002 study.

4 Study Design

4.1 Overall Design

The Gentrix Ventral Hernia Repair Long Term Follow Up study is a single-arm, prospective, single-center, post-market study which includes Long Term Follow Up (LTFU) safety and performance outcomes of a sub-population of subjects who underwent minimally invasive (e.g., laparoscopic or robotic) surgical repair using Gentrix® Surgical Matrix post index procedure to date, including not previously reported in T-GENVIH-002 study.

4.2 Scientific Rationale for Study Design

This study adds to the available data evaluating the safety and effectiveness of Gentrix Surgical Matrix in ventral hernia repair, particularly in a real-world population, and particularly in the MIS sub-population described.

4.3 End of Study Definition Overview

The end of the study is defined as completion of Case Report Forms (CRFs) for the last subject in this prospective study.

5 Study Population

5.1 Inclusion Criteria

1. Patient was a subject in the T-GENVIH-002 study and underwent minimally invasive (i.e., laparoscopic or robotic) surgical abdominal wall reconstruction for a primary hernia repair using Integra Gentrix® Surgical Matrix.
2. Subject has participated in the informed consent process and signed a study-specific informed consent document.
3. Subject is fluent in US English or US Spanish language.
4. Subject is willing to complete an e-consent and phone or in-office visit.

5.2 Exclusion Criteria

Not applicable.

5.3 Description of the site

One site in the US will be selected to participate in this study. The study site was selected based upon their prior participation in the T-GENVIH-002 study, experience with the subject device, their clinical expertise, expected commitment to have available data for eligible study patients, and their ability to fulfill general requirements in the Sponsor's SOPs and to comply with this protocol.

5.4 Point of Enrollment & Enrollment Period

The patients will provide informed consent to allow use of their data. There is no traditional enrollment period in this study. Data will begin to be collected from the first patient who meets all the eligibility criteria.

The total expected duration of the study is approximately 3 months.

5.5 Strategies for Recruitment

A one-off subject phone (call) visit will constitute the source of data and will be collected using a study-specific eCRF delivered via a phone script by the site responsible or their designee(s). Each patient should be included in the study only once. Patient screening will rely on site identification and contact of prior T-GENVIH-002 study subjects (Sponsor remains blinded) and e-consent process. In these cases, every effort should be made to identify every possible eligible patient. For those that are lost to follow up, site may work directly with a Sponsor approved people search service (Sponsor remains blinded). In order to be eligible for the study, patients should meet all of the eligibility criteria.

For subjects who decline an electronic consent collected remotely, an in-office interview and assistance with completing the electronic consent in person with the site study coordinator or their designee(s) will be offered for the convenience of the subjects and to maximize data collection efforts.

5.6 Risk/Benefit Assessment

5.6.1 Risks associated with Study device

Complications and reactions are possible with any soft tissue repair, including but not limited to infection, increased chronic inflammation, allergic reaction, unexplained fever or chills, excessive redness, acute and chronic pain, swelling, tender scars, adhesions, seroma formation, fistula formation, hematoma, recurrence of tissue defect, delayed or failed

incorporation of graft, urinary or fecal incontinence, delayed or failed incorporation of graft (mesh) or suture erosion or extrusion, and injury to the bladder, bowel, blood vessels.

5.6.2 Risks Associated with Participation in the study and mitigation

As this prospective study involves data collection, there are only minimal risks associated with participation. There are no additional device-related risks for this study. There are, however, privacy (loss of confidentiality) risks associated with participation in the study.

Participation in the study does not submit the patient to any additional procedures or exams outside the customary standard of care. Patient confidentiality and privacy is strictly held in trust by the participating investigator, their staff, and the Sponsor. The patient's data will be given a code to assure that the data can only be traced with the use of an identifier. The identifier will be stored securely in the local research institute. Data that is shared with the sponsor will only contain the code. The patient's name and any other identifiable information will be omitted. All national data protection laws will be respected including the US Health Insurance Portability and Accountability Act of 1996 (HIPAA). Data shared with the Sponsor will be encoded and maintained in a secure electronic database that is compliant with 21 CFR Part 11 requirements on electronic records and electronic signatures.

5.6.3 Anticipated Clinical and device Benefits

There is no direct benefit. Information learned from this study might help researchers to better understand medical treatments and disease processes or procedures in order to better help others in the future.

The data collected from the study will be used to inform the device manufacturer about the safety and performance of the device when used in accordance with the device labelling.

5.6.4 Rationale of Risks/Benefits Ratio

The participation in the study does not add risks to the patients, thus the benefit is judged to outweigh the overall residual risks.

6 Study Assessments and Procedures

6.1 Schedule of Data Collection

6.1.1 Eligibility/Consent

- The procedures to be completed are:

- ✓ Identification of the full consecutive series of patients who underwent abdominal wall reconstruction for a minimally invasive surgical approach (i.e., laparoscopic or robotic) hernia with Integra® Gentrix® Surgical Matrix from the prior T-GENVIH-002 study and informed consent for those who volunteer to participate.
- ✓ Creation on the CRF of a new case book for each eligible subject. Each created case book assigns the eligible subject with a study number.
- ✓ Completion of Worksheets/ CRFs: Site will transcribe/transmit the below-mentioned patients' data in study CRFs. The patients' data will originate from a direct interview with the subject by the study coordinator.

