Medtronic

Clinical Investigation Plan

Clinical Investigation Plan/Study Title	A multi-center post-market single arm prospective study of Parietene™ DS Composite Mesh in subjects undergoing ventral hernia repair
Clinical Investigation Plan Identifier	MDT17051PDS
Study Product Name	Parietene™ DS Composite Mesh
Sponsor/Local Sponsor	Covidien-Medtronic Minimally Invasive Therapies Group Surgical Innovations 15 Hampshire St Mansfield, MA, 02048 USA
Document Version	4.0
Version Date	03 December 2021

1. Investigator Agreement and Signature Page

Study Product Name	Parietene™ DS Composite Mesh
Sponsor	Covidien-Medtronic Minimally Invasive Therapies Group Surgical Innovations 15 Hampshire St Mansfield, MA, 02048 USA
Clinical Investigation Plan Identifier	MDT17051PDS
Version Number / Date	4.0, 03 DEC 2021
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 the International Conference on Harmonization Guidelines on Good Clinical Practice, United States Food and Drug Administration regulations. 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:	

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2. Glossary

Term	Definition
ADE	Adverse Device Effect
AE	Adverse Event
"Bridging" repair technique with the mesh placed in an "inlay" position	"Bridging" repair technique with the mesh placed in an "inlay" position is defined as cutting mesh to the size of the defect, positioning the mesh in the abdominal wall defect and then suturing the edges of the mesh to the edges of the defect.
BMI	Body Mass Index, calculated as per kg/m2 (Kg is person's weight in Kg and m is the height in meters)
CDC	Centers for Disease Control and Prevention (USA)
CI	Confidence Interval
CIP	Clinical Investigation Plan (can be used synonymously with Protocol)
DD	Device Deficiency
eCRF	Electronic Case Report Form
FAS	Full Analysis Set – An analysis set including any subjects enrolled and receiving study device
General Surgeon	A surgeon who has received a "basic certificate", commonly referred to as "General Surgery Certificate"
GCP	Good Clinical Practice
Hernia Recurrence	A clinically manifested bulge or a protrusion exacerbated by a Valsalva maneuver
ICMJE	International Committee of Medical Journal Editors
ICH	International Conference on Harmonization
IFU	Instructions for Use
Incisional Ventral Hernia	A ventral hernia that developed after surgical trauma to the abdominal wall, including recurrences after repair of primary ventral hernias. (1)
IRB	Institutional Review Board
ISO	International Organization for Standardization

Term	Definition
MedDRA	Medical Dictionary for Regulatory Activities
Parastomal Hernia	An incisional hernia through the abdominal wall defect created during placement of a colostomy, ileostomy, or ileal conduit stoma
PMCF	Post Market Clinical Follow-Up
PPAS	Per Protocol Analysis Set – An analysis set consisting of a subset of the full analysis set of subjects who meet the primary endpoint (12-month assessment) and who did not deviate (major) from the protocol
Primary Ventral Hernia	A primary ventral hernia is a ventral hernia that was present at birth or that developed spontaneously without trauma to the abdominal wall as the cause of the hernia. (1)
QOL	Quality of Life
SAE	Serious Adverse Event
SADE	Serious Adverse Device Effect
USA	United States of America
Ventral Hernia	A ventral hernia is a hernia of the abdominal wall excluding the inguinal area, the pelvic area, and the diaphragm. (1)

3. Synopsis

Title	A multi-center post-market single arm prospective study of Parietene™ DS Composite Mesh in subjects undergoing ventral hernia repair
Clinical Study Type	Post-Market Study
Product Name	Parietene™ DS Composite Mesh
Sponsor	Covidien-Medtronic Minimally Invasive Therapies Group Surgical Innovations 15 Hampshire St Mansfield, MA, 02048 USA
Indication Under Investigation	Parietene™ DS Composite Mesh is indicated for the repair of ventral hernias. This on label indication will be investigated during this study.
Investigation Purpose	To confirm the clinical safety and performance of Parietene™ DS Composite Mesh in the short (1, 3 months), mid (12 months) and long term (24 months) when used for the repair of ventral hernias.
Product Status	Parietene™ DS Composite Mesh received 510(k) clearance by the FDA (USA) in June 2017. (K163212)
Primary Objective	The primary objective of this study is to assess hernia recurrence, within 12 months following the use of Parietene™ DS Composite Mesh in ventral hernia repair.
Secondary Objective	The secondary objective of this study is to assess clinical outcomes, within 24 months following the use of Parietene™ DS Composite Mesh in ventral hernia repair.
Study Design	This study is a single arm, prospective, multi-center, observational, post-market study to confirm the clinical safety and performance of Parietene™ DS Composite Mesh in ventral hernia repair. After IRB approvals, subjects who have signed an informed consent form (and who meet the eligibility criteria) and have received Parietene™ DS Composite Mesh will be enrolled in the study. Subjects will undergo elective ventral hernia repair using Parietene™ DS Composite Mesh and be evaluated pre- operatively, at the procedure, at discharge, within 1 month, 3 months, 12 months, and 24 months post-surgery. An interim analysis based on 30 subjects with complete 3-month visits to assess the short-term safety of the device will be used to support regulatory

