Medtronic

Clinical Investigation Plan

Clinical Investigation Plan/Study Title	**POETRY Study - PrOGrip™ Self-gripping Polyester Mesh Prospective Embedded REgisTRY for Abdominal Wall Sutureline Reinforcement in Patients Undergoing Midline Laparotomy to Prevent Incisional Hernia**
Clinical Investigation Plan Identifier	MDT17048POETRY
Study Product Name	ProGrip™ Self-gripping Polyester Mesh
Sponsor	Medtronic, Covidien LP, MITG Surgical Innovations 555 Long Wharf Drive New Haven, CT 06511 USA
Local Sponsor	Medtronic, Sofradim Production 116 avenue du Formans 01600 Trevoux France
Document Version	4.0
Version Date	25 Sep 2020
Lead Principal Investigator(s)	[redacted]

Confidentiality Statement

[redacted]

Covidien LP and Sofradim Production are indirect wholly owned subsidiary of Medtronic plc

1. Investigator Commitment

Study product Name	ProGrip™ Self-gripping Polyester Mesh
Sponsor	Medtronic, Covidien LP, MITG Surgical Innovations 555 Long Wharf Drive New Haven, CT 06511 USA
Local Sponsor	Medtronic, Sofradim Production 116 avenue du Formans 01600 Trevoux, France
Clinical Investigation Plan Identifier	MDT17048POETRY
Version Number/Date	4.0 – 25 Sep 2020
I have read the protocol, including all appendices, and I agree that it contains all necessary details for me and my staff to conduct this study as described. I will conduct this study as outlined herein and will make a reasonable effort to complete the study within the time designated. I agree to comply with International Conference on Harmonization Guidelines on Good Clinical Practice and ISO 14155:2020. I agree to ensure that the confidential information contained in this document will not be used for any purpose other than the evaluation and conduct of the clinical investigation without the prior written consent of Medtronic. I will provide all study personnel under my supervision copies of the protocol and access to all information provided by Medtronic. I will discuss this material with them to ensure that they are fully informed about the products and the study.	
Investigator's Signature:	
Investigator's Name:	
Institution:	
Date:	

2. Table of Contents

3. Glossary

Term	Definition
ADE	Adverse Device Effect
AE	Adverse Event
ASA	American Society of Anesthesiologists
ASADE	Anticipated Serious Adverse Device Effect
BMI	Body Mass Index (kg/m^2)
CA	Competent Authority
CI	Confidence Interval
CIP	Clinical Investigation Plan
CNIL	Commission Nationale de l'Informatique et des Libertés
CRF	Case Report Form
CTA	Clinical Trial Agreement
CV	Curriculum Vitae
DD	Device Deficiency
DoH	Declaration of Helsinki
EC	Ethics Committee
EU MDR	European Medical Device Regulation
FD	Financial Disclosure
FDA	Food and Drug Administration
FDAAA	Food and Drug Administration Amendments Act
GCP	Good Clinical Practice
Hernia	A clinically manifested bulge or a protrusion exacerbated by a Valsalva maneuver.

Term	Definition
IC	Informed Consent
ICH	International Conference of Harmonization
ICJME	International Committee of Medical Journal Editors
IFU	Instructions For Use
MedDRA	Medical Dictionary for Regulatory Activities
PMCF	Post-Market Clinical Follow-up
QoL	Quality of Life
RA	Regulatory Authority
QOL	Quality of Life
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SSI	Surgical Site Infection
U(S)ADE	Unanticipated (Serious) Adverse Device Effect
VAS	Visual Analog Scale - a psychometric response scale (0-10) which can be used in questionnaires to determine how much pain a subject is feeling.

4. Synopsis

Title	**Poetry Study - PrOGrip™ Self-gripping Polyester Mesh Prospective Embedded REgisTRY for Abdominal Wall Suture Line Reinforcement in Patients Undergoing Midline Laparotomy to Prevent Incisional Hernia**
Clinical Study Type	Post-Market Clinical Follow-up (PMCF) interventional study
Product Name	ProGrip™ Self-gripping Polyester Mesh
Sponsor	Medtronic, Covidien LP, MITG Surgical Innovations 555 Long Wharf Drive New Haven, CT 06511 USA
Local Sponsor	Medtronic, Sofradim Production 116 avenue du Formans 01600 Trevoux, France
External Organizations	Club Hernie - CRO 8 allée Mozart 92190 Meudon, France
Indication under investigation	Reinforcement of abdominal suture line / Incisional hernia prevention
Investigation Purpose	To confirm the efficacy and safety of ProGrip™ Self-gripping Polyester Mesh for suture line reinforcement to reduce the incisional hernia incidence within 24 months after midline laparotomy.
Product Status	ProGrip™ Self-gripping Polyester Mesh is a CE-Mark cleared device.
Primary Objective	The primary objective of this investigation is to confirm the efficacy of ProGrip™ Self-gripping Polyester Mesh to reduce the incidence of incisional hernia within 24 months post-operatively in subjects undergoing procedures with midline laparotomies.
Secondary Objective	The secondary objective of this investigation is to confirm the safety of ProGrip™ Self-gripping Polyester Mesh through the occurrence of adverse device effects or procedure related adverse events following the use of ProGrip™ Self- gripping Polyester Mesh in subjects undergoing procedures with midline laparotomies.
Primary Endpoint	Incisional hernia rate within 24 months of midline laparotomy assessed by CT-scan and physical examination including hernia clinical examination.
Secondary Endpoints	▪ AE incidence reported by number, seriousness, and relationship to the procedure and device from the surgery to the 24-month visit ▪ Time to incisional hernia occurrence ▪ Post-operative pain at the site of surgery

	▪ Club Hernie Registry Quality of Life Questionnaire ▪ Patient satisfaction ▪ Surgeon satisfaction via questionnaire
Study Design	Prospective embedded registry study capturing outcomes after use of ProGrip™ Self-gripping Polyester mesh This study is a prospective, multicenter, PMCF embedded registry study evaluating the use of the ProGrip™ Self-gripping Polyester Mesh in subjects undergoing midline laparotomy in order to prevent incisional hernia using the embedded registry data of Club Hernie in France. The Club Hernie is a non-profit organization created in 2009, currently including 40 permanent French surgeon members, with the aim to improve the healthcare treatments in parietal surgery by an assessment of surgical practices, promoting research in abdominal wall surgery using an internet database open to surgeon members to monitor their own hernia practice and outcomes. This study utilizes the Club Hernie established registry database. This online database consists of systematic and consecutive data entry of all subjects treated for abdominal wall surgery with standard data capture of all preoperative, perioperative and post-operative data. Subjects who meet the eligibility criteria will be considered for study participation and will be evaluated at screening/baseline, procedure, Day 1, discharge, Day 8, and 1, 12, and 24 months post-surgery. The planned enrollment period is 22 months in up to 12 sites in France. For this study select Club Hernie permanent members, non-permanent and new members are considered for participation. The planned follow-up period is 24 months after the last subject enrolled
Sample Size	At least 135 subjects may be enrolled in up to 12 French study sites using the embedded registry data of Club Hernie.
Inclusion/Exclusion Criteria	**Inclusion Criteria** **Subjects are eligible to be enrolled in the study only if they meet all of the following criteria:** 1. Subject has provided informed consent. 2. Subject is ≥ 18 years of age at the time of consent.

	3. Subject will be undergoing an elective midline laparotomy. 4. Subject may have a combination of low- and high-risk factors but cannot exceed a total of 5 risk factors or have more than 2 high-risk factors. Subject must have at least 2 low-risk factors if subject does not have any high-risk factors. High- and low-risk factors include: a. High-Risk Factors (maximum of 2): i. BMI ≥ 35 ii. Prior open abdominal surgery iii. Daily active smoker or Chronic Obstructive Pulmonary disease (COPD) diagnosis iv. Current or recent (within 1 year) cancer diagnosis or chemotherapy treatment v. History of or current abdominal aorta aneurism or surgery for abdominal aorta aneurism b. Low-Risk Factors (minimum of 2, if no high-risk factors): i. 25 ≤ BMI < 35 ii. Age > 45 iii. Uncontrolled diabetes iv. Malnutrition as defined by 10% weight loss within the last 3 months v. Current immunosuppressive treatment vi. Undergoing colorectal surgery **Exclusion Criteria** **Subjects will be excluded from enrollment in the study if they meet any of the following criteria:** 1. Subject is undergoing emergency surgery, i.e. lifesaving procedures performed where subject is in imminent danger of death. 2. Subject for which the device is used outside the product IFU, including; a. Pregnant women: Women who are known or suspected to be pregnant, or who are planning to become pregnant during the study follow-up period b. Subject who has an infection within 30 days of enrollment or, at the time of the surgery, has any active, acute or chronic infection(s) that are uncontrolled and/or requiring treatment such as antibiotics c. Subject whose surgical site is contaminated or

	dirty/infected intraoperatively, as assessed by the Investigator (Exclude Altemeier classification III-IV). 3. Subject who had received a mesh in a previous ventral hernia repair or has a ventral hernia. 4. Investigator determined that a planned future surgery would interfere with application of mesh reinforcement. 5. Subject has participated in an investigational drug or device research study within 30 days of enrollment. 6. Subject has a life expectancy of <2 years. 7. Subject has an ASA Physical Status Classification System score >3. 8. Subject has >5 total risk factors or >2 high-risk factors
Study Procedures and Assessments	Subjects will be evaluated at baseline/screening, during the procedure, at day 1, at discharge, day 8, 1 Month, 12 Months, and 24 Months post-surgery. Assessments to be conducted/data collected include: **Preoperative data (Day -30 to 0)** ▪ Informed consent ▪ Eligibility assessment ▪ Demographic data (age, gender, ASA score, BMI, subject's ▪ occupation) ▪ Relevant prior medical/surgical history (previous surgical ▪ procedure) ▪ Serum or urine pregnancy test, for female subjects (unless the patient is surgically sterile or postmenopausal for at least two years). **Operative data (Day 0)** ▪ Date of surgery ▪ Indication of the procedure ▪ Surgical technique for laparotomy closure (closure technique ▪ and type of suture) ▪ Mesh reference (TMP1509G, TMP1515G, TMP2015G, TMP3015G, TMP1008G, TMP2008G, TMP3008G, TMP4008G) and lot number ▪ Type of fixation ▪ Operative time (from incision to closure, skin to skin), ▪ Mesh positioning and time ▪ Peri-operative events including adverse device effects or procedure related adverse events ▪ Surgeon satisfaction (Mesh handling, mesh manipulability, ease of use) **Post-operative course (Day 0) Follow up** ▪ Post-operative pain assessment measured utilizing a 0-10

	▪ Visual Analog Scale (VAS) (Worst pain experienced over the last 24 hours). **Post-operative course (Day 1) Follow up** ▪ Pain assessment measured with VAS score ▪ Post-operative adverse events (including adverse device effects or procedure related adverse events: SSI, hematoma, seroma, etc.) Data will be recorded in the discharge data **Discharge data** ▪ Date of discharge ▪ Length of Hospital stay (number of nights in the institution after the surgery) ▪ Post-operative adverse events (including adverse device effects or procedure related adverse events: SSI, hematoma, seroma, etc.). **Post-operative course (Day 8, +/- 2days) Follow up** ▪ Pain assessment measured with VAS score, either during systematic clinical visit or by phone call when a subject is already discharged. **1 month (Day 30, +/- 1week) Follow up** ▪ Pain assessment measured with VAS score ▪ Physical exam including hernia clinical examination ▪ Post-operative adverse events (including adverse device effects or procedure related adverse events). ▪ Club Hernie Registry Quality of Life (QoL) Questionnaire **12 months (-1/+4weeks) Follow up** ▪ Physical exam including hernia clinical examination ▪ Abdominal CT-Scan ▪ Post-operative adverse events (including adverse device effects or procedure related adverse events) ▪ Club Hernie Registry QoL questionnaire and patient satisfaction ▪ Pain assessment measured with VAS score NOTE: 1 Month prior, all subject will be contacted by phone in order to complete a self-assessment questionnaire and to remind them of the 1-year follow-up visit. **24 months (-1/+4weeks) Follow up** ▪ Physical exam including hernia clinical examination ▪ Abdominal CT-Scan ▪ Post-operative adverse events (including adverse device effects or procedure related adverse events) ▪ Club Hernie Registry QoL questionnaire and patient satisfaction ▪ Pain assessment measured with VAS score