- The patients' data to be collected are:
  - ✓ Eligibility:
    - Inclusion Criteria: Ensure the subject meets all the inclusion criteria.

6.1.2 Visit 1 Questionnaire

The patients' data to be collected from the last data collection of GENVIH-002 study to date, including not previously reported, are:

- Clinically confirmed recurrence of the primary hernia repair
- Self-reported recurrence (i.e., bulge) of the primary hernia
- Surgical Site Occurrences requiring Procedural Intervention (SSOPI)
- Surgical Site Occurrences (SSOs)
- Surgical Site Infections (SSIs)

6.1.3 Adverse Events

Information will be collected on post-operative adverse events that relate to the primary hernia repair procedure, including those not previously reported in the T-GENVIH-002 study.

6.1.4 Device Deficiencies

Information will be collected for post-operative device deficiencies that relate to the primary hernia repair procedure, including those not previously reported in the T-GENVIH-002 study.

6.1.5 Study Completion/Exit

Information will be collected by the study coordinator for each enrolled subject to reflect study exit type.

6.2 Monitoring

Monitoring of the study may be conducted either remotely or in-person, as determined by the Sponsor per Sponsor's Monitoring Visit Plan.

7 Safety Assessments and Reporting

7.1 Definitions

The table below contains the definitions being used for safety assessment as part of this study:

Table 2: List of AE Terms and Definitions

This list of terms should be edited to remove those which do not concern the study.	
Term	**Definition**
Adverse Device Effect (ADE)	An adverse event related to the use of an investigational medical device. This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device. And this definition includes any event resulting from use error or from intentional misuse of the investigational device.
Adverse Event (AE)	Any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users, or other persons, whether or not related to the investigational medical device and whether anticipated of unanticipated. This definition includes events related to the investigational medical device; events related to the procedures involved and, for users or other persons, this definition is restricted to events related to investigational medical devices.
Anticipated Serious Adverse Device Effect (ASADE)	A serious adverse device effect which by its nature, incidence, severity or outcome has been identified in the risk assessment

This list of terms should be edited to remove those which do not concern the study.	
Term	**Definition**
Device Deficiency (DD)	Inadequacy of a medical device with respect to its identity, quality, durability, reliability, usability, safety or performance. **Note 1:** Device deficiencies include malfunctions, use errors, and inadequacy in the information supplied by the manufacturer including labelling. **Note 2:** This definition includes device deficiencies related to the investigational medical device or the comparator.
Malfunction	Failure of an investigational medical device to perform in accordance with its intended purpose when used in accordance with the instruction for use.
Serious Adverse Device Effect (SADE)	Adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event. **Note:** SAEs related to procedures imposed by the clinical investigation plan but not with the use of the device should not be considered Serious Adverse Device Effects.
Serious Adverse Event (SAE)	Adverse event that led to any of the following: a) death, b) serious deterioration in the health of the subject, users or other persons as defined by one or more of the following: a life-threatening illness or injury, or a permanent impairment of a body structure or a body function including chronic diseases, or in-patient or prolonged hospitalization, or medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function, c) fetal distress, fetal death or a congenital abnormality or birth defect including physical or mental impairment. **Note:** Planned hospitalization for a pre-existing condition, or a procedure required by the CIP, without serious deterioration in health, is not considered a serious adverse event.

This list of terms should be edited to remove those which do not concern the study.	
Term	**Definition**
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.
Unanticipated Serious Adverse Device Effect (USADE)	Serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the current risk assessment. **Note 1:** Anticipated serious adverse device effect (ASADE) is an effect which by its nature, incidence, severity or outcome has been identified in the risk assessment. **Note 2:** Procedures associated with the use of a device should be addressed in the risk assessment, which makes it possible to determine whether the procedure related SAEs are Unanticipated Serious Adverse Device Effect or not.

7.2 Reporting of Safety Information

7.2.1 Non-Reportable Event

Adverse Events not related to the primary hernia repair procedure will not be required to be reported by the investigator in this study.

7.2.2 Severity

Each adverse event will be classified according to three (3) levels of severity. The Sponsor and the investigator will use the following definitions to assess the severity of the adverse event:

Mild – Awareness of signs or symptoms, but easily tolerated and are of minor irritant type causing no loss of time from normal activities. Symptoms do not require therapy or a medical evaluation; signs and symptoms are transient.

Moderate – Events introduce a low level of inconvenience or concern to the participant and may interfere with daily activities but are usually improved by simple therapeutic measures; moderate experiences may cause some interference with functioning.

Severe – Events interrupt the participant's normal daily activities and generally require systemic drug therapy or other treatment; they are usually incapacitating.

7.2.3 Causality

The relationship between the use of the medical device (including the medical - surgical procedure) and the occurrence of each adverse event shall be assessed and categorized.