	approval. Study enrollment will continue during interim analysis. The study will continue as a post market clinical follow-up (PMCF) with extended follow-up of subjects to assess the mid (12 months) and long (24 months) term safety and performance of the device. The study will include a minimum of 125 subjects who will be followed 24 months post-surgery. Subject participation in the study will last a maximum of 26 months and overall, the study is estimated to proceed for up to 38 months.
Primary Endpoint	Incidence of hernia recurrence within 12 months following Parietene™ DS Composite Mesh use in ventral hernia repair
Secondary Endpoints	The secondary endpoints will include: - Incidence of adverse device effects (ADEs) intra-operatively, at discharge, within 1 month, 3 months, 12 months, and 24 months following Parietene™ DS Composite Mesh use in ventral hernia repair - Incidence of hernia recurrence at 1, 3 and 24 months. The evaluation of hernia recurrence will be performed during a physical examination - Time to hernia recurrence and time to adverse device effect occurrence (from surgery time-point) - Carolinas Comfort Scale™ QOL questionnaire completed pre-operatively and at 1, 12 and 24 months postoperatively
Randomization	Study will not utilize any randomization or blinding
Sample Size	125 male or female adult subjects will be enrolled in a minimum of 4 USA sites who are undergoing elective ventral hernia repair
Inclusion/Exclusion Criteria	**Subjects are eligible to be enrolled in the study only if they meet all of the following criteria:** <u>Pre-Operative Inclusion Criteria</u> 1. Subject has provided informed consent 2. Subject is ≥18 years of age (at the time of consent) 3. Subject is undergoing elective ventral hernia repair (primary or incisional) with intraperitoneal mesh placement **Subjects will be excluded from the study if they meet any of the following criteria:** <u>Pre-Operative Exclusion Criteria</u> 1. BMI > 45 kg/m2 2. Subject is undergoing emergency surgery 3. Subject is pregnant or planning to become pregnant during study participation period 4. Subject is unable or unwilling to comply with the study requirements or follow-up schedule 5. Subject has comorbidities which, in the opinion of the Investigator,

	will not be appropriate for the study or the subject has an estimated life expectancy of less than 6 months 6. The subject has participated in another investigational drug or device research study within 30 days of enrollment 7. Subject has a parastomal hernia <u>Intra-operative Exclusion Criteria</u> 1. Subject's hernia repair is in a contaminated or infected site (CDC wound class 2-4; Section 17.2) as assessed by the Investigator(s) 2. Subject is undergoing "bridging" repair technique with the mesh placed in an "inlay" position 3. Surgeon is unable to completely remove existing mesh from prior surgery 4. Surgeon overlays 2 meshes Subject receives any mesh other than Parietene™ DS composite mesh
Study Procedures and Assessments	Subjects will be evaluated pre-operatively, during the procedure, at discharge, within 1 month, 3 months, 12 months, and 24 months post-procedure via in person visit or remote follow-up. Assessments to be conducted/data collected include: **Pre-operative data (Day -30 to 0):** • Eligibility criteria • Subject demographics • Informed consent • Pregnancy status • Medical and abdominal surgical history and relevant risk factors • Carolinas Comfort Scale™ QOL questionnaire – Pre-Operative assessment **Operative data (Day 0):** • Eligibility criteria (Intra-operative criteria) • Pregnancy status • Hernia defect description • Recurrence history, if applicable • Date of surgery, Operative time • Condition of Anesthesia / ASA Grade • Intraoperative wound contamination class (CDC classification) • Indication for ventral hernia surgery • Type of access, defect closure and surgical technique approach • Mesh size, mesh shape, lot number, positioning, and fixation • Antibiotic prophylaxis