	NOTE: 1 Month prior, all subjects will be contacted by phone in order to complete a self-assessment questionnaire and to remind them of the 2-year follow-up visit
Safety Assessments	The incidence of AEs related to device and/or procedure will be recorded from the surgery through the 24 months post-operative follow-up. The data will be analyzed in the Safety Analysis Set.
Statistics	**Sample size determination** Sample size is determined based on primary performance endpoint assuming the superiority of ProGrip™ Self-gripping Polyester Mesh use to prevent incisional hernia vs no prevention of incisional hernia within 2-years following a midline laparotomy procedure. The literature review showed an incisional hernia rate after midline laparotomies around 20%. Using a power (1-β) of 80% and a 5% error type I (two-sided) and considering a hypothetic incisional hernia rate of 10% for subjects with ProGrip™ Self-gripping Polyester Mesh, versus a theoretical hypothetic incisional hernia rate of 20% for subjects without any prevention following a midline laparotomy procedure, N= 108 evaluable subjects are required. Assuming an attrition rate of 20% at 2-years, N=135 subjects will need to be enrolled. **Statistical method** <u>Primary endpoint</u> Statistical analysis of primary endpoint will be comparative. Binomial one-way test will be used to compare the observed ProGrip™ Self gripping Polyester Mesh incisional hernia incidence rate to the 20% theoretical incidence rate (from no prevention population), using a two- sided alpha-level of 5%. Other endpoints will be analyzed using descriptive methods: ▪ Qualitative variables will be described by their absolute and relative (%) frequencies of each class or value, and by two tailed 95% confidence intervals. ▪ Quantitative variables will be described by their mean, standard deviation (SD), extreme values (minimum and maximum values), and number of missing data and by two tailed 95% confidence intervals. <u>Performance analyses will be run on:</u> ▪ Performance Analysis Set includes all enrolled subjects excluding subjects who became pregnant during the follow-

	up, or subjects who undergo unscheduled abdominal surgery during study follow-up, which may increase the risk and cause of incisional hernia occurrence*. *Subject follow-up data, starting from the event's occurrence, will be excluded/remove from the performance analysis. ▪ Per Protocol Analysis Set (PPAS) is a subset of PAS excluding subjects with protocol violation and major protocol deviation(s) that may impact the primary endpoint assessment. More precisely, reason for exclusion may include but is not limited to: ▪ Patient wrongly included (i.e. patient was enrolled but does not meet all the eligibility criteria). ▪ Failure to obtain informed consent. ▪ Deviation resulting from device use outside the recommended use in the IFU. ▪ Patient who receives the incorrect device or device is misused. <u>Safety analyses will be run on:</u> ▪ Safety Analysis Set includes all enrolled subjects. <u>Interim Analysis</u> After half the enrolled subjects complete the 1-year follow-up timepoint, an interim analysis will be conducted for regulatory purposes. An additional interim analysis for regulatory needs may also be conducted as needed.

5. Introduction

5.1. Background

Although laparoscopic minimally invasive surgeries have increased in frequency, midline laparotomies are still common in both elective and emergency cases. After midline laparotomy, the prevalence of incisional hernias ranges between 10% and 54% depending on if the procedure was elective or emergency (1-3). The presence of an incisional hernia can lead to complications such as bowel obstruction, incarceration, strangulation, and/or patient discomfort and pain (4). Repair of incisional hernias requires additional procedure adding additional risk to the patient and finical costs. As a result, prevention of incisional hernias has become a common goal and in recent years, multiple studies have shown decreased frequency of incisional hernias when using prophylactic polypropylene mesh after midline laparotomies.

To that end, based on the extensive long-term data attained during the development of multiple surgical meshes for use in a variety of soft tissue repairs, Medtronic has developed the ProGrip™ self-gripping polyester mesh. Composed of knitted monofilament polyester with polylactic acid monofilament resorbable pins ProGrip™ self-gripping polyester mesh is intended for use in reinforcement of soft tissue where weakness exists, in procedures involving the repair of inguinal and incisional hernias or abdominal suture line reinforcement.

Medtronic has conducted a biocompatibility evaluation of ProGrip™ self-gripping polyester mesh, compliant with the standard EN ISO 10993-1 (2009), which demonstrates the biological safety of the device. Pre-clinical animal testing of ProGrip™ self-gripping polyester mesh demonstrates that the mesh shows the same inflammatory reaction as Parietex™ mesh, similar gripping power to ProGrip™ self-gripping polypropylene mesh and contributes to the fixation of the mesh to the surrounding tissues better than Parietex™ mesh. Along with this data, ProGrip™ Self Gripping Polyester has been available for use in inguinal and incisional hernia repair since 2008 and the available data support a positive risk/benefit ratio for the device.

5.2. Purpose

Medtronic is sponsoring the POETRY study, a multi-site, prospective registry-embedded, post-market clinical follow up interventional study. The purpose of this study is to confirm the efficacy and safety of ProGrip™ Self-gripping Polyester Mesh for suture line reinforcement to reduce the incisional hernia incidence within 24 months in a minimum of 135 enrolled subjects undergoing procedures with midline laparotomies.

6. Objectives and Endpoints

6.1. Objectives

6.1.1. Primary Objective

The primary objective of this investigation is to confirm the efficacy of ProGrip™ Self-gripping Polyester Mesh to reduce the incidence of incisional hernia within 24 months post-operatively in subjects undergoing procedure with midline laparotomies.

6.1.2. Secondary Objective

The secondary objective of this investigation is to confirm the safety of ProGrip™ Self-gripping Polyester Mesh through the occurrence of adverse device effects or procedure related adverse events following the

use of ProGrip™ Self-gripping Polyester Mesh in subjects undergoing procedures with midline laparotomies.

6.2. Endpoints

6.2.1. Primary Endpoint

The primary endpoint is the incisional hernia incidence rate within 24 months of midline laparotomy assessed by CT-scan and physical examination including hernia clinical examination. CT scan is one of the medical imagery exams that are used to confirm the incisional hernia. A confirmation to the clinical assessment is essential in order to not miss any incisional hernia occurrence. CT scans are already part of the standard of care follow-up for the patient undergoing colorectal procedures. To avoid an additional imagery procedure for those patients and homogenize the type of imagery for the other patients, all the patients will have a CT scan.

6.2.2. Secondary Endpoints

The following secondary endpoints will be assessed;

- Adverse event (AE) incidence reported by number, seriousness, and relationship to the procedure and device from the surgery to the 24-month visit
- Time to incisional hernia occurrence
- Post-operative pain at the site of surgery
- Club Hernie Registry Quality of Life Questionnaire
- Patient satisfaction
- Surgeon satisfaction via questionnaire

7. Study Design

This study is a prospective, multicenter, PMCF embedded registry study evaluating the use of the ProGrip™ Self-gripping Polyester Mesh in subjects undergoing midline laparotomy in order to prevent incisional hernia using the embedded registry data of Club Hernie in France. ProGrip™ Self-gripping Polyester Mesh is a CE-Mark cleared device.

The study is expected to be conducted at up to 12 study sites located in France and at least 135 subjects will be enrolled in the study. To ensure a widespread distribution of data and minimize study site bias in study results, the maximum number of subjects to be enrolled at a single study site is 25 subjects.

The Club Hernie is a non-profit organization created in 2009, currently including 40 French surgeon permanent members, with the aim to improve the healthcare treatments in parietal surgery by an

assessment of surgical practices, promoting research in abdominal wall surgery using an internet database open to surgeon members to monitor their own hernia practice and outcomes.

This study utilizes the Club Hernie established registry database. This online database consists of systematic and consecutive data entry of all patients treated for abdominal wall surgery with standard data captured of all preoperative, perioperative and post-operative data.

Out of the Club Hernie patient population, patients who meet the eligibility criteria will be considered for study participation and will sign the informed consent form and will be evaluated at screening/baseline. After the informed consent has been signed and the mesh has been implanted, the subject is considered enrolled, and they will also be evaluated at procedure, Day 1, discharge, Day 8, and 1, 12, and 24 months post-surgery. Enrollment period planned is 22 months in up to 12 sites in France. For this study Club Hernie select permanent members, non-permanent and new members are considered for participation. Subjects that withdraw or are lost to follow-up will not be replaced. Full details of subject exit, withdrawal, or discontinuation can be found in Section 11.13.

7.1. Duration

The expected total study duration is approximately 52 months, representing 28 months enrollment and 24 months of follow-up. Screening for subject eligibility may occur up to 30 days (inclusive) prior to the procedure and post-procedure subjects will be assessed at Day 1, discharge, Day 8, and 1, 12, and 24 months post-surgery. At least 135 subjects will participate in the study for a maximum of approximately 26 months.

7.2. Rationale

ProGrip™ Self-gripping Polyester Mesh is a CE-Mark cleared device for abdominal suture line reinforcement since January 2018.

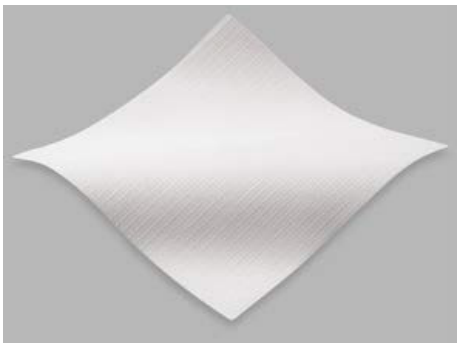
To confirm the efficacy and safety of ProGrip™ Self-gripping Polyester Mesh for suture line reinforcement to reduce the incisional hernia Medtronic is performing an embedded registry study. Following use of ProGrip™ Self-gripping Polyester Mesh, incisional hernia rate and adverse event rates will be followed for 24 months. Currently there are no known factors (apart from those identified in the IFU) that may compromise study outcomes or the interpretation of results (e.g., baseline characteristics, the use of other study products, or subject-related factors such as age, gender or lifestyle). If any adverse device effect occurrences are identified they will be assessed, reported and documented in the Club Hernie Registry Database as well as in the AE report form. As a single arm safety study, no comparator device will be used.

7.3 Study Oversight

The Steering Committee will consist of select Investigators participating in this study, Club Hernie leadership, as well as appropriate members of Medtronic Clinical and Medical Affairs. The role of the Steering Committee is to make recommendations on the design and conduct of the study, the analysis of data, and the communication of results in alignment with the Medtronic Publication and Authorship Policy. The Steering Committee will also review aggregate adverse event data on an as needed basis, as described in the Steering Committee Charter.

8. Product Description

ProGrip™ self-gripping polyester mesh is made of knitted monofilament polyester with polylactic acid monofilament resorbable pins on one of the sides. These pins facilitate placing, positioning and fixation of the mesh to the surrounding tissue. The monofilament polylactic acid pins are bioresorbable and contribute to the fixation of the mesh to surrounding tissue during at least 8 weeks. The polylactic acid pins degrade and resorb in vivo by hydrolysis and are metabolized by the body into carbon dioxide (CO_2) and water (H_2O). The mesh is available in different sizes of rectangular sheet.



TMP1509G: Rectangular 15 x 9 cm
TMP1515G: Rectangular 15 x 15 cm
TMP2015G: Rectangular 20 x 15 cm
TMP3015G: Rectangular 30 x 15 cm
TMP1008G: Rectangular 10 x 8 cm*
TMP2008G: Rectangular 20 x 8 cm*
TMP3008G: Rectangular 30 x 8 cm*
TMP4008G: Rectangular 40 x 8 cm*

Figure 1. ProGrip™ Self-Gripping Polyester Mesh (rectangular) and TMP Codes with sizes for this study
*Added to the study 25 Sep 2020

All materials that may be in contact with tissues and/or body fluids are presented in Table 1.

Table 1: Materials in contact with tissues and/or body fluids

ProGrip™ self-gripping polyester mesh components	Materials
Mesh	Monofilament polyester
Resorbable pins	Polylactic acid monofilament

This CE marked device will be used within intended use as described in the approved IFU for which CE mark has been obtained.

8.1. Manufacturer

ProGrip™ Self-Gripping Polyester Mesh is manufactured by Sofradim Production, (wholly owned subsidiary of Medtronic plc.) in Trévoux, France.

8.2. Packaging

The device is intended for single use only and is provided in an ethylene oxide sterilized package which includes an expiration date and lot number. A single (1) mesh is contained in each box.

8.3. Intended Population

ProGrip™ self-gripping polyester mesh is intended for use in reinforcement of soft tissue where weakness exists, in procedures involving abdominal suture line reinforcement. A thorough assessment of each patient's medical history and conditions shall be performed to determine the suitability for prophylactic mesh augmentation with ProGrip™ self-gripping polyester mesh in the prevention of incisional hernia.

8.4. Product Use

Full operating steps are described in the instructions for use (Appendix B, Section 19.2). Briefly,

- The device is designed to be implanted outside of the peritoneal cavity.
- This mesh can be used whole or cut to the required dimensions.
- In case of abdominal suture line reinforcement, the placement of the mesh should ensure necessary overlap of the weakness, according to the surgeon's practice.
- Only a single mesh should be used per subject.

Approximately 135 mesh devices (one per subject) of TMP1509G, TMP1515G, TMP2015G, TMP3015G, TMP1008G, TMP2008G, TMP3008G, or TMP4008G are expected to be used for the study.

8.5. Product Training Requirements

Each Investigator participating in the clinical study and the associated clinical study staff will receive training on ProGrip™ self-gripping polyester mesh, if necessary. Investigators and study staff will be trained on device characteristics, shelf life, storage requirements, device use, and warnings, precautions and contraindications.