Each AE will be classified according to four (4) different levels of causality:

Not related: Relationship to the device, or procedures can be excluded when:

- the event has no temporal relationship with the use of the study devices, or the procedures related to application of the study devices;
- the serious adverse event does not follow a known response pattern to the medical device (if the response pattern is previously known) and is biologically implausible;
- the discontinuation of medical device application or the reduction of the level of activation/exposure - when clinically feasible - and reintroduction of its use (or increase of the level of activation/exposure), do not impact on the serious adverse event;
- the event involves a body-site or an organ that cannot be affected by the device or procedure;
- the serious adverse event can be attributed to another cause (e.g., an underlying or concurrent illness/ clinical condition, an effect of another device, drug, treatment or other risk factors);
- the event does not depend on a false result given by the investigational device used for diagnosis, when applicable;

In order to establish the non-relatedness, not all the criteria listed above might be met at the same time, depending on the type of device/procedures and the serious adverse event.

Possible: The relationship with the use of the investigational device or comparator, or the relationship with procedures, is weak but cannot be ruled out completely. Alternative causes are also possible (e.g., an underlying or concurrent illness/ clinical condition or/and an effect of another device, drug or treatment). Cases where relatedness cannot be assessed, or no information has been obtained should also be classified as possible.

Probable: The relationship with the use of the investigational device or comparator, or the relationship with procedures, seems relevant and/or the event cannot be reasonably explained by another cause.

Causal relationship: The serious adverse event is associated with the investigational device, or with procedures beyond reasonable doubt when:

- the event is a known side effect of the product category the device belongs to or of similar devices and procedures;
- the event has a temporal relationship with investigational device use/application or procedures;
- the event involves a body-site or organ that
    - the investigational device or procedures are applied to;
    - the investigational device or procedures have an effect on;
- the serious adverse event follows a known response pattern to the medical device (if the response pattern is previously known);
- the discontinuation of medical device application (or reduction of the level of activation/exposure) and reintroduction of its use (or increase of the level of activation/exposure), impact on the serious adverse event (when clinically feasible);
- other possible causes (e.g., an underlying or concurrent illness/ clinical condition or/and an effect of another device, drug or treatment) have been adequately ruled out;
- harm to the subject is due to error in use;
- the event depends on a false result given by the investigational device used for diagnosis, when applicable;

In order to establish the relatedness, not all the criteria listed above might be met at the same time, depending on the type of device/procedures and the serious adverse event.

The Sponsor and the investigator will distinguish between the adverse events related to the study device and those related to the procedures (any procedure specific to the study). An adverse event can be related both to procedure and the study device.

During causality assessment activity, clinical judgement shall be used and the relevant documents, such as the IFU, the Clinical Investigation Plan or the Risk Analysis Report shall be consulted, as all the foreseeable serious adverse events and the potential risks are listed and assessed there. The presence of confounding factors, such as concomitant medication/treatment, the natural history of the underlying disease, other concurrent illness or risk factors shall also be considered.

Complications caused by concomitant treatments not imposed by the clinical investigation plan are considered not related. Similarly, several routine diagnostic or patient management procedures are applied to patients regardless of the clinical investigation plan. If routine

procedures are not imposed by the clinical investigation plan, complications caused by them are also considered not related.

In some particular cases the event may not be adequately assessed because information is insufficient or contradictory and/or the data cannot be verified or supplemented. The Sponsor and the investigator will make the maximum effort to define and categorize the event and avoid these situations. Where an investigator assessment is not available and/or the Sponsor remains uncertain about classifying the adverse event, the sponsor should not exclude the relatedness; the event should be classified as “possible” and the reporting not be delayed. Particular attention shall be given to the causality evaluation of unanticipated serious adverse events. The occurrence of unanticipated events related to the use of the device could suggest that the clinical investigation places subjects at increased risk of harm than was to be expected beforehand.

7.2.4 Foreseeable adverse events and anticipated adverse device effects

The following adverse events are outlined, and therefore anticipated, in the device’s Instructions for Use (IFU):

Infection, increased chronic inflammation, allergic reaction, unexplained fever or chills, excessive redness, acute and chronic pain, swelling, tender scars, adhesions, seroma formation, fistula formation, hematoma, recurrence of tissue defect, anastomotic stricture formation and leaks, dyspareunia, vaginal shortening, vaginal bleeding, atypical vaginal discharge, groin and/or buttock and/or leg pain, urinary or fecal incontinence, delayed or failed incorporation of graft, failure to repair a prolapse, recurrent prolapse, mesh or suture erosion or extrusion, and injury to the bladder, bowel, blood vessels, and/or nerves of the pelvis.

7.3 Reporting Requirements

7.3.1 Reporting of AEs and SAEs

The investigator will determine if there has been a potentially device or procedure related adverse event or potentially device or procedure related serious adverse event. All potentially device or procedure related adverse events and potentially device or procedure related serious adverse events must be reported on the “Adverse Event” form.