	• Area of mesh overlap • Adverse events assessment • Surgeon satisfaction questionnaire **Discharge Data:** • Adverse events assessment • Length of hospital stay **1 Month Follow-up (± 14days)** • Hernia recurrence/reoperation • Adverse events assessment • Carolinas Comfort Scale™ QOL questionnaire - Post-Operative assessment • Adverse events assessment **3 Month Follow-up (± 14 days)** • Hernia recurrence/reoperation • Adverse events assessment **12 Month and 24 Month Follow-ups (± 30 days)** • Hernia recurrence/reoperation • Adverse events assessment • Carolinas Comfort Scale™ QOL questionnaire - Post-Operative assessment
Safety Assessments	All intra-operative and post-operative adverse events will be reported in the eCRF database. Listings of AEs will be generated including event description, severity and seriousness, relation to procedure, relation to the device and outcome. Adverse events will be reported to IRBs and regulatory authorities in accordance with the local IRB regulations and FDA regulations.
Statistics	**Sample size** Sample size has been determined based on an acceptable level of accuracy for the estimated rate of hernia recurrence at 12 months (primary endpoint). Previous studies of the predicate device (Proceed™ Surgical mesh) with similar study indications, population, and design (prospective study with a long-term follow-up with more than 100 subjects), have reported the incidence of recurrence at 12 months to range from 3.5% to 5.2%.*

95% confidence intervals obtained from incidence rates between 3.5% and 5.2% with N=100 subjects are shown below. Precision of the recurrence rates range from ± 3.6% to ± 4.4% as the recurrence rate increases.

	Recurrence rate at 12-month			
	3.5%	**4.0%**	**4.5%**	**5.2%**
N	100	100	100	100
95% CI	[0.0 % - 7.1 %]	[0.2% -	[0.4% - 8.6%]	[0.8% - 9.6%]
accuracy (+/-)	3.6%	3.8%	4.1%	4.4%

Anticipating an attrition rate of 20% at 12 months, 125 subjects will be enrolled for this study.

Statistical methods & Analysis Populations

Statistical analysis (mainly descriptive) for primary and secondary endpoints will be performed on the Full Analysis Set (FAS, including any subject enrolled and receiving study device) and on the Per Protocol Analysis Set (PPAS, a subset of the FAS of subjects who meet the primary endpoint and who did not deviate (major deviation from the protocol), for confirmatory analysis.

- Continuous variables will be summarized using counts, means, standard deviations, medians, minimum and maximum. Categorical variables will be summarized using frequencies and percentages.
- Time to events analyses using Kaplan Meier estimates and curve will be performed for time to recurrence or to adverse event occurrence

Statistical analysis will be performed using SAS version 9.4 and Minitab® Version 15.0.

Interim Analyses (During which enrollment will continue)

- Upon data entry of 30 subject's completion at 3-month follow-up
- Upon data entry of subjects at 12-month follow-up

*Berrevoet et al., 2009, Berreveot et al., 2014

4. Introduction

4.1 Background

A ventral hernia is a hernia of the abdominal wall excluding the inguinal area, pelvic area, and the diaphragm (1). It is comprised of an abnormal protrusion of abdominal cavity contents or pre-peritoneal fat through a defect or weakness in the abdominal wall. Hernias may occur spontaneously (primary hernia) or at the site of a previous surgical incision (incisional hernia).

Hernias can only be repaired by surgical procedure (2). Operative repair of abdominal wall hernias forms a part of the daily routine practiced by every general and visceral surgeon. Approximately 4 million laparotomies are performed in the United States annually, up to 30%- 45% of them resulting in incisional hernia (3). Approximately 250,000 ventral incisional hernia repairs are performed annually in the United States (4-6). The repair of ventral hernias can be performed through either an open or a laparoscopic technique by a simple interrupted suture repair or a mesh repair.

Use of prosthetic mesh repair is considered as standard of care for ventral hernia treatment (7). Depending on the surgical technique, the mesh may be implanted either in an intraperitoneal position, or outside of the abdominal cavity, such as onlay or inlay techniques. Surgical meshes are medical devices used to provide additional support to weakened or damaged tissue. The majority of surgical mesh devices currently available for use are constructed from synthetic materials and/or animal tissue. The mode of action of the mesh primarily relies on the strength provided by the structural component of the implant, i.e., the textile/tissue structure. The surgical mesh is intended to be progressively colonized by the host tissue following the cascade of biological mechanisms inherent to the wound healing and soft tissue remodeling, so that the mesh will ensure a long-term reinforcement of soft tissues.