For investigators who do not know ProGrip™ self-gripping polyester mesh prior to enrolling subjects, they must certify their understanding of the operative technique and anticipated complications associated with the use of this device by completing at least (1) case using the device.

8.6. Product Receipt and Tracking

ProGrip™ self-gripping polyester mesh will be provided to each site upon Sponsor collection and approval of all required regulatory documentation. The ProGrip™ self-gripping polyester mesh will be labeled "For MDT17048POETRY Clinical Investigation". Device accountability logs and clinical material shipment/return forms will be provided to the site. It is the site's responsibility to document the receipt (maintain material shipment/return forms), disposition of the product (per subject use, including amount used, amount remaining, etc.), transfer (if applicable) and return of all unopened study devices.

8.7. Product Storage

Once received at the study site, ProGrip™ self-gripping polyester mesh must be stored at room temperature in a secure (locked) location at the study site. Access should be limited to designated study staff only. It is the responsibility of the investigator to correctly handle and store market released product. These products will be used according to their labeling. The investigator shall make sure that all investigational devices will be stored in such a manner as to be easily identifiable. If the investigational device cannot be identified, the device shall not be used.

8.8. Product Return

All unused or expired ProGrip™ self-gripping polyester mesh should be returned to Medtronic within 30 days of the last subject enrolled at the site and it will be documented in the product accountability log and clinical material shipment/return form. If the products are explanted but not returned, a justification will be reported on the appropriate case report forms or disposition logs. To receive a Returned Product Mailer Kit, please contact your local Medtronic field personnel. Additionally, all products involved in a device deficiency and those removed from subjects should be returned to Medtronic as soon as reasonably possible.

8.9. Product Accountability

All products used in this study will be market released in the geographies they are used. Device Traceability may be required per local laws and regulations. If there are additional local requirements related to the ProGrip™ self-gripping polyester mesh beyond what is collected by Medtronic on the CRF, this is the Investigator's responsibility and should be recorded in the subject's medical records, but will not be collected by Medtronic (e.g., national registration card number, identification code linked to names and contact information, log of all subjects enrolled in the study, lot or batch number).

Medtronic will perform periodic reconciliation of the investigational product to ensure traceability.

9. Study Site Requirements

9.1 Investigator / Investigation Study Site Selection

All investigators managing the subject's hernia must be qualified practitioners. All implanting physicians must be experienced and/or trained in the handling of ProGrip™ self-gripping polyester mesh.

The role of the principal investigator is to implement and manage the day-to-day conduct of the clinical investigation as well as ensure data integrity and the rights, safety and well-being of the subjects involved in the clinical investigation.

The principal investigator shall:

- Be qualified by education, training, and experience to assume responsibility for the proper conduct of the clinical investigation
- Be experienced in the field of application and training in the use of ProGrip™ self-gripping polyester mesh
- Disclose potential conflicts of interest, that interfere with the conduct of the clinical investigation or interpretation of results
- Has the ability to comply with the applicable EC and regulatory requirements
- Is not disbarred, disqualified, or working under sanctions in applicable regions
- Be registered at the CNOM
- Be able to demonstrate that the proposed investigational study site:
    - Has adequate time and resources to conduct the study throughout the duration of the study
    - Has access to the required number of eligible subjects needed within the recruitment period
    - Has one or more qualified investigators, a qualified investigational study site team and adequate facilities for the foreseen duration of the clinical investigation
    - Has not had early termination and/or known instances of non-compliance from other clinical studies
    - Adequate study device storage location(s) and processes
    - Acceptable audit or inspection history
    - Acceptable anticipated study startup timeline
    - Lack of potential competition for the same subject population from other ongoing studies

Study site personnel training will be completed and documented prior to participation in this study.

9.2 Study Site Activation

During the activation process (prior to subject enrollment), Medtronic will train study site personnel on the clinical investigation plan, on relevant standards and regulations, informed consent, and on data

collection and reporting tools. If new members join the study site team, they will receive training on the applicable study requirements relevant to their role before contributing to the study.
Prior to performing study related activities, all regulatory requirements shall be fulfilled, including, but not limited to the following:

- EC approval (and voting list, as required by local law) of the current version of the CIP and IC.
- RA approval or notification (as required per local law)
- Fully executed CTA
- CV of investigators and key members of the investigation study site team (as required). The signature on the CV must be dated within 3 years prior to the date of activation of the study site.
- Documentation of delegated tasks
- Documentation of study training
- Additional requirements imposed by local regulations, the EC and RA shall be followed, if appropriate.

In addition, all participating study site staff must be trained on the current version of the CIP as well as on the applicable study requirements depending on their role and must be delegated by the principal investigator to perform study related activities.
Medtronic will provide each study site with documentation of study site/investigator readiness; this letter must be received prior to performing study related activities.

9.3 Role of the Sponsor Representatives

Sponsor representatives may provide support at the study site as required for the study under supervision of the Principal Investigator, including:

- Provide study training relevant and pertinent to the involvement of personnel conducting study activities and investigator responsibilities
- Technical support under the supervision of a study investigator, but no data entry, shall be performed by Medtronic personnel or their representatives at study sites
- Monitoring and auditing activities

In addition, for this study, sponsor representatives may be authorized by the Principal Investigator to perform the following significant trial related duties:

- Provide technical support to study investigators performing the study implant procedure

10. Selection of Subjects

10.1. Study Population

At least 135 subjects undergoing midline laparotomy may be enrolled in up to 12 sites in France using the embedded registry data of Club Hernie. Each site will be allowed to enroll between 1 and 25 subjects. To reduce bias, enrollment will not exceed 25 subjects per site. No randomization, or blinding will take place during the study.

10.2. Subject Enrollment

A subject is considered enrolled in the study when it is confirmed they meet all pre-operative inclusion and no exclusion criteria, the ICF is signed and they have been implanted with the device. A subject must be followed for the full 24 months if the procedure was begun or completed with the study device. No study procedures, or data collection will be performed until informed consent form has been completed.

10.3. Inclusion Criteria

Subjects are eligible to be enrolled in the study only if they meet all of the following criteria:

1. Subject has provided informed consent.
2. Subject is ≥ 18 years of age at the time of consent.
3. Subject will be undergoing an elective midline laparotomy.
4. Subject may have a combination of low- and high-risk factors but cannot exceed a total of 5 risk factors or have more than 2 high-risk factors. Subject must have at least 2 low-risk factors if subject does not have any high-risk factors. High- and low-risk factors include:
    a. High-Risk Factors (maximum of 2):
        i. BMI ≥ 35
        ii. Prior open abdominal surgery
        iii. Daily active smoker or Chronic Obstructive Pulmonary Disease (COPD) diagnosis
        iv. Current or recent (within 1 year) cancer diagnosis or chemotherapy treatment
        v. History of or current abdominal aorta aneurism or surgery for abdominal aorta aneurism
    b. Low-Risk Factors (minimum of 2, if no high-risk factors):
        i. 25 ≤ BMI < 35
        ii. Age > 45
        iii. Uncontrolled diabetes
        iv. Malnutrition as defined by 10% weight loss within the last 3 months
        v. Current immunosuppressive treatment
        vi. Colorectal surgery

10.4. Exclusion Criteria

Subjects will be excluded from enrollment in the study if they meet any of the following criteria:

1. Subject is undergoing emergency surgery, i.e. lifesaving procedures performed where subject is in imminent danger of death.
2. Subject for which the device is used outside the product IFU, including;
    a. Pregnant women: Women who are known or suspected to be pregnant, or who are planning to become pregnant during the study follow-up period
    b. Subject who has an infection within 30 days of enrollment or, or at the time of the surgery, has any active, acute or chronic infection(s) that are uncontrolled and/or requiring treatment such as antibiotics
    c. Subject whose surgical site is contaminated or dirty/infected intraoperativly, as assessed by the Investigator (Exclude Altemeier classification III-IV)
3. Subject who had received a mesh in a previous ventral hernia repair or has a ventral hernia.
4. Investigator determined that a planned future surgery would interfere with application of mesh reinforcement.
5. Subject has participated in an investigational drug or device research study within 30 days of enrollment.
6. Subject has a life expectancy of <2 years.
7. Subject has an ASA Physical Status Classification System score >3.
8. Subject has > 5 total risk factors or > 2 high-risk factors.

11. Study Procedures

11.1 Schedule of Events

Subjects will be evaluated at screening/baseline, procedure, Day 1, discharge, Day 8, and 1, 12, and 24 months post-surgery. Refer to Section 11.2 for procedure/assessments collected at each visit.

11.2 Data Collection

Table 2: Schedule of Events

Procedure/Assessment	Screening (Day -30 to 0)	Operative (Day 0)	Post-operative course (Day 0) Follow up	Post-operative course (Day 1) Follow up	Discharge Assessment	Post-operative course (Day 8, +/-2days) Follow Up	1 Month (Day 30, +/-1week) Follow-up	12 Months (-1/+4 weeks) Follow-up	24 Months (-1/+4 weeks) Follow-up
	Can be combined								
Eligibility criteria	X[1]	X[1]							
Informed consent	X[2]								
Pregnancy Test	X[3]								
Subject demographics	X								
Relevant prior medical/surgical history	X								
Surgical Data									
Date of surgery		X							
Procedure indication		X							
Surgical technique for laparotomy closure		X							
Mesh reference and lot number		X							
Type of fixation		X							
Operative time		X							

Procedure/Assessment	Screening (Day -30 to 0)	Operative (Day 0)	Post-operative course (Day 0) Follow up	Post-operative course (Day 1) Follow up	Discharge Assessment	Post-operative course (Day 8, +/-2days) Follow Up	1 Month (Day 30, +/-1week) Follow-up	12 Months (-1/+4 weeks) Follow-up	24 Months (-1/+4 weeks) Follow-up
	Can be combined								
Mesh positioning and time		X							
Peri-operative events (including adverse device effects or procedure related adverse events)		X							
Surgeon satisfaction		X							
Post-operative data									
AE, SAE, & DD Data			X	X	X	X	X	X	X
VAS pain assessment[4]			X	X		X	X	X	X
Post-operative adverse events				X	X		X	X	X
Date of discharge					X				
Length of Hospital stay					X				
Physical exam including hernia clinical examination[4]							X	X	X
Abdominal CT Scan[4]								X	X
Quality of Life Questionnaire[4]							X	X	X
Patient Satisfaction[4]								X	X
1-month prior phone call including self-assessments[4]								X	X
Study Exit									X

1. If Screening and Surgery occur on different days, these procedures should occur during Screening and be reconfirmed on the day of surgery.
2. No study procedures will be performed until informed consent form has been completed. Subject should be re-consented if date of original consent is greater than 30 days.
3. Serum or urine pregnancy test for female subjects (unless the patient is surgically sterile or postmenopausal for at least two years).
4. These procedures/assessments may not be considered standard of care based upon local standards or index procedure type

11.3 Scheduled Follow-up Visit Windows

Should a subject miss a visit or the visit fall outside the pre-specified window, a study deviation must be reported, and the original follow-up schedule maintained for subsequent visits.

Data analyses include follow-up visits, regardless of whether the visit occurs within the window. Therefore, a late visit is preferred over a missed visit but must be accompanied by a deviation report. Follow-up visit windows are listed in Table 3 and are based on days post-operative.

Table 3: Data collection and study procedure requirements at subject visits

Study Follow-up Visit	Window (Calculated days post-operative)		
	Window Start (post-implant)	Target (post-implant)	Window End (post-implant)
Follow-up 1	Day 6	Day 8	Day 10
Follow-up 2	Day 23	Day 30	Day 37
Follow-up 3	11 Months, 3 Weeks	12 Months	13 Months
Follow-up 4	23 Months, 3 Weeks	24 Months	25 Months

11.4 Subject Screening

A screening visit will be used to confirm pre-operative eligibility and consent subjects. Subjects will be consented prior any procedures specific to the study are undertaken. The purpose and all aspects of the study will be explained to the subject. Subjects who agree to study participation must sign and personally date the sponsor and an EC-approved informed consent form prior to participating in any study activities.

Once the consent process has been completed, pre-operative eligibility has been confirmed, the following data will be collected:

- Demographic data (e.g. age, gender, ASA score, BMI, subject's occupation)
- Relevant prior medical/surgical history (e.g. previous surgical procedure)
- Serum or urine pregnancy test, for female subjects (unless the patient is surgically sterile or postmenopausal for at least two years).

The screening visit will be performed within 30 days up to the day of the scheduled procedure and may be combined with the surgery procedure visit. If screening and/or ICF signature occur more than 30 days before the procedure the subject is to be rescreened and reconsented.

11.5 Subject Consent

Informed consent is defined as a legally effective documented confirmation of a subject's voluntary agreement to participate in a particular study after information has been given and explained to the subject on all aspects of the study that are relevant to the subject's decision to participate. This process includes obtaining an IC form that has been approved by the study site's EC and signed and dated by the subject. A subject may only consent after information has been given and explained to the subject on all aspects of the clinical investigation that are relevant to the subject's decision to participate.