Potentially device or procedure related adverse events and potentially device or procedure related serious adverse events will be evaluated and differentiated by:

- Seriousness of the event;
- Causality of the event (in relation to the device or procedure);

- Severity of the event.

All potentially device or procedure related AEs and potentially device or procedure related SAEs must be collected for all enrolled subjects starting from the time of enrollment through the last Follow-up. Each AE must be described as follows:

AE Term: A medically defined diagnosis/symptom. Use the highest level of evidence available.

Level 1: Diagnosis (highest level)
Level 2: Symptoms
Level 3: Signs (lower level)

AE Description: Explain the circumstance of becoming aware of the event, how the subject explained the circumstances surrounding the onset of the event, the underlying cause (the diagnosis), coexisting disease, or other condition or complaint involving the event.
AE Duration: Document by entering the date of onset (start date) and date of resolution (stop date).
AE Causality: Document causal relationship between event and the investigational product and Study Procedure (causally related, possible, probably, not related).
AE Seriousness: Document as serious or not serious.
AE Severity: Document as mild (transient and easily tolerated by the subject), moderate (discomfort and interrupts normal activities), or severe (incapacitating with inability to work or do usual activity).
Action(s) Taken and/or Treatment(s): Document as none, medication, hospitalization, surgical, and/or other. Any prescribed medication should be noted in the subject's medical records and transcribed onto the AE and Concomitant Medications CRFs. If a surgical or invasive procedure is required for an AE, document the procedure on the Invasive Procedure Log.
Outcome: Document as recovered without sequelae, recovered with sequelae, ongoing, death, or other. AEs will be followed until a resolution has occurred, until a resolution is no longer expected, the pre-existing condition returns to baseline conditions, or the subject exits the study.

7.3.2 Reporting Device Deficiency

All device deficiencies (DDs) related to the identity, quality, durability, reliability, usability, safety or performance of the study device including the analysis of used or explanted study device, where applicable, shall be documented throughout the study and managed by the sponsor.

The principal investigator shall record every observed device deficiency on the "Device Deficiency" form, together with an assessment for all enrolled subjects starting from the time of enrollment through the last Follow-up visit. Each DD must be described as follows:

Deficiency Type:

- Identity (Packaging/Labeling)
- Quality (Structure/Appearance)
- Durability (ability to withstand wear, pressure, or damage)
- Usability (use error, misuse, abnormal use)
- Reliability (Performs in a consistent manner)
- Safety (Impact on Patient Care)
- Performance (Functions according to the IFU)

When the deficiency was noted

If the deficiency was associated with an AE

If the deficiency might have led to:

- Adverse Effect
- Serious Adverse Device Effect

Device deficiencies shall be managed by the sponsor in accordance with written procedures for the control of non-conforming product. The sponsor shall take appropriate corrective and preventive actions to protect the safety of subjects, users and other persons.

In case of DD that could have led to SADE, the sponsor determines whether the risk analysis needs to be updated and assess whether corrective or preventive action is required.

The Site should make every attempt to save or collect the defective device, and if appropriate, the packaging, for return to the Sponsor. A qualified company representative will investigate and determine root cause and corrective actions as applicable, and directives will be provided to the site if warranted.

If the site documents a DD, the site will report the event in accordance with the following parameters. **It should be noted that no documents should be submitted to any regulatory**

agency without communicating with the Sponsor beforehand to assure accuracy and completeness of the information.

For DDs, the principal investigator shall:

- report to the sponsor, without unjustified delay, all serious adverse events and device deficiencies that could have led to a serious adverse device effect and documented in the AE CRFs as noted above,
- report to the IRB/EC device deficiencies that could have led to a serious adverse device effect, if required by the national regulations or by the IRB,
- report to regulatory authorities device deficiencies that could have led to a serious adverse device effect, as required by the national regulations, and
- supply the sponsor, upon sponsor's request, with any additional information related to the safety reporting of a particular event.

Device deficiencies that did not lead to an adverse event but could have led to a medical occurrence:

a) if either suitable action had not been taken,
b) if intervention had not been made, or
c) if circumstances had been less fortunate,

shall be reported as specified as stated below.

Device deficiencies shall be managed by the sponsor in accordance with written procedures for the control of non-conforming product. The sponsor shall take appropriate corrective and preventive actions to protect the safety of subjects, users and other persons.

For DDs, the sponsor shall:

- report or ensure the reporting, to the IRB by the principal investigator(s), of all serious adverse events and device deficiencies that could have led to a serious adverse device effect, if required by national regulations or by the IRB,
- report to regulatory authorities, within the required time period, all serious adverse events including serious health threat and device deficiencies that could have led to a serious adverse device effect, if required by national regulations or the CIP,
- report all relevant safety information to the DMC, if established, according to written procedures.

7.3.3 Regulatory Reporting and Timelines

- **Report by the Investigator to the Sponsor**

The sponsor shall implement and maintain a system to ensure that the reporting of the reportable events as defined under Section 7.2.1 Non-Reportable Event will be provided by the investigator to the sponsor immediately, but not later than 5 calendar days after investigation site study personnel's awareness of the event.