Currently, various surgical mesh designs exist to accommodate the variety of surgical techniques in soft tissue repair and reconstruction by open and laparoscopic surgeries. In particular, composite meshes such as Parietene™ DS Composite Mesh, are composed of a textile with a temporary adhesion barrier on one side to allow intraperitoneal mesh placement during abdominal wall surgery while minimizing tissue attachment to the mesh in case of direct contact with the viscera.

The development of Parietene™ DS Composite Mesh relies on the long-term knowledge acquired by Medtronic in the development of surgical mesh for a variety of soft tissue repair procedures and the processing of implantable absorbable polymers. Parietene™ DS Composite Mesh was specifically developed as a fully synthetic alternative to the composite meshes currently available.

Medtronic has conducted a biocompatibility evaluation of Parietene™ DS Composite Mesh, compliant with the standard EN ISO 10993-1 (2009), which demonstrates the biological safety of the device. Pre-clinical animal testing comparing of Parietene™ DS Composite Mesh and Proceed™ Surgical Mesh (Studies 197164, 197165 and 198929), its predicate device, demonstrate that Parietene™ DS Composite

Mesh achieves at least equivalent performance in terms of tissue integration and minimizing tissue attachment in case of contact to the viscera.

4.2 Purpose

The purpose of this study is to confirm the clinical safety and performance of Parietene™ DS Composite Mesh in the short (1-month and 3-months), mid (12-months) and long term (24-months) when used for the repair of ventral hernias.

5. Objectives and Endpoints

5.1 Objectives

5.1.1 Primary Objective

The primary objective of this study is to assess hernia recurrence, within 12-months following the use of Parietene™ DS Composite Mesh in ventral hernia repair.

5.1.2 Secondary Objective

The secondary objective of this study is to assess clinical outcomes, within 24-months following the use of Parietene™ DS Composite Mesh in ventral hernia repair.

5.2 Endpoints

5.2.1 Primary Endpoint

Incidence of hernia recurrence within 12-months following Parietene™ DS Composite Mesh use in ventral hernia repair.

Hernia recurrence is defined as: A clinically manifested bulge or a protrusion exacerbated by a Valsalva maneuver. The evaluation of hernia recurrence will be performed during a physical examination and confirmed per site standard of care if necessary.

5.2.2 Secondary Endpoint

The secondary endpoints will include:

- Incidence of adverse device effects (ADEs) intra- operatively, at discharge, within 1-month, 3-months, 12-months, and 24-months following Parietene™ DS Composite Mesh use in ventral hernia repair
- Incidence of hernia recurrence at 1, 3 and 24 months. The evaluation of hernia recurrence will be performed during a physical examination

- Time to hernia recurrence and time to adverse device effect occurrence (from surgery time- point)
- Carolinas Comfort Scale™ QOL questionnaire completed pre-operatively and at 1, 12 and 24 months post-operatively (Section 17.2)

6. Study Design

This study is a USA based, single arm, prospective, multi-center, observational investigation to confirm the clinical safety and performance of Parietene™ DS Composite Mesh in ventral hernia repair.

After IRB approvals, subjects who have signed an informed consent form (who meet the eligibility criteria) and have received Parietene™ DS Composite Mesh will be enrolled in the study. Subjects will undergo elective ventral hernia repair using Parietene™ DS Composite Mesh and be evaluated pre-operatively, at the procedure, at discharge, within 1-month, 3-months, 12-months, and 24-months post-surgery.

An interim analysis based on 30 subjects with completed 3-month visits will assess the short-term safety of the device and will be used to support regulatory submission. Study enrollment will continue during interim analysis. The study will continue as a post market clinical follow-up (PMCF) with extended follow-up of subjects to assess the mid (12-months) and long (24-months) term safety and performance of the device. The study will include a minimum of 125 subjects in a minimum of 4 sites who will be followed 24 months post-surgery.

6.1 Duration

The duration of the study is estimated to be up to 38 months. Screening for subject eligibility may occur up to 30 days (inclusive) prior to the procedure and post-procedure subjects will be assessed at discharge, 1 month, 3 months, 12 months, and 24 months. In total subjects will participate in the study for a maximum of approximately 26 months (not including hospital stay).

6.2 Rationale

Parietene™ DS Composite Mesh was 510(k) Cleared by the FDA (USA) in June 2017 (K163212).

To assess short-, mid- and long-term clinical outcomes following use of Parietene™ DS Composite Mesh in ventral hernia repair, Medtronic is performing a prospective study in the US. Following Parietene™ DS Composite Mesh use, incidence of hernia recurrence and adverse device effects 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 eCRF.