Prior to enrolling subjects, the IC site must be approved by the EC. The document(s) must be controlled (i.e. versioned and/or dated) to ensure it is clear which version(s) were approved by the EC. Any adaptation of the sample IC must be reviewed and approved by Medtronic and the EC reviewing the application prior to enrolling subjects.

The investigator must notify the subject of any significant new findings about the study that become available during the course of the study which are pertinent to the safety and well-being of the subject, as this could impact a subject's willingness to participate in the study. If relevant, consent may be requested from subjects to confirm their continued participation.

Prior to initiation of any study-specific procedures, IC must be obtained from the subject. Likewise, privacy or health information protection regulation may require subjects to sign additional forms to authorize study sites to submit subject information to the study sponsor. The IC process must be conducted by the principal investigator or an authorized designee, and the IC Form and must be given to the subject in a language he/she is able to read and understand. The process of IC must be conducted without using coercion or undue improper influence on or inducement of the subject to participate by the investigator or other study site personnel. The IC process shall not waive or appear to waive subject's legal right. The language used shall be as non-technical as possible and must be understandable to the subject.

The subject must have ample time and opportunity to read and understand the IC form, to inquire about details of the study, and to decide whether or not to participate in the study. All questions about the study should be answered to the satisfaction of the subject.

When the subject decides to participate in the study, the IC must be signed and personally dated by the subject and investigator or authorized designee, as required by the IC, and ensured by the principal investigator or his/her authorized designee.

If the IC is obtained the same day the subject begins participating in study-related procedures, it must be documented in the subject's case history that consent was obtained prior to participation in any study-related procedures. It is best practice for the IC process to be documented in the subject's case history, regardless of circumstance. The date the subject signed the IC and Data Protection Authorization, as required by law, must be documented in the subject's medical records.

The original of the signed IC must be filed in the hospital/clinical chart and/or with the subject's study documents.

The IC must be available for monitoring and auditing. Any Medtronic Field personnel who support the study procedure must be able to review the subject's signed and dated IC and verify its completeness prior to proceeding with the implant. In the event the Medtronic Field personnel identify IC as being incomplete, the study procedure will not be allowed to occur until the consent of the subject can be adequately and appropriately obtained.

A log of all subjects enrolled in the study should be maintained. Enrollment can be a stand-alone visit or can occur on the same day as the screening visit or operative day. Once consent is obtained, report adverse events/deaths, study deviations and subject exits as they occur.

11.6 Operative Day (D0)

The following information is required to be collected on the operative day:

- Date of surgery
- Indication of the procedure
- Surgical technique for laparotomy closure (closure technique and type of suture)
- Mesh reference (TMP1509G, TMP1515G, TMP2015G, TMP3015G, TMP1008G, TMP2008G, TMP3008G, TMP4008G) and lot number
- Type of fixation
- Operative time (from incision to closure, skin to skin),
- Mesh positioning and time
- Peri-operative events including adverse device effects or procedure related adverse events
- Surgeon satisfaction (Club Hernie questionnaire regarding surgeon satisfaction of mesh handling, mesh manipulability, ease of use)

11.7 Scheduled Follow-up Visits

11.7.1 Post-operative course (D0) Follow up

The following information is required to be collected post-operatively on the operative day:

- Post-operative pain assessment measured utilizing a 0-10 Visual Analog Scale (VAS) (Worst pain experienced over the last 24 hours).

11.7.2 Post-operative course (D1) Follow up

The following information is required to be collected during post-operative day 1:

- Pain assessment measured with VAS score
- Post-operative adverse events (including adverse device effects or procedure related adverse events: SSI, hematoma, seroma, etc.). Data will be recorded in the discharge data.

11.7.3 Discharge Data

The following information is required to be collected during discharge:

- Date of discharge
- Length of Hospital stay (number of nights in the institution after the surgery)
- Post-operative adverse events (including adverse device effects or procedure related adverse events: SSI, hematoma, seroma, etc.)

11.7.4 Post-operative course, Day 8, (-/+2days) Follow up

The following information is required to be collected during the Day 8 post-operative follow up (-/+ 2 days):

- Pain assessment measured with VAS score, either during systematic clinical visit or by phone call when a subject is already discharged.

11.7.5 Post-operative course, Day 30, (-/+1 week) Follow up

The following information is required to be collected during the Day 30 post-operative follow up (-/+ 1 week):

- Pain assessment measured with VAS score
- Physical exam including hernia clinical examination
- Post-operative adverse events (including adverse device effects or procedure related adverse events).
- Club Hernie Registry Quality of Life (QoL) Questionnaire

11.7.6 Post-operative course, 12 Months, (-1/+4 week) Follow up

The following information is required to be collected during the 12 Months post-operative follow up (-1/+4 weeks):

- Physical exam including hernia clinical examination
- Abdominal CT-Scan
- Post-operative adverse events (including adverse device effects or procedure related adverse events)
- Club Hernie Registry Quality of Life (QoL) Questionnaire and patient satisfaction
- Pain assessment measured with VAS score

NOTE: 1 Month prior, all subjects will be contacted by phone in order to complete a self-assessment questionnaire and to remind them of the 1-year follow-up visit.

11.7.7 Post-operative course, 24 Months, (-1/+4 week) Follow up

The following information is required to be collected during the 24 Months post-operative follow up (-1/+4 weeks):

- Physical exam including hernia clinical examination

- Abdominal CT-Scan
- Post-operative adverse events (including adverse device effects or procedure related adverse events)
- Club Hernie Registry Quality of Life (QoL) Questionnaire and patient satisfaction
- Pain assessment measured with VAS score

NOTE: 1 Month prior, all subjects will be contacted by phone in order to complete a self-assessment questionnaire and to remind them of the 2-year follow-up visit.

11.7.8 End of Study

After the 24-month follow-up no additional study related medical care will be provided, and subjects will receive the standard of care as determined appropriate by their physician.

If the ProGrip™ Self- gripping polyester mesh is removed from the subject, they will be exited from the study 30 days after mesh removal.

11.8 Subject Questionnaires

During this study the Visual Analog Scale (VAS) will be used to measure subject pain. VAS is a psychometric response scale, first used by Hayes and Patterson in 1921 (1, 2) and currently referenced in more than 950 published manuscripts. Scores are based on self-reported measures of symptoms that are recorded with a single handwritten mark placed at one point along the length of a 10-cm line that represents a continuum between the two ends of the scale, “no pain” on the left end (0 cm) of the scale and the “worst pain” on the right end of the scale (10 cm), which can be used in questionnaires to determine how much pain a subject is feeling.

The Club Hernie Quality of Life and Patient Satisfaction Survey will be used to determine how satisfied a subject is with the mesh placement and what impact it has had on their quality of life. Along with the Surgeon Satisfaction Questionnaire, the Club Hernie Quality of Life and Patient Satisfaction Surveys used in this study were developed by Club Hernie and have been in use in their database since 1999. To date, these questionnaires have been published in numerous manuscripts (3-9), including a recent Medtronic sponsored study (10).

11.9 Assessment of Efficacy

Incisional hernia rate within 24 months of midline laparotomy as assessed by a CT-scan and a physical examination including a hernia clinical examination will be recorded in the Club Hernie Registry Database and used to assess the efficacy of the ProGrip™ Self- gripping polyester mesh.

11.10 Assessment of Safety

The incidence of AEs related to device and/or procedure will be recorded starting at the time of informed consent signature through the 24 months post-operative follow-up. The data will be analyzed in the Safety Analysis Set. See Section 13 for further information on the collection of AEs and safety information.

11.11 Recording Data

This study will utilize the Club Hernie electronic database. All data requested on the Club Hernie Registry Database are required. Study visits or measurements not collected and/or recorded will be considered deviations unless otherwise specified. The Principal Investigator or authorized designee(s) must ensure the accuracy and completeness of the recorded data and then provide his/her electronic signature on the Club Hernie Registry Database (CNIL – Commission Nationale de l'Informatique et des Libertés – approved database). Each Principal Investigator or authorized designee(s) will be trained on the use of the Club Hernie database. Club Hernie does not have the capability to maintain an audit trail, data trail and edit trail; this is a deviation from ISO 14155:2020. All data (new, updated, previously entered) will be reviewed by sponsor with each Club Hernie database extraction. Data accuracy will be assessed by source data verification during monitoring visits. Prior to study closure each Principle Investigator will approve their final set of study data.

Data entered must be traceable to source documents. Source documentation is defined as the first time data appear, and may include original documents, data, and records (e.g., hospital records, clinical and office charts, procedure reports, laboratory notes, memoranda or evaluation checklists, pharmacy dispensing records, copies or transcriptions certified after verification as being accurate copies, microfiches, photographic negatives, microfilm or magnetic media, X-rays, subject files, device data and records kept at the pharmacy, at the laboratories and at medico-technical departments involved in the study).

In general, CRFs may not serve as source documents. The data reported on the CRFs and into Club Hernie shall be derived from and consistent with source documents, and any discrepancies shall be explained in writing by the site staff. If data elements are not documented in the medical record, but are required for CRFs or Club Hernie an exception may be made (e.g., the completion of QoL Questionnaires, clinical scales, Inclusion CFRs, Study Exit CFRs, Protocol Deficiency CRFs, Device Deficiency CRFs, and Adverse Event CRFs). Source documentation for data elements not routinely captured in medical records may vary from study site to study site; the study site may use source document worksheets if identified as source documents.

The investigator must ensure the availability of source documents from which the information on the CRFs or Club Hernie entry was derived. The type and location of source documents should be documented. Where printouts of electronic medical records, are provided as source documents, or where copies of

source documents are retained as source documents, those should be certified. Certification must contain (1) the signature of the individual making the copy, (2) the date the copy was made and (3) a statement attesting to the accuracy and completeness of the copy.

11.12 Deviation Handling

A study deviation is defined as an event within a study that did not occur according to the CIP or the CTA. Prior approval by Medtronic is expected in situations where the investigator anticipates, contemplates, or makes a conscious decision to deviate. The investigator is not allowed to deviate from the CIP, except under emergency circumstances to protect the rights, safety and well-being of human subjects. Prior approval is not required when a deviation is necessary to protect the safety, rights or well-being of a subject in an emergency or in unforeseen situations beyond the investigator's control (e.g. subject failure to attend scheduled follow-up visits, inadvertent loss of data due to computer malfunction, inability to perform required procedures due to subject illness).

For medically justifiable conditions which preempt a subject's ability to complete a study-required procedure, it may be permitted to report only one deviation which will apply to all visits going forward. This may also apply for other unforeseen situations (e.g. the subject permanently refuses to complete a study required procedure and the data will not contribute to the primary end point analysis). However, prior approval from Medtronic is required for such situations.

All study deviations must be reported on the CRF regardless of whether medically justifiable, pre-approved by Medtronic, an inadvertent occurrence, or taken to protect the subject in an emergency. Multiple deviations of the same type at the same visit may be reported on one case report form.

In the event the deviation involves a failure to obtain a subject's consent, or is made to protect the life or physical well-being of a subject in an emergency, the deviation must be reported to the EC as well as Medtronic within five (5) working days. Reporting of all other study deviations should comply with EC policies and/or local laws and must be reported to Medtronic as soon as possible upon the study site becoming aware of the deviation. Reporting of deviations must comply with EC policies, local laws, and/or RA requirements.

Medtronic is responsible for analyzing deviations, assessing their significance, and identifying any additional corrective and/or preventive actions (e.g. amend the CIP, conduct additional training, terminate the investigation). Repetitive or serious investigator compliance issues may result in initiation of a corrective or preventative action plan with the investigator and study site, and in some cases, may necessitate suspending enrollment until the problem is resolved or ultimately terminating the investigator's participation in the study. Medtronic will provide study site-specific reports to investigators summarizing information on deviations that occurred at the investigational study site on a periodic basis.

Examples of study deviations include but are not limited to:

- Failure to obtain proper IC
- Failure to collect required study data (e.g. required abdominal CT scan)
- Required study data collected outside of visit window
- Inclusion/exclusion criteria not met

11.13 Subject Exit, Withdrawal or Discontinuation

11.13.1 Study Exit

A study exit CRF is required for all subjects. Prior to exiting a subject from the study, it is recommended to follow the subject until all ongoing system and/or procedure related AEs are resolved or unresolved with no further actions planned. Following exit, subjects will continue to receive standard medical care. Upon exiting from the study, no further study data will be collected or study visits will occur for the subject. All data available through the time of the subject's exit will be used for analysis.

Subjects are urged to remain in the study as long as possible but may be exited from the study for any of the following situations:

- Study completed
- Subject lost to follow-up
- Subject death
- Subject chooses to withdraw (e.g., consent withdrawal)
- Investigator deems withdrawal necessary (e.g., medically justified, inclusion/exclusion criteria not met, failure of subject to maintain adequate study compliance)
- Mesh removal

11.13.2 Screen Failure

Subjects who provide study consent, but then are determined to be ineligible will be considered a screen failure and will not require additional study follow-up visits. The reason for the screening failure will be clearly recorded in the applicable POETRY Study Exit Form.