- **Report to the IRB**

Prior to initiation of the study, reporting requirements of AEs and DDs for the IRB will be verified and documented. Reporting will occur according to the requirements set forth by the involved IRB and/or national requirements.

8 Lost to follow up

A participant will be considered lost to follow up if not able to be contacted and/or not responsive. Site will conduct a due diligence attempt per site standard operating procedures. A person search vendor approved by the Sponsor may be utilized by the site to find latest contact information for subjects on an as needed basis (Sponsor remains blinded to this activity). The site will document these proceedings for local records and complete the Sponsor's Study Completion/Exit Form.

9 Data Management

9.1 Methods for data collection and data entry

An EDC system which is a 21 CFR Part 11-compliant data capture system with eCRF designed and the study database built will be used for the purposes of this clinical investigation. The data entered into the EDC system will be reviewed and cleaned. Queries will be issued to the site via the EDC system and are to be resolved by the investigator or his designee using the EDC system. An audit trail in the system is available for tracking all information including the site user enters, modifies, or deletes the study data and query resolution.

Data review and data cleaning will be completed on a regular basis. The study data will be reviewed and cleaned to ensure that there are no outstanding data discrepancies prior to database lock. Any changes to the database after that time will require written agreement by Integra LifeSciences Corporation.

A Data Management Plan is prepared to document precisely the procedures for the study database development, data review, data cleaning and query resolution.

9.2 Source Data Requirements

Data collection is the responsibility of the clinical trial staff at the site under the supervision of the site investigator. The investigator is responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported.

The investigator or its delegate will perform primary data collection drawn directly from the subject by use of an interview (either by phone or in-person) by the study coordinator, using a paper Case Report Form that the coordinator will fill out. Source data is defined as all information in original records, certified copies of original records of clinical findings, observations, or other activities in a clinical investigation, necessary for the reconstruction and evaluation of the clinical investigation. All source documents should be completed in a neat, legible manner to ensure accurate interpretation of data. In this study, the Case Report Form is a Source Document.

Clinical data (including adverse events (AEs) will be entered into EDC system, a 21 CFR Part 11-compliant data capture system, provided by the Sponsor. The data system includes password protection and internal quality checks, such as automatic range checks, to identify data that appear inconsistent, incomplete, or inaccurate. Clinical data will be entered directly from the source documents.

The investigator shall ensure the accuracy, completeness, legibility, and timelines of the data reported in CRF and in all required documentation. Data reported on the CRF shall be supported by the source documents with any discrepancies being explained. Any corrections made to documents will be done according to ISO 14155 guidelines. If an item is not available or is not applicable, this fact should be indicated; no space is to be left blank. The investigator who has signed the clinical investigation plan signature page or his/her authorized designee is to personally sign the CRFs to validate that the observations and findings are recorded on the eCRFs correctly and completely. The CRFs are to be completed in a timely manner after the subject's visit. Failure to meet the documentation requirements may lead to the disqualification of an investigator.

9.3 Confidentiality and Data privacy

Participant confidentiality and privacy is strictly held in trust by the participating investigator, their staff, and the sponsor(s) and their interventions. This confidentiality is extended to cover testing of biological samples and genetic tests in addition to the clinical information relating to participants. Therefore, the study protocol, documentation, data, and all other information

generated will be held in strict confidence. No information concerning the study or the data will be released to any unauthorized third party without prior written approval of the sponsor.

All research activities will be conducted in as private a setting as possible.

The study monitor, other authorized representatives of the sponsor, representatives of the Institutional Review Board (IRB), or regulatory agencies may inspect all documents and records required to be maintained by the investigator, including but not limited to, medical records (office, clinic, or hospital) and pharmacy records for the participants in this study. The clinical study site will permit access to such records.

The study participant's contact information will be securely stored at each clinical site for internal use during the study. At the end of the study, all records will continue to be kept in a secure location for as long a period as dictated by the reviewing IRB, Institutional policies, or sponsor requirements.

9.4 Study Record Retention

The Principal Investigator and Integra LifeSciences will maintain accurate, complete, and current records relating to participation in this study. If the Principal Investigator wishes to assign the responsibility of maintaining the study files to someone else or move them to another location, he/she should consult with Integra LifeSciences in writing regarding the change. The Principal Investigator will take measures to ensure that these essential documents are not accidentally damaged or destroyed.

Upon study completion, the investigator on one hand and Integra LifeSciences on the other hand will maintain all study records for the minimum time required by the US law and regulation and in accordance with 21 CFR 812, Subpart G.

10 Statistical Considerations

The detailed analyses methods will be described in the Statistical Analyses Plan (SAP).

10.1 Statistical Hypotheses

This is a prospective, single-arm, single center post-market study to capture existing clinical performance data to confirm the continued performance of the Gentrix® Surgical Matrix. A formal hypothesis does not apply to this study. Subjects from that consecutive series will be included in the study based on the defined inclusion and exclusion criteria.