6.3 Study Oversight

This study will utilize a Steering Committee. The Steering Committee advises on the scientific content of the study and provides input for execution. Members will be study site investigators. The purpose of the Steering Committee is to make recommendations on the conduct of the study, the analysis of data, and the communication of results in alignment with the Medtronic Publication and Authorship Policy as well as the Development of Clinical Publications standard operating procedures. The Steering Committee may also review aggregate adverse event data on an as needed basis. As membership may change, the current list of members can be made available upon request.

7. Product Description

7.1 General

Parietene™ DS Composite Mesh is designed to be placed in an intraperitoneal site by a laparoscopic or open approach. The mesh is composed of a permanent macroporous polypropylene textile on one side and a fully absorbable synthetic film on the other side. The film is adhered to the textile using a binding agent localized on the textile fibers. A violet marking is positioned on the mesh to help center and orient the mesh. Two non-absorbable pre-placed sutures are tied to the mesh to guarantee side differentiation.

- The macroporous textile is knitted from a permanent monofilament polypropylene yarn. This macroporous polypropylene textile, commercialized by Medtronic since 2014 (ie: Parietene™ macroporous mesh) was chosen for its optimized mesh performance that offers balanced mechanical properties meeting physiological needs – without any compromise on mesh resistance – and acceptable tissue integration.
- The synthetic film is made of an absorbable synthetic copolymer of glycolide, caprolactone, trimethylene carbonate, and lactide which is a polymer produced by Medtronic and clinically used since 2002 in the absorbable suture Caprosyn™.
- The binding agent and the violet marking are made of absorbable polycaprolactone. The D&C Violet No. 2 dye is used for the marking. The violet dye (D&C Violet No. 2) is used in the absorbable components of the device Parietex™ Composite Ventral Patch, which is marketed by Medtronic since 2012.
- The pre-placed sutures are made of an isotactic crystalline stereoisomer of polypropylene (a synthetic linear polyolefin) and polyethylene. The Copper Phthalocyanine Blue is used to color the sutures. These pre-placed sutures are Surgipro™ sutures which are manufactured by Medtronic have been and clinically used for more than 20 years.
- The permanent macroporous textile is designed to be placed over the abdominal wall to

ensure long term reinforcement of soft tissues, while the continuous absorbable film is designed to minimize tissue attachment to the mesh in case of direct contact with the viscera. The absorbable film is degraded within 105 days by hydrolysis.

It is estimated that 125 Parietene™ DS Composite Mesh devices will be used for this study.

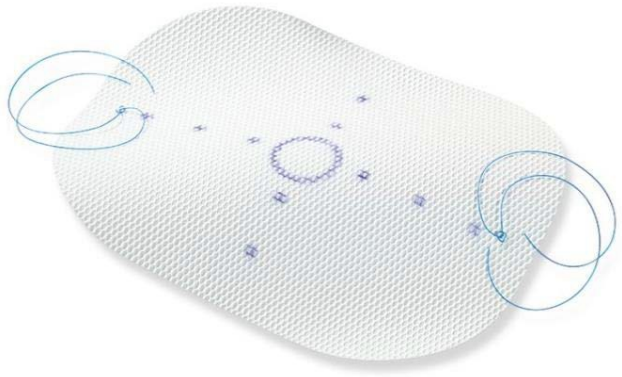

Figure 1. Parietene™ DS Composite Mesh

The product is available in multiples shapes with the following sizes:

Rectangular with round edges	Number of products per box	Circle	Number of products per box
10x15cm	1 or 3	Round 12cm	1 or 3
15x20cm	1 or 3	Round 15cm	1 or 3
20x25cm	1		
20x30cm	1		
30x35cm*	1		
*This mesh size can be used if it becomes available during the course of the study.			

7.2 Manufacturer

Parietene™ DS Composite Mesh is manufactured by Sofradim Production, (wholly owned subsidiary of Medtronic plc.) in Trévoux, France.

7.3 Packaging

The device is provided in a single sterile package that includes an expiration date and lot number and is intended for single use only.

7.4 Intended Population

Parietene™ DS Composite Mesh is intended for the reinforcement of abdominal wall soft tissue where a weakness exists. It is indicated for the repair of ventral hernias in accordance with the IFUs. Parietene™ DS Composite Mesh is not intended for the repair of parastomal hernias. Contraindications can be found in the device instructions for use.

7.5 Product Use

The Study Investigator(s) should use Parietene™ DS Composite Mesh according to the instructions for use (Section 17.4).