11.13.3 Discontinuation

Subjects who provide study consent, and are deemed eligible, but do not undergo the procedure with the study device will be considered "discontinued" and will be followed until discharge (no additional follow-up visits will be required). The reason for discontinuation will be clearly recorded in the applicable POETRY Study Exit Form and Club Hernie Registry Database.

11.13.4 Withdrawal

The reason for study exit will be documented on the POETRY Study Exit form and Club Hernie Registry Database. A subject can withdraw from the study at any time. In the event the subject withdraws consent during the study, the date and reason for withdrawal (if known) will be documented. If the study Investigator voluntarily removes a subject from further study participation, supporting documentation

must be in place for the rationale and date of removal. Follow up of subjects withdrawn will be determined by investigator. Withdrawn subjects will not be replaced.

11.13.5 Lost to Follow-Up

Attempts to reach the subject will be performed by the site after each missed follow-up visit. For each visit, the following should be performed;

- Three (3) phone calls should be made to the subject at various times and least a day apart. Each attempt should be clearly documented in the source documents and the response or lack thereof should be captured.
- If there is no response to the phone calls, then an official, certified letter should be written to the subject. A copy of the letter and return or delivery receipts should be retained in the subject's source document.

The subject will not be considered lost to follow-up until the end of the study. Four (4) failed documented attempts of meticulous postal reminders and phone calls for each visit will be used to minimize the non-response bias. Lost to Follow-up subjects will not be replaced.

11.13.6 Mesh Removal

In the case that the study mesh is removed from the subject the subject will be exited from the study 30 day after mesh removal. The reason for study exit will be documented on the POETRY Study Exit form and the mesh shall be returned to the sponsor.

11.13.7 Study Completed

At the completion of the 24-month follow-up visit, subjects will be exited from the study. The 24-month follow-up visit and exit visit should be combined, and both a 24-month follow-up CRF and a Study Exit CRF need to be completed.

12. Risks and Benefits

12.1. Potential Risks

Medtronic follows rigorous Quality Assurance and Control procedures throughout the life of a product, from the business analysis phase through development, market release, and post-market surveillance. For studies following ISO 14155, the risk analysis process for the ProGrip™ self-gripping polyester mesh is being performed in accordance with ISO 14971, and will ensure that the level of risk is acceptable prior to starting the study. The residual risks have been classified as acceptable in the worst cases.

Possible additional risks for participating in this study include the following (although others are possible): hematoma, seroma, adhesion, infection, fistula, chronic pain, inflammation, and recurrence, allergic

reaction to the components of the product and urinary retention (which may occur with the use of anesthetics). Details can be found in the device IFUs (Section 19.2).

For subjects that are operated for an oncologic colorectal procedure, the abdominal CT-Scan is part of standard of care. For other procedures, as a result of participation in this study, subjects may be exposed to radiation from x-ray procedures. In addition to the routine procedures, the x-ray exams used for this study include a CT scan evaluation of the abdominal cavity. These x-ray exams deliver up to a total radiation dose of approximately 8 mSv each, and subjects will undergo 1 CT scans at the 1 and 2 year post-operative visits. A milliSievert (mSv) is a unit of radiation dose. For comparison, the average person in France receives 2.9mSv each year from natural sources of radiation. A slight increase in cancer risk may exist for people exposed to radiation.

Following the fluoroscopic procedure, as with any X-ray exposure in everyday life, the skin area exposed to those x-rays could react to produce an effect similar to a sun burn. A skin reaction, if it occurs at all, could show up from a few hours to a few weeks after the procedure, and usually goes away on its own. If a skin reaction is found the subject should promptly report this to the study physician.

The mesh will not stretch to accommodate growth so it may be inappropriate to have a mesh implanted if the subject is planning a future pregnancy. A pregnancy after a laparotomy is a risk factor for developing an incisional hernia.

There may be additional risks related to this study that are not yet known.

12.2. Risk Minimization

The potential risks associated with the ProGrip™ self-gripping polyester mesh were identified and have been successfully mitigated. Any potential risks associated with this study are further minimized by selecting qualified investigators and training study personnel on the CIP. Additionally, the study is performed per IFU indications and is on label use for the product.

In addition, investigators will be actively involved in the implantation and follow-up of the subjects implanted with ProGrip™ self-gripping polyester mesh.

Risks will be minimized by careful assessment of each subject prior to, during, and after implant of the ProGrip™ self-gripping polyester mesh. Prior to implant, it is recommended subjects undergo a complete physical evaluation.

Medtronic has further minimized the possibility of risks by performing required laboratory and pre-clinical testing prior to the POETRY study, implementing quality control measures into production processes, providing guidelines for subject selection and evaluation, and providing adequate instructions and labeling.

12.3. Potential Benefits

The information obtained from this study will be used to confirm the safety and efficacy of ProGrip™ self-gripping polyester mesh in abdominal suture line reinforcement. This information may lead to findings that could result in a reduction of adverse events for future subjects. The use of a preventative mesh could reduce the 10-50% rate of incisional hernias that occur after midline laparotomy and decrease complications associated with new surgery and incisional hernia repair. Additionally, information collected from this study may assist in the design of new product(s)/therapy(ies) and/or IFU.

12.4. Risk-Benefit Rationale

In use since 2008 for repair of inguinal and incisional hernia repair, numerous clinical trials have demonstrated the safety and effectiveness of ProGrip™ self-gripping polyester mesh (5-8). Including more than 2,400 patients in more than 20 clinical studies, ProGrip™ self-gripping polyester mesh demonstrates both a low global complication rate as well as a low device related complication rate (Publication summaries and data can be found in the ProGrip™ self-gripping polyester mesh Clinical Evaluation Report). Overall, a positive risk/benefit ratio has been demonstrated with ProGrip™ self-gripping polyester mesh as evidenced by these clinical studies, preclinical and biocompatibility testing. ProGrip™ self-gripping polyester mesh is a CE-Mark cleared device. Consequently, ProGrip™ self-gripping polyester mesh presents a favorable risk/benefit ratio to the subject. The instructions for use in addition to surgeon training, will instruct surgeons on proper use of the device to mitigate risk. There are currently no known interactions between ProGrip™ self-gripping polyester mesh and concurrent medical interventions.

13. Adverse Events and Device Deficiencies

Adverse event (AE) definitions used in this study are based on ISO 14155:2020 (Clinical Investigation of Medical Devices for Human Subjects -- Good Clinical Practice).

13.1. Adverse Events

AE definitions are provided in Section 13.4 (Table 4). During this study, only device and procedure related AEs, SAEs, DDs, and DDs with SADE potential will be collected throughout the study duration, starting at the time of signing the IC (this is a deviation from ISO 14155:2020).

Reporting of these events to Medtronic will occur on a paper AE Form. Each event must be reported separately. Documented pre-existing conditions are not considered AEs unless the nature or severity of the condition has worsened.

Anticipated Adverse Events following surgical procedures (primarily associated with anesthesia, listed in Table 4, need not be reported unless the adverse event worsens or is present outside the stated timeframe post-implant.

For AEs that require immediate reporting, initial reporting may be done by phone, fax, email or on the CRF completing as much information as possible. The completed AE CRF must be submitted to Medtronic as soon as possible.

Any medication/treatment associated with the treatment of an AE must be reported.

Subject deaths are also required to be reported. Refer to Section 13.8 for Subject Death collection and reporting requirements.

13.2. Device Deficiency

The device deficiency (DD) definition is provided in Section 13.4 (Table 4). DD and DD with SADE potential information will be collected throughout the study and reported to Medtronic. Note that a DD that results in an AE to the subject should be captured as an AE only.

DD that did not lead to an AE but could have led to a SADE (i.e., if suitable action had not been taken, if intervention had not been made, or if the circumstances had been less fortunate) require immediate reporting.

13.3 Processing Updates and Resolution

For any changes in status of a previously reported adverse event or DD (i.e. change in actions taken, change in outcome, change in relatedness), information needs to be updated on, or added to a new AE or DD paper form. All AEs must be followed until the AE has been resolved, is unresolved with no further actions planned, the subject dies or exits the study, or until study closure, whichever occurs first.

In the event that a subject is exited from the study prior to study completion, all efforts should be made to continue following the subject until all unresolved system or procedure related AEs, as classified by the investigator, are resolved, unresolved with no further actions planned, or 30 days, whichever occurs first.

At the time of study exit, all collected adverse events that are unresolved must be reviewed and an update must be reported.

13.4 Definitions/Classifications

Where the definition indicates “device”, it refers to any device used in the study. This might be the device under investigation and includes but is not restricted to: ProGrip™ self-gripping polyester mesh.

Table 4: Adverse Event and Device Deficiency Definitions

General	
Adverse Event (AE)	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 or unanticipated NOTE 1: This definition includes events related to the investigational medical device or the comparator. NOTE 2: This definition includes events related to the procedures involved. NOTE 3: For users or other persons, this definition is restricted to events related to investigational medical devices or comparators. (ISO 14155:2020, 3.2)
Adverse Device Effect (ADE)	AE related to the use of an investigational medical device NOTE 1: This definition includes AEs resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device. NOTE 2: This definition includes any event resulting from an error use or from intentional misuse of the investigational medical device. NOTE 3: this includes 'comparator' if the comparator is a medical device. (ISO 14155:2020, 3.1)
Device Deficiency (DD)	Inadequacy of a medical device with respect to its identity, quality, durability, reliability, usability, safety or performance. NOTE 1: DD include malfunctions, use errors and inadequacy in the information supplied by the manufacturer including labeling. NOTE2: This definition includes device deficiencies related to the investigational medical device or the comparator. (ISO 14155:2020, 3.19)

Relatedness	
Mesh Placement Procedure Related	An AE that occurs due to any procedure related to the implantation or surgical modification of the device.
Index Procedure Related	An AE that occurs due to the standard of care index surgical procedure
Device Related	An AE that results from the presence or performance (intended or otherwise) of the device.
Seriousness	
Serious Adverse Event (SAE)	AE 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: 1) a life-threatening illness or injury, or 2) a permanent impairment of a body structure or a body function, including chronic disease, 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, c) foetal distress, foetal death or a congenital abnormality or birth defect including physical or mental impairment NOTE 1: Planned hospitalization for a pre-existing condition, or a procedure required by the CIP, without serious deterioration in health, is not considered an SAE. (ISO 14155:2020, 3.45)
Serious Adverse Device Effect (SADE)	Adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event. (ISO 14155:2020, 3.44)
Other	
Anticipated Adverse Event	An AE inherent to a surgical procedure that is expected to occur in all subjects for a projected duration according to the Investigator's opinion, including, but not limited to: ▪ Postoperative transient nausea determined to be procedure related within the first 24 postoperative hours. ▪ Postoperative transient emesis determined to be

	procedure related within the first 24 postoperative hours. ▪ Postoperative constipation determined to be procedure and/or medication related for the duration of medication administration for management of pain. ▪ Postop pain that the Investigator considers common and within normal limits for the procedure and is well-managed with medication.
Unanticipated Serious Adverse Device Effect (U(S)ADE)	(Serious adverse) device effect which by its nature, incidence, severity or outcome has not been identified in the current risk assessment NOTE 1: ASADE is an effect which by its nature, incidence, severity or outcome has been identified in the risk assessment. (ISO 14155:2020, 3.51)
Serious Health Threat	Signal from any adverse event or device deficiency that indicates an imminent risk of death or a serious deterioration in the health in subjects, users or other persons, and that requires prompt remedial action for other subjects, users or other persons NOTE 1: This would include events that are of significant and unexpected nature such that they become alarming as a potential serious health hazard or possibility of multiple deaths occurring at short intervals. (ISO 14155:2020, 3.46)

13.5 Reporting of Adverse Events

The following events are generally considered reportable during the course of this study and should be reported to the sponsor:

- any DD,
- any procedure or device related AE or SAE,
- any Device Deficiency/Malfunction that might have led to an SADE if,
  - suitable action had not been taken or,
  - intervention had not been made or,
  - if circumstances had been less fortunate,
- new findings/updates in relation to already reported events.

Events will be reviewed by the sponsor to determine any reporting obligations to EC.

SAEs & Device Deficiencies/Malfunctions that might have led to an SADE need to be reported to the sponsor within 24 hours of becoming aware by completing an AE report form and sending it to Medtronic BOX [redacted]. When the AE report form is received by the sponsor, it will be marked as received and reviewed and saved in TMF. A deviation form is required if AE report form is not completed and AE was only reported via email to sponsor or if the event was reported outside of the required timeframe. Refer to Table 5 for reporting requirements of applicable events and device deficiencies.

Table 5: Reporting requirements of applicable events and device deficiencies.