Primary Endpoint(s):

The primary endpoint of this prospective study is to determine the incidence of clinically confirmed recurrence of the primary hernia to date, including not previously reported in T-GENVIH-002 study.

Secondary Endpoint(s):

1. Incidence of self-reported recurrence (i.e., bulge) of the primary hernia to date, including not previously reported in T-GENVIH-003 study.
2. Incidence of Surgical Site Occurrences requiring Procedural Intervention (SSOPI) of the primary hernia repair to date, including not previously reported in T-GENVIH-002.
3. Incidence of Surgical Site Occurrences (SSOs) of the primary hernia repair to date (seroma, abscess, dehiscence, hematoma, wound necrosis, ileus, fistula, delayed wound healing), including not previously reported in T-GENVIH-002 study.
4. Incidence of Surgical Site Infections (SSIs) post primary hernia repair to date, including not previously reported in GENVIH-002 study.
5. Incidence of reoperation requirement of the primary hernia repair to date, including not previously reported in GENVIH-002 study.

10.2 Sample Size Determination

Subjects from that consecutive series will be included in the study based on the defined inclusion and exclusion criteria. The planned sample size for this study will be approximately 21 treated subjects.

10.3 Populations for Analyses

Full Analysis Set (FAS): All subjects who enroll in the study, provide informed consent , and receive study intervention.

Per-Protocol (PP) Set: All subjects in the Full Analysis Set not identified as major protocol violations (defined to be protocol violations that may have a significant impact on subject outcomes, i.e., eligibility criteria not met). This population will be clearly defined prior to data analysis.

The primary analysis will be based on the full analysis set. The per-protocol set will be supportive and will be used to assess the robustness of study results. Safety analysis will be based on the full analysis set.

10.4 Statistical Analyses

10.4.1 General Approach

Descriptive statistics will be used to summarize study outcomes. For categorical data, frequency counts and percentages will be provided. For continuous data, descriptive statistics, including sample size, mean, median, standard deviation, and range of values (i.e., minimum and maximum values) will be provided.

All data collected in this study will be provided in subject data listings. Data collected in this study will be reported using summary tables and graphs as appropriate to the data. Descriptive summary statistics (n, mean, median, standard deviation, minimum and maximum) will be calculated for the continuous variables and/or frequencies and percentages will be produced for the categorical variables.

10.4.2 Measures to Minimize Bias: Randomization and Blinding

This study does not include a randomization or blinding component. When screening subjects for the study, the investigators or designee should offer participation to any/all patients who meet the inclusion and exclusion and who completed the prior T-GENVIH-002 study.

10.4.3 Analysis of the Primary Endpoint(s)

The primary endpoint for this study is descriptive statistics of clinically confirmed recurrence of the primary hernia to date, including not previously reported in T-GENVIH-002 study.

10.4.4 Analysis of the Secondary Endpoint(s)

Descriptive statistics will be provided for the following secondary endpoints:

1. Incidence of self-reported recurrence (i.e., bulge) of the primary hernia to date, including not previously reported in T-GENVIH-003 study.
2. Incidence of Surgical Site Occurrences requiring Procedural Intervention (SSOPI) of the primary hernia repair to date, including not previously reported in T-GENVIH-002.
3. Incidence of Surgical Site Occurrences (SSOs) of the primary hernia repair to date (seroma, abscess, dehiscence, hematoma, wound necrosis, ileus, fistula, delayed wound healing), including not previously reported in T-GENVIH-002 study.
4. Incidence of Surgical Site Infections (SSIs) post primary hernia repair to date, including not previously reported in GENVIH-002 study.
5. Incidence of reoperation requirement of the primary hernia repair to date, including not previously reported in GENVIH-002 study.

10.4.5 Safety Analyses

All AEs will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) and presented in by-subject listings. The number and percent of subjects experiencing any AE, any related AE, and discontinuations due to an AE will be tabulated. Treatment-emergent AEs will be tabulated (frequencies and percentages) by Preferred Term (PT) within System Organ Class (SOC). If a subject experiences more than one occurrence of the same AE, and these differ in severity and/or causality, the AE will be tabulated according to the greatest severity and nearest relationship to the device. Deaths and SAEs will be listed should they occur.

10.4.6 Baseline Descriptive Statistics

Nonapplicable.

10.4.7 Planned Interim Analyses

There is no planned Interim analysis.

10.4.8 Sub-Group Analyses

Subgroup analyses may be performed for surgical approach and type of the Gentrix Surgical Matrix used for cases of recurrence with reoperation post index procedure, if used.

10.4.9 Tabulation of Individual participant Data

All data collected in this study will be provided in subject data listings by study visit.

10.4.10 Sensitivity Analyses

All data will be analyzed as they were collected in the database. Missing data will not be imputed.

11 Regulatory, Ethical, Compliance and Operational Considerations

11.1 Informed Consent and Informed Consent Process

For this study, an IRB approved consent and consent process were used.

11.2 Protocol Amendment

Investigator may not modify (amend) this clinical investigation plan without obtaining written concurrence of the Sponsor, involved Ethics Committee(s), and applicable regulatory authorities.