7.5.1 Summary of Operating Steps

1. Parietene™ DS Composite Mesh can be trimmed to the desired size.
    a. CAUTION: The pre-placed sutures are necessary to guarantee sides differentiation when deploying the mesh. If it is required to trim the device, ensure that the pre-placed sutures remain on the device. When trimming, the central marking may no longer be centered.
2. Should it be used in a laparoscopic approach, Parietene™ DS Composite Mesh can be rolled on either side (film side or textile side) without damaging the device.
    a. To facilitate mesh deployment within the abdominal cavity, it is suggested to roll the Parietene™ DS Composite Mesh with the film inside.
    b. It is recommended to introduce a mesh of size up to 20 x 15 cm in a trocar with minimum internal diameter of 10 mm, a mesh of size up to 30 x 20 cm in a trocar with minimum internal diameter of 12 mm. Mesh insertion capability may vary depending on rolled mesh size and graspers/trocars used.
    c. CAUTION: Do not force the mesh through the trocar. Inappropriate insertion may lead to textile and/or film damage. The meshes equal or larger than 35 x 30 cm are not designed for laparoscopic use.
3. The textile side (the porous side) should be placed against the abdominal wall for tissue integration, while the film side (the smooth side) should be facing the viscera to minimize tissue attachment.

4. The pre-placed sutures are positioned on the textile side to help with the mesh handling once it is unrolled in the abdominal cavity. These yarns allow to easily pinpoint the mesh textile side. They can be used for the transparietal fixation of the mesh.

    a. CAUTION: If the pre-placed sutures are not used for transparietal fixation, do not remove them until the placement of the mesh is secured.

5. The device should be centered on the defect. The central marking is designed to help centering. Use the violet dots on the mesh to facilitate its placement and orientation.

6. The choice of mesh size is determined by the surgeon. The edge of the mesh should be at least 3 cm over the edges of the defect(s).

    NOTE: The distance between two violet dots is approximately 2.5 cm.

7. The technique used to anchor the mesh (suture and/or tack) is left up to the practitioner.

    If the pre-placed sutures are used for transparietal fixation, it must be combined with standard fixation means (suture and/or tack) to guarantee a secured mesh fixation. It is suggested to fixate the mesh to the abdominal wall at a distance of approximately 1 cm from the edge of the mesh. A moderate and equal tension should be applied in all directions for fixation in order to account for wound shrinkage during the healing process and to prevent damage to the mesh.

For study purpose, it is recommended a minimum of 5 cm mesh overlap beyond the edges of the defect. In all study cases, every effort should be made to close the defect.

If barbed sutures are used for fixation, these sutures must have the specific indication for mesh fixation.

7.6 Product Training Requirements

Each Investigator participating in the clinical study and the associated clinical study staff will receive training on the clinical protocol, as well as Parietene™ DS composite mesh. Investigator(s) and study staff will be trained on device characteristics, shelf life, storage requirements, device use, and warnings, precautions, and contraindications.

7.7 Product Receipt and Tracking

Parietene™ DS Composite Mesh will be shipped to each site upon Sponsor collection and approval of all required regulatory documentation and each site will document the quantity, lot number(s), serial number(s), expiration date(s), and any additional details upon receipt in the Product Accountability Log.

7.8 Product Return

Any unused Parietene™ DS Composite Mesh will be returned to Medtronic after the last subject enrolled at the site and it will be documented in the product accountability log.

7.9 Product Accountability

Parietene™ DS Composite Mesh will be provided to each site upon Sponsor collection and approval of all required regulatory documentation. The Parietene™ DS Composite Mesh will be labeled "Exclusively for Clinical Investigations" and should be stored in a secure (locked) area at room temperature. Access should be limited to only authorized personnel listed on the Delegation of Authority log. Device accountability logs 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, lot number, etc.), transfer (if applicable) and return of all unopened study devices.

8. Study Site Requirements

8.1 Investigator/Investigation Site Selection

This study will be conducted by experienced surgeons in the field of hernia surgery, who are board certified/board eligible, qualified by education and training in accordance with US and hospital guidelines, education, and relevant experience appropriate to the use of the product and associated procedures. Investigator(s)/sites must have adequate time and resources to conduct the study throughout the duration of the study and have access to an adequate number of eligible subjects.

Investigator(s)/sites must be able to comply with applicable Institutional Review Board and regulatory requirements. Investigator(s) must not be debarred, disqualified, or working under sanctions in applicable regions. Qualifications are verified through valid CV and current licensing and maintained with study documentation.