Report	Responsible party	Submit to	Description / Time constraints
ADE, or DD	Investigator	Medtronic	Notify within **24h** of notification of the event via data entry into Club Hernie database and AE form, telephone call and fax
	Medtronic	EC	Review within 48 hours per EC requirements
SAE, SADE, or Device Deficiency that might have led to a SADE	Investigator	Medtronic	Notify within **24h** of notification of the event via data entry into Club Hernie database and AE form, telephone call and fax
	Medtronic	EC	Review within 48 hours per EC requirements Per EC requirements
U(S)ADE	Medtronic	IEC	Review within 48 hours per EC requirements Per EC requirements
	Medtronic or designee	Alternate applicable regulatory body	Report the results of an evaluation to EC and all participating investigators within **7 working days** after Medtronic first receives notice of the effect, and **2 days** if the U(S)ADE indicates an imminent risk of death, serious injury or serious illness and requires prompt remedial action.

Assessment of the occurrence of an AE will be based on changes in the subject's abbreviated physical examination, laboratory results and/or signs and symptoms. Adverse events will be monitored until a subject completes the study unless the Investigator determines the event is related to the device, in which case they will be monitored until resolution, if possible. Medical care will be provided, as defined in the informed consent, for any AE related to study participation. Adverse events will be collected on the Club Hernie database, and on an AE paper form to be sent to the sponsor and applicable source documentation. AE data will include but is not limited to; date of the AE, treatment, resolution, assessment of both seriousness and relationship to the investigational medical device. To the extent possible, the event to be recorded and reported is the event diagnosis as opposed to event symptoms (e.g., fever, chills, nausea and vomiting in the presence of a clinically diagnosed infection is to be reported as infection only). AEs occurring at procedure and up to and including 24 months follow-up will be recorded.

The following should not be considered an AE:

- A condition requiring a preplanned procedure unless the condition worsened since screening
- A preexisting condition found as a result of screening, unless the condition has worsened since enrollment.

All responses to the above events that require treatment beyond the institution's standard procedures will be reported as AEs.

All procedure AEs and ADEs as described above that are observed during the course of this study, regardless of severity or relationship to the device will be recorded on the appropriate the Club Hernie database tab and on an AE paper form.

The sponsor is responsible for ensuring all Adverse Events reported by the sites are also reported to the EC and to Regulatory Affairs – Medtronic France as required.

13.5.1 Adverse Event and Device Deficiency Classification

Causality assessments define the relationship between the use of the medical device (including the medical-surgical procedure) and the occurrence of each adverse event, according to MEDDEV (Guidelines On A Medical Devices Vigilance System). 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. Each AE will be classified according to five different levels of causality. The sponsor and the investigators will use the following definitions to assess the relationship of the serious adverse event to the investigational medical device or procedures:

- Possible Relationship: An AE that follows a reasonable temporal sequence from administration of the study treatment and follows a known response pattern to the study treatment but could have been produced by the participant's clinical state or by other therapies.
- Probable Relationship: An AE that follows a reasonable temporal sequence from administration

of the study treatment; follows a known response pattern to the study treatment; and cannot be reasonably explained by the known characteristics of the participant's clinical state or by other therapies.

- Causal Relationship: An AE that follows a plausible temporal sequence from administration of the study treatment and follows a known response pattern to the study treatment. The reaction cannot be reasonably explained by the known characteristics of the subject's clinical state or other modes of therapy administered to the subject.
- Unknown relationship: Given the information available, sequence and timing of events, it is unknown or impossible to determine the relationship of the AE with the study treatment.

The Sponsor and the Investigators will distinguish between the serious adverse events related to the device and those related to the index procedures and to mesh placement procedure. An adverse event can be related both to the index and mesh procedures and the device. Complications of procedures are considered not related if the PI said procedures would have been applied to the subjects also in the absence of device use/application.

In some particular cases the event may be not adequately assessed because information is insufficient or contradictory and/or the data cannot be verified or supplemented. The sponsor and the Investigators will make the maximum effort to define and categorize the event and avoid these situations. Where the sponsor remains uncertain about classifying the serious event, it should not exclude the relatedness and classify the event as "possible".

Particular attention shall be given to the causality evaluation of unanticipated serious adverse (device) events. The occurrence of unanticipated events related to the use of the device (USADE) could suggest that the clinical investigation places subjects at increased risk of harm than was to be expected beforehand.

13.6 Adverse Event Outcome Classification

Outcome of the event will be defined according to the following:

- Fatal: This event is determined to be the cause of death.
- Not Recovering/Not Resolved: The event has retained pathological conditions resulting from the prior disease or injury.
- Recovered/Resolved: The event has fully resolved at the end of the study.
- Recovering/Resolving: The event is ongoing at the end of the study.
- Unknown: The event has been unclassified at the end of the study.

13.7 Study Contact Information

Questions regarding safety or medical procedures should be directed to Medtronic MITG Medical Affairs. All other questions including emergency contact for reporting serious adverse events and serious adverse device effects should be directed to Medtronic MITG Surgical Innovations, Clinical Research.

Table 6: Study Contact Information

Medical Affairs	Clinical Research
[redacted]	[redacted]

13.8 Subject Death

All subject deaths must be reported by the investigator to Medtronic on an AE form (AE with outcome of death) as soon as possible after the investigator first learns of the death. In case of death, there should be one AE with the outcome of death.

A copy of the death certificate, if available and allowed by state/local law, should be provided to the Medtronic clinical study team. When a death occurs in a hospital, a copy of the death summary report and all relevant hospital records, if available should be provided to the Medtronic clinical study team. If an autopsy is conducted, a copy of the autopsy report should also be provided to the Medtronic clinical study team if available and allowed by local law. When the death occurs at a remote study site, it is the investigative study site's responsibility to attempt retrieval of information about the death.

In summary, the following data will be collected:

- Date of death
- Detailed description of death
- Cause of death
- Relatedness to system and/or procedure
- Device disposition information
- Death summary/hospital records (if available and allowed by local law)
- Autopsy report (if available and allowed by local law)
- Death certificate (if available and allowed by local law)

13.9 Product Complaint Reporting

Product complaint reporting and vigilance reporting are applicable and AEs related to any market-released device during the study must be reported. The reporting of product complaints is not part of the study and should be done in addition to the AE reporting requirements. Refer to local regulations for reporting requirements.

Product Complaint: Any written, electronic or oral communication that alleges deficiencies related to the identity, quality, durability, reliability, safety, effectiveness or performance of a medical device that has been placed on the market.

- Abuse: Abnormal use (definition acc. #4.1 of MDR 2.12-1)
- Misuse: Use error (definition acc. #4.20 of MDR 2.12-1)

It is the responsibility of the investigator to report all product complaint(s) associated with a medical device distributed by Medtronic, regardless whether they are related to intended use, misuse or abuse of the product. Reporting must be done immediately and via the regular channels for market-released products. The reporting of product complaints by the clinical team must be done according to the local Standard Operating Procedures. Medtronic will notify the RAs (e.g. CA) as applicable for the following incidents immediately upon learning of them and is not limited to AEs and DDs only:

- Any malfunction or deterioration in the characteristics and/or performance of a device, as well as any inadequacy in the labeling or instructions for use which led or might have led to the death or serious deterioration in the state of health of a patient, user, or other person.
- Any technical or medical reason resulting in withdrawal of a device from the market by the manufacturer.
- Any serious deterioration in the state of health, including:
  - Life-threatening illness or injury
  - Permanent impairment of a body function or permanent damage to a body structure
  - A condition necessitating medical or surgical intervention to prevent permanent impairment of a body function or permanent damage to a body structure

14. Data Review Committees

Due to the design of this post-market study in association with Club Hernie, it was determined that a Data Monitoring Committee and Clinical Events Committee would not be chosen specifically, but that the study Steering Committee would review the data as needed. See section 7.3 Study Oversight for details on the Steering Committee.

14.1 Safety Committee

An internal Medtronic Safety Team will review the overall rates of protocol defined adverse events (SAEs and events related to the primary and safety endpoints) on a quarterly basis. The committee will have the ability to make recommendations and request further information as required.

15. Statistical Design and Methods

15.1 General Aspects of Analysis

For each of the objectives the available data will be summarized and missing data will be discussed. The main analysis of the study objectives will be based on available data and missing data will not be imputed unless otherwise noted in the statistical analysis plan. All practical monitoring and follow-up steps will be taken to ensure complete and accurate data collection. Deviations to the statistical analysis plan (SAP) will be reported per section 11.12 (Deviation Handling).

15.2 Analysis Execution

Analysis will include both primary and all secondary objectives. A final report will be prepared once all data collection has ended and all subjects have completed the 24-month follow-up or have been exited.

15.3 Interim Analysis

After half the enrolled subjects complete the 1-year follow-up timepoint, an interim analysis will be conducted for regulatory purpose. An additional interim analysis for regulatory needs may also be conducted as needed.

15.4 Endpoints

15.4.1 Primary Endpoints

Statistical analysis of the primary endpoint will be comparative. Binomial one-way test will be used to compare the observed ProGrip™ Self- gripping Polyester Mesh incisional hernia incidence rate to the 20% theoretical incidence rate (from no prevention population), using a two- sided alpha-level of 5%.

15.4.2 Other Endpoints

Other endpoints will be analyzed using descriptive methods:

- Qualitative variables will be described by their absolute and relative (%) frequencies of each class or value, and by two-tailed 95% confidence intervals.
- Quantitative variables will be described by their mean, standard deviation (SD), extreme values

(minimum and maximum values), and number of missing data and by two-tailed 95% confidence intervals.

15.5 Analysis Sets

- The Performance Analysis Set (PAS) includes all enrolled subjects excluding subjects who became pregnant during the follow-up, or subjects who undergo unscheduled abdominal surgery during study follow-up, which may increase the risk and cause of incisional hernia occurrence*.

*Subject follow-up data, starting from the event's occurrence, will be excluded/remove from the performance analysis.

- Per Protocol Analysis Set (PPAS) is a subset of PAS excluding subjects with protocol violation and major protocol deviation(s) that may impact the primary endpoint assessment. More precisely, reason for exclusion may include but is not limited to,
  - Patient wrongly included (*i.e.* patient was enrolled but does not meet all the eligibility criteria).
  - Failure to obtain informed consent.
  - Deviation resulting from device use outside the recommended use in the IFU.
  - Patient who receives the incorrect device or device is misused

- Safety Analysis Set includes all enrolled subjects.

15.6 Sample Size Determination

Sample size is determined based on primary performance endpoint, assuming the superiority of ProGrip™ Self-gripping Polyester Mesh use to prevent incisional hernia vs no prevention of incisional hernia within 2-years following a midline laparotomy procedure.
The literature review showed an incisional hernia rate after midline laparotomies around 20% (9-16). Using a power (1-β) of 80% and a 5% error type I (two-sided), and considering a hypothetic incisional hernia rate of 10% for subjects with ProGrip™ Self-gripping Polyester Mesh, vs a theoretical hypothetic incisional hernia rate of 20% for subjects without any prevention following a midline laparotomy procedure, N= 108 evaluable subjects are required.
Assuming an attrition rate of 20% at 2-years, N=135 subjects will need to be enrolled.

15.7 Minimization of Bias

Selection of subjects, treatment of subjects, and evaluation of study data are potential sources of bias. Methods incorporated in the study design to minimize potential bias include (but are not limited to):

- Enrollment will not exceed 25 subjects per site.

In summary, potential sources of bias that may be encountered in this study have been considered and minimized by careful study design.

16. Ethics

16.1. Statement(s) of Compliance

This study is designed to reflect the good clinical practice (GCP) principles outlined in ISO 14155:2020. These include the protection of the rights, safety and well-being of human subjects, controls to ensure the scientific conduct and credibility of the clinical investigation and the definition of responsibilities of the sponsor and investigators.

The study will also be conducted in accordance with the Declaration of Helsinki (2013). The principles of the Declaration of Helsinki are implemented in this study by means of the Subject Informed Consent (IC) process, Ethics Committee approval, study training, clinical study registration, pre-clinical testing, risk benefit assessment, and publication policy.

Ultimately, all study sites in all geographies will follow and comply with:

- Principles of DoH
- The Clinical Trial Agreement (CTA)
- The procedures described within this CIP
- Local EC Requirements

In addition to the regulatory requirements outlined above, the study will be conducted according to federal, national and local laws, regulations, standards, and requirements of the countries/geographies where the study is being conducted. These include but are not limited to:

- In Europe the study will be conducted in compliance with DoH version 2013.

The study will be publicly registered prior to in accordance with the 2007 FDAAA and DoH on http://clinicaltrials.gov (PL 110-85, section 810(a)). This study will be publicly registered on www.clinicaltrials.gov prior to first enrollment. In addition, the study may be registered in local regulatory databases where required by local law.

Approval of the CIP and CIP amendments is required from the following groups prior to any study procedures at a study site:

- Medtronic
- An independent medical EC.