11.3 Protocol Deviations

A Deviation is an Instance of failure to follow, intentionally or unintentionally, the requirements of the CIP. The investigator is not allowed a planned deviation from the CIP without first receiving approval in writing from the Sponsor.

Such deviations are documented on eCRFs and reported to the Sponsor as soon as possible.

11.4 Publication Policy

Integra LifeSciences Corporation may at any time publish the results of and information pertaining to the participating subject only to compliance with regulatory requirements pertaining to patient protected health information.

After closure of the clinical investigation, the results will be summarized in a Clinical Investigation Report, which will be submitted to the investigator and appropriate regulatory authorities. This Clinical Investigation Report will include a summary of the results based on a statistical evaluation and clinical assessment.

The conditions under which an investigator may publish results from this study in any form are defined in detail in the clinical trial agreement.

The clinical investigation will be registered in a publicly accessible database (www.clinicaltrials.gov) prior to start of recruitment, contents will be updated throughout study conduct and results will be entered at study completion.

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13 APPENDIX I

Table 3: List of 45Devices and SKU #

Device Name	Type:	SKU #	Size(s)
Gentrix® Surgical Matrix (6-Layer)	PSMX	PSMX0505	5cm x 5cm
		PSMX0710	7cm x 10cm
		PSMX1015	10cm x 15cm
Gentrix® Surgical Matrix Plus (8-Layer)	MSPL	MSPL0507	5cm x 7cm
		MSPL0710	7cm x 10cm
		MSPL1010	10cm x 10cm
		MSPL1015	10cm x 15cm
Gentrix® Surgical Matrix Thick	PSMT	PSMT1020	10cm x 20cm
		PSMT1620	16cm x 20cm
		PSMT2020	20cm x 20cm
		PSMT2025	20cm x 25cm
		PSMT2030	20cm x 30cm
		PSMT3030	30cm x 30cm
		PSMT3040	30cm x 40cm

Document History

SignNow E-Signature Audit Log

All dates expressed in DD-MON-YYYY (EU)

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Sender: andrew.tummon@integralife.com
Signers: david.sheleheda@integralife.com, dennis.young@integralife.com, nicole.kotter@integralife.com, karen.bartku@integralife.com, laurence.tong@integralife.com, weiwei.xu@integralife.com
CC: karen.bartku@integralife.com