The Investigator(s) and the associated clinical study staff will receive training on the management of the clinical study and the device according to the instructions for use.

9. Selection of Subjects

9.1 Study Population

One hundred and twenty-five (125) male or female subjects, aged ≥18 years at the time of consent, who meet the eligibility criteria and are undergoing elective ventral hernia repair using Parietene™ DS Composite Mesh will be enrolled at a minimum of 4 sites in the US. To reduce bias, enrollment will not exceed 40 subjects per site.

9.2 Subject Enrollment

After being informed of the nature of the study, the subject will provide written informed consent that has been approved by the sponsor and the appropriate IRB of the respective clinical site. A minimum of one hundred and twenty-five (125) subjects will be enrolled in the study at a minimum of 4 US sites with competitive enrollment not to exceed 40 subjects per site.

A subject is considered enrolled in the study when:

- it is confirmed that the ICF is signed,
- they meet all pre-operative inclusion criteria,
- they meet no pre- or intra-operative exclusion criteria,
- they have received Parietene™ DS Composite Mesh intraoperatively.

Adverse events will be collected starting at the time of skin incision and the subject must be followed for the full 24 months if the procedure was begun or completed with the study device. If ICF signature occurs more than 30 days before the procedure the subject is to be reconsented. No study procedures will be performed until informed consent form has been completed.

The elective ventral hernia repair procedure will be performed per the intraperitoneal onlay mesh technique (IPOM) by open or laparoscopic approach.

9.3 Inclusion Criteria

Pre-Operative Inclusion Criteria

1. Subject has provided informed consent
2. Subject is ≥18 years of age (at the time of consent)
3. Subject is undergoing elective ventral hernia repair (primary or incisional) with intraperitoneal mesh placement

9.4 Exclusion Criteria

Pre-Operative Exclusion Criteria

1. BMI > 45
2. Subject is undergoing emergency surgery
3. Subject is pregnant or planning to become pregnant during study participation period
4. Subject is unable or unwilling to comply with the study requirements or follow-up schedule
5. Subject has comorbidities which, in the opinion of the Investigator, will not be appropriate for the study or the subject has an estimated life expectancy of less than 6 months
6. The subject has participated in another investigational drug or device research study within 30

days of enrollment

7. Subject has a parastomal hernia

Intra-operative Exclusion Criteria

1. Subject's hernia repair is in a contaminated or infected site as assessed by the Investigator (Exclude CDC wound class 2-4; See Section 17.3)
2. Subject is undergoing "bridging" repair technique with the mesh placed in an "inlay" position
3. Surgeon is unable to completely remove existing mesh from prior surgery
4. Surgeon overlays 2 meshes
5. Subject receives any mesh other than Parietene™ DS composite mesh

10. Study Procedures

10.1 Schedule of Events

Procedure / Assessment	Screening (Day -30 to 0)	Operative (Day 0)	Discharge Assessment	1-Month (±14 days) Follow-up (Clinic / Remote Visit)	3-Month (±14 days) Follow-up (Clinic / Remote Visit)	12-Months (±30 days) Follow-up (Clinic / Remote Visit)	24-Months (±30 days) Follow-up (Clinic / Remote Visit)
	Can be combined						
Eligibility criteria	X[1]	X[1]					
Informed consent	X[2]						
Subject demographics	X						
Pregnancy status	X[1]	X[1]					
Medical and abdominal surgical history and relevant risk factors	X						
Carolina Comfort Scale™ (Appendix B)	X			X		X	X
Hernia defect description		X					
Recurrence history if applicable		X					
Date of surgery, Operative time		X					
Anesthesia / ASA grade		X					
Intraoperative wound contamination class		X					
Indication for ventral hernia surgery		X					
Type of access, defect closure and Surgical technique approach		X					
Mesh size, lot number, positioning, and fixation		X					
Antibiotic prophylaxis		X					
Area of mesh overlap		X					
Surgeon satisfaction questionnaire		X					
Adverse events		X	X	X	X	X	X
Length of hospital stay			X				
Hernia recurrence/reoperation				X	X	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.

10.2 Subject Screening (Day -30 to 0)

A screening visit will be used to confirm pre-operative eligibility and consent subjects. Subjects will be consented prior to the start of any study specific procedures. Data collected as part as standard of care may be utilized to establish eligibility. 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 IRB-approved informed consent form prior to participating in any study activities.