Similarly, approval of subsequent revisions to the CIP is required at each study site from the above-mentioned groups prior to implementation of the revised CIP at the study site.

This study contains 3 deviations from ISO14155:2020;

- To ensure only data is collected from subjects who have received ProGrip™ Self-gripping Polyester Mesh, a subject is considered enrolled when it is confirmed they meet all pre-operative

inclusion and no exclusion criteria, the ICF is signed and they have been implanted with the device. Those subjects who sign the ICF but do not receive ProGrip™ Self-gripping Polyester Mesh will not be included in the study.

- As an on-label Post-Market Clinical Follow-up study to confirm the efficacy and safety of ProGrip™ Self-gripping Polyester Mesh for suture line reinforcement, only device and procedure related AEs will be collected. Non-related AEs (flu, broken limbs, etc.) will not be collected.
- The Club Hernie Data base does not have the capabilities to maintain an audit trail, data trail and edit trail. The sponsor will review all database entries monthly and file securely as an audit trail.

17. Study Administration

17.1.Monitoring

It is the responsibility of Medtronic to ensure proper monitoring of this study. Trained Medtronic personnel or delegates appointed by Medtronic may perform study monitoring in order to ensure that the study is conducted in accordance with the CIP, the CTA, and the applicable regulatory and local requirements. Medtronic, or delegates, must therefore be allowed direct access to the subjects' case histories (clinic and hospital records, and other source data/documentation) upon request as per the IC, Research Authorization (where applicable) and CTA. The principal investigator should also be available during monitoring visits. Although on-site monitoring is preferred, remote study monitoring is also acceptable when necessary and study sites should make all efforts to comply with the needs of the study monitors.

17.1.1 Monitoring Visits

Frequency of monitoring visits may be based upon subject enrollment, but additional visits may be scheduled due to study compliance, number of adverse events, number of deviations, observations from previous monitoring visits and any suspected inconsistency in data that requires investigation. Regulatory documents will be reviewed at each study site. Monitoring for the study, including site qualification visits, site initiation visits, interim monitoring visits, and closeout visits, will be done in accordance to the study-specific monitoring plan.

Monitoring visits may be conducted periodically to assess study site progress, the investigator's adherence to the CIP, regulatory compliance including but not limited to EC approval and review of the study, maintenance of records and reports, and review of source documents against subject CRFs in accordance to the study-specific monitoring plan. Monitors review study site regulatory and study compliance by identifying observations of non-compliance and communicating those observations along with recommendations for preventative/corrective actions to study site personnel. Monitors may work with study personnel to determine appropriate corrective action recommendations and to identify trends within the study or at a particular study site.

17.2. Data Management

Data will be collected using an electronic database (Club Hernie) and paper CRFs. The Club Hernie database is free for use by surgeons. Only Hernia Club surgeon members or designees are allowed to get an account for the database, protected by identifier and password. Members only have access to their data and cannot view or modify/manipulate other member's data. Data entered into the database is required to be completed pseudonymously. Therefore, it does not contain any patient data such as name, date of birth, social security number or address of the patient. Club Hernie maintains a list of individuals who have access to the database.

Database extractions will be transferred by a Club Hernie representative to sponsor securely by upload into Medtronic Box. All database extractions will be retained for audit and inspection purposes. Data review of all new, updated and previously entered data will be performed after receipt of each database extraction to ensure the accuracy of the report and identify possible data discrepancies by Medtronic and Data Clarification Forms will be issued to the sites for appropriate response. The site staff will be responsible for resolving all queries in the database. All discrepancy resolutions will be retained for audit and inspection purposes in a discrepancy tracker.

Adverse Events will be coded per Medical Dictionary for Regulatory Activities (MedDRA).

All records and other information about subjects participating in this study will be treated as confidential.

Procedures in the CIP require source documentation. Source documentation will be maintained at the study site. Source documents, which may include worksheets or subject medical records, must be created and maintained by the investigational study site team.

The investigator will clearly mark clinical records to indicate that the subject is enrolled in this clinical investigation.

Paper CRFs will consist of Inclusion Form, AE Form, DD Form, Protocol Deviation and Study Exit Form. The data reported on the CRFs and into Club Hernie shall be derived from source documents and be consistent with these source documents, and any discrepancies shall be explained in writing. Please refer to section 11.11 Data Recording for exceptions to this requirement.

17.3. Direct Access to Source Data/Documents

Medtronic may conduct audits at participating study sites. The purpose of an audit is to verify the performance of the monitoring process and the study conduct, independently of the personnel directly involved in the study. Regulatory authorities (RAs) may also perform inspections at participating study sites. The investigator and/or institution shall permit Medtronic, ECs and RAs direct access to source data and documents during monitoring, audits and regulatory inspections.

17.4. Confidentiality

All records identifying the subject will be kept confidential and, to the extent permitted by the applicable laws and/or regulations, will not be made publicly available. Subject names will be kept confidential. Only the site identification number and subject number will be recorded in the Club Hernie electronic database, and if the subject name appears on any other document, it must be redacted. Study findings stored on a computer will be stored in accordance with local data protection laws. The subjects will be informed in writing that representatives of the sponsor, EC, or Regulatory Authorities may inspect their medical records to verify the information collected, and that all personal information made available for inspection will be handled in strictest confidence and in accordance with local data protection laws. Subjects will also be informed that information regarding the study that does not include subject identifiers will be posted on clinicaltrials.gov. When the results of the study are published, the subject's identity will remain confidential. The investigator will maintain a master list to enable subjects' records to be identified.

17.5. Liability

17.5.1. Warranty

Sofradim Production is a wholly owned subsidiary of Medtronic, which as the parent company of such entity maintains appropriate clinical study liability insurance coverage as required under applicable laws and regulations and will comply with applicable local law and custom concerning specific insurance coverage. If required, a clinical study insurance statement/certificate will be provided to the EC.
Subjects will not be provided with compensation for participation in this study.

17.6. CIP Amendments

A CIP/Protocol amendment will be prepared when there are revisions that are significant changes or corrections, or modification that impact subject safety, ethical conduct, data integrity or study design. CIP/Protocol amendments must undergo review and approval by the sponsor, EC and any appropriate regulatory authority, and will be logged in the document version history (Section 20). EC approval regulatory authority approval (if applicable), site training and a new Investigator Commitment form will be signed and returned before any new procedures take place.

17.7. Record Retention

The investigator and the sponsor will maintain the records of the study including all pertinent correspondence, the study protocol with any/all amendments, all correspondence with and approval from the EC, the Investigator Agreement, device accountability records, individual subject records, and signed informed consent forms. Subject files, other source data and essential documentation kept in the Investigator study files and should be retained until at least 2 years after the last approval of a marketing

application in an ICH region and until there are no pending or contemplated marketing applications in an ICH region or at least 2 years have elapsed since the formal discontinuation of clinical development of the investigational product. Records may need to be maintained by the Principal Investigator for a longer duration if national regulations require or if agreed to in writing with Medtronic. Prior to the destruction of the study related data, the investigator must notify the sponsor. The principal investigator will ensure that essential study documents are not destroyed until written permission has been obtained from Medtronic. All data and documents should be made available if requested by relevant authorities.

After closure of the study Medtronic will archive records and reports per Medtronic standards and applicable regulations.

17.8. Reporting Requirements

17.8.1. Investigator Reports

The investigator is responsible for the preparation (review and signature) and submission to the sponsor of all case report forms, adverse events and adverse device effects (reported per the country-specific collection requirements), device deficiencies, deaths, and any deviations from the clinical investigation plan. Any deviation from the clinical investigational plan shall be recorded together with the explanation of the deviation. Notice of deviations from the CIP to protect the life or physical well-being of a subject in an emergency shall be given as soon as possible, but no later than 5 working days after the emergency occurred. Except in such emergency, prior approval is required for changes in the plan or deviations.

Table 7: Investigator reports applicable to Europe, Middle East and Africa per ISO 14155

Report	Submit to	Description/Constraints
Study Deviations	Sponsor	Any deviation from the CIP shall be recorded together with an explanation for the deviation. Deviations shall be reported to the sponsor who is responsible for analyzing them and assessing their significance. Note: When relevant, ethics committees, CAs or the appropriate RAs should be informed. (ISO 14155:2020)
Failure to obtain IC	Sponsor	IC shall be obtained in writing and documented before a subject is enrolled into the clinical investigation. (ISO 14155:2020)

17.8.2. Sponsor Reports

Medtronic shall prepare and submit the following complete, accurate, and timely reports listed in the table below. In addition to the reports listed below, Medtronic shall, upon request of the reviewing EC or RA, provide accurate, complete and current information about any aspect of the investigation.

Table 8: Sponsor reports for Europe, Middle East and Africa

Report	Submit to	Description/Constraints
Premature termination or suspension of the clinical investigation	Investigators, EC, Relevant authorities and Head of the Institution	Provide prompt notification of termination or suspension and reason(s). (ISO 14155:2020)
Withdrawal of EC approval	Investigators, Head of Institution, EC and relevant authorities	Investigators, ECs will be notified only if required by local laws or by the EC.
Withdrawal of CA approval	Investigators, Head of Institution, EC, and relevant authorities	Investigators, ECs will be notified only if required by local laws or by the EC.
Progress Reports	EC and RAs	This will be submitted to the EC only if required by the EC).
Final report	Investigators, EC, and RAs if required	For studies with study sites complying to ISO 14155: ▪ The investigator shall have the opportunity to review and comment on the final report. ▪ If a clinical investigator does not agree with the final report, his/her comments shall be communicated to the other investigator(s). ▪ The coordinating investigator shall sign the report. If no coordinating investigator is appointed, then the signature of the principal Investigator in each study site should be obtained. (ISO 14155:2020)

Report	Submit to	Description/Constraints
Study deviation	Investigators	Ensure that all deviations from the CIP are reviewed with the appropriate clinical investigator(s), are reported on the CRFs and the final report of the clinical investigation. (ISO 14155:2020) Study site specific study deviations will be submitted to investigators periodically.

17.9. Publication and Use of Information

The Medtronic Publication and Authorship Policy is aligned with the International Committee of Medical Journal Editors (ICMJE) recommendations (www.icmje.org). Medtronic will seek to publish, in appropriate peer-reviewed journals and scientific conferences, results of clinical studies where human subjects are involved, regardless of outcome. While study results are owned by Medtronic, all data on which a publication is based will be made available to all authors as required for their participation in the publication process. Furthermore, data may be published or used by study investigators provided that such publication or use is in accordance with this protocol, the Medtronic Publication and Authorship Policy, and the Clinical Investigation Agreement. Investigators must submit a copy of all manuscripts and/or abstracts to Medtronic for review and comment 30 days prior to planned submission. Medtronic acknowledges that its right to review and comment shall relate solely to the proprietary, licensing, and/or confidential rights Medtronic may have in such proposed publication, rather than whether such results and/or opinions are favorable to Medtronic.

The publication of post-hoc analyses, regional results, or single-center experiences based on multicenter clinical studies should not precede that of the primary multicenter publication, and should cite the primary publication whenever possible, as required by specific journal and scientific meeting guidelines.

Medtronic involvement in a publication (e.g., funding of the study; sponsor of the study; collection, analysis, and interpretation of data; professional writing assistance) must be disclosed according to journal-specific policies, submission requirements, and prevailing editorial standards, in addition to those specified by International Committee of Medical Journal Editors. Authors must ensure that an acknowledgement/disclosure statement is included in the body of the manuscript for Medtronic to review for accuracy. All authors must also disclose financial or personal affiliations that could be considered conflicts of interest as per journal/conference requirements.

To enable health care providers, payers, and subjects' access to the wealth of Medtronic's research, Medtronic will report its scientific data in accordance with the principles outlined in the Guidance Document on Registration and Reporting Results of Company-Sponsored Clinical Trials under FDAAA 2007 (Title VIII).

17.9.1. Transparency

Transparency of clinical study results will be maintained by the following means:

- A final report, describing the results of all objectives and analysis, will be distributed to all investigators, ECs and CAs of participating countries when required by local law
- Registering and posting the study results on ClinicalTrials.gov based on the posting rules stipulated
- Submitting for publication the primary study results after the study ends
- Disclosing conflicts of interest (e.g., financial) of the co-authors of publications according to the policies set forth by the corresponding journals and conferences
- Making an individual study sites study data accessible to the corresponding investigator after the completion of the study, if requested

17.10. Suspension or Early Termination

17.10.1. Planned Study Closure

Study Closure is a process initiated by distribution of a study closure letter. Study closure is defined as closure of a study that occurs when Medtronic and/or regulatory requirements have been satisfied per the CIP and/or by a decision by Medtronic or RA, whichever occurs first. The study closure process is complete upon distribution of the Final Report or after final payments, whichever occurs last. Ongoing EC oversight is required until the overall study closure process is complete. Refer to Section 11.13 for additional information regarding study exit procedures.