Client	Event	By	Server Time	Client Time	IP Address
SignNow SSO	Uploaded the Document	andrew.tummon@integralife.com	03-Aug-2023 12:50:24 pm UTC	03-Aug-2023 12:50:18 pm UTC	50.228.64.126
SignNow SSO	Viewed the Document	andrew.tummon@integralife.com	03-Aug-2023 12:51:02 pm UTC	03-Aug-2023 12:51:02 pm UTC	50.228.64.126
SignNow SSO	Document Saved	andrew.tummon@integralife.com	03-Aug-2023 12:56:09 pm UTC	03-Aug-2023 12:56:09 pm UTC	50.228.64.126
SignNow SSO	Invite Sent to: david.sheleheda@integralife.com, dennis.young@integralife.com, nicole.kotter@integralife.com, karen.bartku@integralife.com, laurence.tong@integralife.com, weiwei.xu@integralife.com	andrew.tummon@integralife.com	03-Aug-2023 12:56:47 pm UTC	03-Aug-2023 12:56:46 pm UTC	50.228.64.126
SignNow SSO	Signer Authenticated Using Password	david.sheleheda@integralife.com	03-Aug-2023 13:27:36 pm UTC	03-Aug-2023 13:27:34 pm UTC	50.228.64.126
SignNow SSO	Viewed the Document	david.sheleheda@integralife.com	03-Aug-2023 13:27:41 pm UTC	03-Aug-2023 13:27:41 pm UTC	50.228.64.126
SignNow SSO	User logged in	david.sheleheda@integralife.com	03-Aug-2023 13:27:41 pm UTC	03-Aug-2023 13:27:41 pm UTC	50.228.64.126
SignNow SSO	Signed the Document, Signature ID: 50aafb085ee14fb6bf7d	david.sheleheda@integralife.com	03-Aug-2023 13:27:48 pm UTC	03-Aug-2023 13:27:48 pm UTC	50.228.64.126
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SignNow SSO	Signer Authenticated Using Password	karen.bartku@integralife.com	03-Aug-2023 13:46:20 pm UTC	03-Aug-2023 13:46:19 pm UTC	35.145.159.128
SignNow SSO	User logged in	karen.bartku@integralife.com	03-Aug-2023 13:46:36 pm UTC	03-Aug-2023 13:46:36 pm UTC	35.145.159.128
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SignNow SSO	Document Saved	karen.bartku@integralife.com	03-Aug-2023 13:46:47 pm UTC	03-Aug-2023 13:46:46 pm UTC	35.145.159.128
SignNow SSO	Signed the Document, Signature ID: c8f4539756a84c85bc20	karen.bartku@integralife.com	03-Aug-2023 13:46:47 pm UTC	03-Aug-2023 13:46:46 pm UTC	35.145.159.128
SignNow SSO	Signer Authenticated Using Password	karen.bartku@integralife.com	03-Aug-2023 13:47:46 pm UTC	03-Aug-2023 13:47:45 pm UTC	35.145.159.128
SignNow SSO	Viewed the Document	karen.bartku@integralife.com	03-Aug-2023 13:47:54 pm UTC	03-Aug-2023 13:47:54 pm UTC	35.145.159.128
SignNow SSO	Signer Authenticated Using Password	weiwei.xu@integralife.com	03-Aug-2023 14:30:14 pm UTC	03-Aug-2023 14:30:11 pm UTC	50.216.153.100
SignNow SSO	Viewed the Document	weiwei.xu@integralife.com	03-Aug-2023 14:30:38 pm UTC	03-Aug-2023 14:30:35 pm UTC	50.216.153.100
SignNow SSO	User logged in	weiwei.xu@integralife.com	03-Aug-2023 14:30:39 pm UTC	03-Aug-2023 14:30:36 pm UTC	50.216.153.100
SignNow SSO	Signed the Document, Signature ID: 29a94f3dde8541898447	weiwei.xu@integralife.com	03-Aug-2023 14:30:59 pm UTC	03-Aug-2023 14:30:57 pm UTC	50.216.153.100
SignNow SSO	Document Saved	weiwei.xu@integralife.com	03-Aug-2023 14:31:00 pm UTC	03-Aug-2023 14:30:57 pm UTC	50.216.153.100
SignNow SSO	Signer Authenticated Using Password	dennis.young@integralife.com	04-Aug-2023 12:56:49 pm UTC	04-Aug-2023 12:56:48 pm UTC	162.207.160.114
SignNow SSO	User logged in	dennis.young@integralife.com	04-Aug-2023 12:57:01 pm UTC	04-Aug-2023 12:57:01 pm UTC	162.207.160.114
SignNow SSO	Viewed the Document	dennis.young@integralife.com	04-Aug-2023 12:57:01 pm UTC	04-Aug-2023 12:57:01 pm UTC	162.207.160.114
SignNow SSO	Document Saved	dennis.young@integralife.com	04-Aug-2023 12:58:42 pm UTC	04-Aug-2023 12:58:41 pm UTC	162.207.160.114
SignNow SSO	Signed the Document, Signature ID: ca4e2febb8cb4a238367	dennis.young@integralife.com	04-Aug-2023 12:58:42 pm UTC	04-Aug-2023 12:58:41 pm UTC	162.207.160.114
SignNow SSO	Resent invite for the Document	andrew.tummon@integralife.com	04-Aug-2023 16:34:44 pm UTC	04-Aug-2023 16:34:43 pm UTC	50.228.64.126
SignNow SSO	Signer Authenticated Using Password	laurence.tong@integralife.com	04-Aug-2023 16:35:02 pm UTC	04-Aug-2023 16:35:02 pm UTC	50.228.64.126
SignNow SSO	User logged in	laurence.tong@integralife.com	04-Aug-2023 16:35:12 pm UTC	04-Aug-2023 16:35:12 pm UTC	50.228.64.126
SignNow SSO	Viewed the Document	laurence.tong@integralife.com	04-Aug-2023 16:35:12 pm UTC	04-Aug-2023 16:35:12 pm UTC	50.228.64.126
SignNow SSO	Signed the Document, Signature ID: cf015d6c9cd94b5297f8	laurence.tong@integralife.com	04-Aug-2023 16:36:54 pm UTC	04-Aug-2023 16:36:53 pm UTC	50.228.64.126
SignNow SSO	Document Saved	laurence.tong@integralife.com	04-Aug-2023 16:36:54 pm UTC	04-Aug-2023 16:36:53 pm UTC	50.228.64.126
SignNow SSO	Signer Authenticated Using Password	laurence.tong@integralife.com	04-Aug-2023 17:43:46 pm UTC	04-Aug-2023 17:43:45 pm UTC	98.223.176.152
SignNow SSO	Signer Authenticated Using Password	nicole.kotter@integralife.com	07-Aug-2023 16:20:48 pm UTC	07-Aug-2023 16:20:47 pm UTC	50.228.64.126
SignNow SSO	Viewed the Document	nicole.kotter@integralife.com	07-Aug-2023 16:20:55 pm UTC	07-Aug-2023 16:20:55 pm UTC	50.228.64.126
SignNow SSO	User logged in	nicole.kotter@integralife.com	07-Aug-2023 16:20:55 pm UTC	07-Aug-2023 16:20:55 pm UTC	50.228.64.126

SignNow SSO	Signed the Document, Signature ID: 1af883a482834d308ae2	nicole.kotter@integralife.com	07-Aug-2023 16:27:26 pm UTC	07-Aug-2023 16:27:25 pm UTC	50.228.64.126
SignNow SSO	Document Saved	nicole.kotter@integralife.com	07-Aug-2023 16:27:27 pm UTC	07-Aug-2023 16:27:25 pm UTC	50.228.64.126