17.10.2. Early Termination or Suspension

Early Termination is the closure of a study that occurs prior to meeting defined endpoints. This is possible for the whole study or a single study site. Suspension is a temporary postponement of study activities related to enrollment and distribution of the product. This is possible for the whole study or a single study site.

17.10.2.1. Study-wide termination or suspension

Possible reasons for considering study-wide suspension or termination of the study include but are not limited to:

- AEs associated with the system or product under investigation which might endanger the safety or welfare of the subject
- Observed/suspected performance different from the product's design intent
- Decision by Medtronic or RA (where the study is operating under RA)
- Technical issues during the manufacturing process

17.10.2.2. Investigator/ study site termination or suspension

Possible reasons for investigator or study site termination or suspension include but are not limited to:

- Failure to obtain initial EC approval or annual renewal of the study
- Persistent non-compliance to the clinical investigation (e.g. failure to adhere to inclusion/exclusion criteria, failure to follow subjects per scheduled follow-ups)
- Lack of enrollment
- Noncompliance to regulations and the terms of the CTA (e.g. failure to submit data in a timely manner, failure to follow-up on data queries and monitoring observations in a timely manner, etc.)
- EC suspension of the study site
- Fraud or fraudulent misconduct is discovered (as defined by local law and regulations)
- Investigator request (e.g. no longer able to support the study)

17.10.3. Procedures for Termination or Suspension

17.10.3.1. Medtronic-initiated and regulatory authority-initiated

- Medtronic will promptly inform the clinical investigators of the termination or suspension and the reasons and inform the RAs where required
- In the case of study termination or suspension for reasons other than a temporary EC approval lapse, the investigator will promptly inform the EC
- In the case of study termination, the investigator must inform the subjects and may inform the personal physician of the subjects to ensure appropriate care and follow-up is provided
- In the case of a study suspension, subject enrollment must stop until the suspension is lifted by Medtronic
- In the case of a study suspension, enrolled subjects should continue to be followed out of consideration of their safety, rights and welfare

17.10.3.2. Investigator-initiated

- The investigator will inform Medtronic and provide a detailed written explanation of the termination or suspension
- The investigator will promptly inform the institution (where required per regulatory requirements)
- The investigator will promptly inform the EC
- the investigator will promptly inform the regulatory authorities, if applicable
- The investigator will promptly inform the subjects and/or the personal physician of the subjects to ensure appropriate care and follow-up is provided
- In the case of a study suspension, subjects enrolled should continue to be followed out of consideration of their safety, rights and welfare

17.10.3.3. Ethics committee-initiated

- Subject enrollment must stop until the suspension is lifted
- Subjects already enrolled should continue to be followed in accordance with EC policy or its determination that an overriding safety concern or ethical issue is involved
- The investigator will inform his/her institution (where required per local requirements)
- The investigator will promptly inform the subjects or the personal physician of the subjects, with the rationale for the study termination or suspension
- the investigator will promptly inform the RAs

18. References

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19. Appendices

19.1. APPENDIX A: List of Investigators and Institutions

Investigational Sites information including addresses, contact information, Principal Investigators, and the EC will be retained in a separate document from the body of the clinical investigation plan document. This will be provided to investigational sites and updated as necessary.

19.2. APPENDIX B: Instructions for Use


Box size: 220 mm x 310 mm
Overall Size: 453 mm x 645 mm
Folds to: 75.5 mm x 215 mm

COVIDIEN

ProGrip™
Self-Gripping Polyester Mesh

Medtronic

19.3. APPENDIX C: Financial Statement

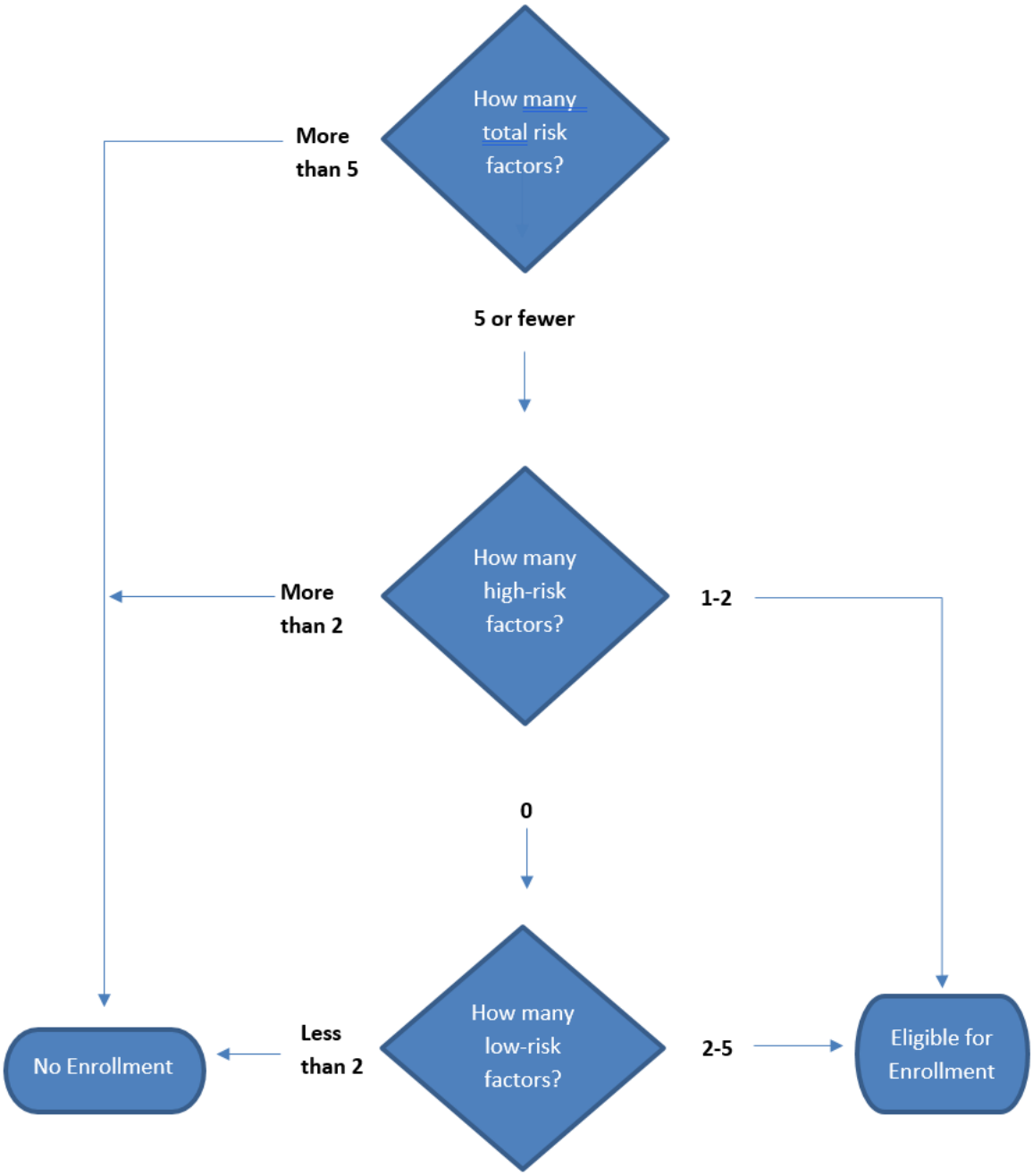
Medtronic contracts with participating institutions/investigators through a Clinical Trial Agreement (CTA) that defines the scope and responsibilities and associated compensation related to carrying out the obligations under a clinical study sponsored by Medtronic.

The CTA will be retained in the Trial Master File per the Document Management Plan.

19.4. APPENDIX D: Subject Forms

Site-specific Patient Informed Consent (PIC) templates will be retained in a separate document from the body of the clinical investigation plan document. This will be provided to investigational sites and updated as necessary.

19.5. APPENDIX E: Subject Enrollment Decision Tree



20. Version History

Version	Summary of Changes	Author(s)/Title
1.0	'Not Applicable, New Document'	[redacted] Senior Medical Writer
2.0	▪ Minor typos correction ▪ Title: Correction of the title, subject has replaced patient by error in version 1.0. ▪ Front page: Confidentiality Statement: added Sofradim Production to indicate relationship with Medtronic plc. ▪ Section 2. Deletion of FAS definition as it is not used in the CIP, correction of PPAS definition and addition of PAS and SAS definition. ▪ Section 3. Update of synopsis for the title and statistical section ▪ Section 6.1. Addition of the use of the AE report form for safety reporting to be complaint with section 11. ▪ Section 9.6. Correction of example for major deviation ▪ Section 9.7.2 and 9.7.4 Clarification that screen failure and withdrawal will also be recorded in the POETRY Study Exit Form. ▪ Section 9.7.3. Addition that reason for discontinuation will be clearly recorded in the applicable POETRY Study Exit Form and Club Hernie Registry Database ▪ Section 9.7.5. Clarification that attempts to contact Lost to Follow-Up patient must be documented. ▪ Section 11.1.6. Addition of RA Medtronic France email. ▪ Section 11.2. update of study email for the reporting of AE. ▪ Section 11.3 Study Contact Information update ▪ Section 13. Addition of Per Protocol Analysis Set definition Appendix B. Update of IFU	[redacted] Clinical Study Manager
3.0	▪ Change of template 056-F275, v A Clinical Investigation Plan Template ▪ Section 2. Addition of EU MDR definition ▪ Section 3. Clarification of Clinical Study type	[redacted] Clinical Study Manager

	▪ Section 3. Update of inclusion/exclusion criteria and Study Procedures and Assessments per change in section 8.2, 8.4 and 9.1.2 ▪ Section 5. Update of section title per new template ▪ Section 6. Change of sub-section categories per the new template ▪ Section 8.3. Clarification of the risk factors linked to hernia history ▪ Section 8.4. Clarification of exclusion criteria #2 by highlighting two contra-indications ▪ Section 9.1.2 Addition of the pregnancy test (for exclusion criteria) ▪ Section 9.7.2 Deletion of record of screen Failure in the Club Hernie database ▪ Section 11.2. Addition of reporting requirement to RA Medtronic France per 056-G140 Global Safety Reporting Requirements for Clinical Studies ▪ Section 14.1 Addition of the EU MDR for study compliance	
4.0	▪ Change of template 056-F275, v B Clinical Investigation Plan Template ▪ Document updated for ISO14155:2020 ▪ Document updated to allow for up to 12 sites ▪ Document updated for minor typos ▪ Document updated to clarify Sponsor vs Local Sponsor ▪ Glossary updated to include additional terms and abbreviations ▪ Section 1 Investigator Statement is now called the Investigator Commitment ▪ Section 4 Synopsis section updated to reflect document changes ▪ Section 6.2.2 updated to include additional secondary endpoint ▪ Section 7 Study Design has been updated ▪ Section 7.3 Study Oversight section added ▪ Section 8 Product Description updated to include additional meshes ▪ Section 8.5 updated to clarify product training requirements	[redacted], Senior Medical Writer

	▪ Sections 8.7 Product Storage added ▪ Section 8.8 Product Return and 8.9 Product Accountability have been updated ▪ Section 9 Study Site Requirements added ▪ Section 10.2 Subject Enrollment has been edited for clarity ▪ Section 10.3 Inclusion Criteria has been updated ▪ Section 10.4 Exclusion Criteria has been updated ▪ Section 11.1 Schedule of Events has been updated ▪ Section 11.2 Data Collection has been updated ▪ Section 11.2 Table 2 updated to clarify adverse event collection to occur at all visits ▪ Section 11.3 Scheduled Follow-up Visit Windows has been added ▪ Section 11.5 Subject Consent updated ▪ Section 11.7 Scheduled Follow-up Visits has been edited for clarity ▪ Section 11.8 Subject Questionnaires has been added ▪ Section 11.11 Recording Data has been updated ▪ Section 11.12 Deviation Handling has been updated ▪ Section 11.13.1. Study Exit has been updated ▪ Section 11.13.5 Lost to Follow-up has been updated with details ▪ Section 11.13.6 updated to clarify when to exit a subject if a mesh has been removed ▪ Section 11.13.7 Study Completed has been added ▪ Section 12.1 Potential Risks has been updated ▪ Section 12.2 Risk Minimization has been updated ▪ Section 13 Adverse Events and Device Deficiencies updated ▪ Section 13.1 updated to clarify procedure related adverse events ▪ Section 13.8 Subject Death added ▪ Section 13.9 Product Complaint Reporting added ▪ Section 14 Data Review Committees updated ▪ Section 15 Statistical Design and Methods updated	

	▪ Section 15.3. updated to allow for an additional interim analysis ▪ Section 16.1 Statement(s) of Compliance updated ▪ Section 17.1 Monitoring updated for remote monitoring ▪ Section 17.2 Data Management has been updated ▪ Section 17.3 Direct access to Source Data/Document updated ▪ Section 17.8 Reporting requirements added ▪ Section 17.10 Suspension or Early Termination updated ▪ Appendix B added in additional IFU for additional meshes ▪ Appendix E Subject Enrollment Decision Tree added	