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

- Subject demographics (e.g., gender, age, ethnicity and race, weight, height)
- Serum or urine pregnancy test for females of child-bearing potential unless subject is surgically sterile or postmenopausal for at least 2 years, as documented in the Medical Record
- Medical and abdominal surgical history and relevant risk factors
- Carolinas Comfort Scale™ QOL questionnaire – Pre-Operative assessment (Section 17.2: Appendix B)

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.

10.3 Subject Consent

Subjects will be consented prior to any study procedures are undertaken. Subjects will be provided with a description of the device and procedure; risks, benefits, and alternative procedures; length of participation required; and information regarding injury and confidentiality. Subjects will be informed that their participation in this study is voluntary and they may refuse to participate or discontinue from the study at any time. Subjects will be given the opportunity to ask the Investigator and/or designee(s) questions so that they are adequately informed about the research. The informed consent form must be signed and dated by subject and Investigator or authorized designee(s) at time of consent. The informed consent process will be documented in the source records and a copy of the consent will be provided to the subject. If the consent form is signed outside of 30-day screening window, a new consent must be signed/dated within 30 days prior to surgery.

If new information becomes available that may affect a subject's decision to continue to take part in the study, this information will be discussed with the subject by the investigator or designee and new consent will be obtained in writing. The informed consent process will be documented in the source records and a copy of the consent will be provided to the subject.

10.4 Operative (Day 0)

The Study Investigator(s) should perform the elective surgical procedure according to the appropriate standard procedures and practices at the institution using Parietene™ DS Composite Mesh by Open or Laparoscopic approach with intra-peritoneal positioning. During the procedure, every effort should be made to close the defect and Parietene™ DS Composite Mesh used according to the instructions for use (Section 17.4 and 7.5). For study purpose, it is recommended a minimum of 5 cm mesh overlap beyond the edges of the defect and barbed sutures may be used for mesh fixation only if these sutures are claiming such indication. Additionally, the following procedures and assessments will be performed:

- Eligibility Criteria (Intra-operative criteria)
- Serum or urine pregnancy test for females of child-bearing potential unless the subject is surgically sterile or postmenopausal for at least 2 years (reconfirmed as necessary)
- Hernia defect description
- Recurrence history if applicable
- Date of surgery, Operative time (from time of skin incision to closure)
- Conditions of Anesthesia / ASA grade
- Intraoperative wound contamination class (CDC classification, Section 17.3: Appendix C)
- Indication for ventral hernia surgery
- Type of access, defect closure and surgical technique approach
- Mesh size, mesh shape, lot number, positioning, and type of fixation
- Antibiotic prophylaxis
- Area of mesh overlap
- Adverse events assessment
- Surgeon satisfaction questionnaire

10.4.1 Discharge Assessment

On the day of discharge the following assessments will be made:

- Adverse events assessment
- Length of hospital stay

10.4.2 1-Month Follow-up (+/- 14 Days) Visit

One (1) month post-operative, assessments will take place by delegated study personnel via an on-site visit. Assessments will include:

- Hernia recurrence/reoperation
- Adverse events assessment
- Carolinas Comfort Scale™ QOL questionnaire - Post-Operative assessment

  (Section 17.2: Appendix B)

10.4.3 3-Month Follow-up (+/- 14 Days) Visit

Three (3) months post-operative, the following assessment will take place during a subject visit:

- Hernia recurrence/reoperation
- Adverse events assessment

10.4.4 12-Month and 24-Month Follow-up (+/- 30 Days) Visit

Twelve (12) and twenty-four (24) months post-operative, the following assessment will take place during a subject visit:

- Hernia recurrence/reoperation
- Adverse events assessment
- Carolinas Comfort Scale™ QOL questionnaire- Post-Operative assessment

  (Section 17.2: Appendix B)

If at the twenty-four (24) month post-operative visit, after three (3) attempts, the subject is unwilling or unable to be seen by the investigator, medical records from primary care physician may be used. In addition, the Carolinas Comfort Scale™ QOL questionnaire may be answered over the phone to study personnel. In the event of these occurrences, subjects will not be compensated.

After the study has been completed no further study specific medical care will be provided and subjects will receive standard of care.

10.5 Unscheduled Follow-up Visits

In the event that a subject needs to be seen by the investigator for a complication outside of the study schedule of events, an unscheduled visit form must be completed. During any additional unscheduled visit(s) the following assessments will take place:

- Hernia recurrence/reoperation
- Adverse events assessment

10.6 Conducting Remote Subject Follow-up Visits

When an in-person subject follow-up visit is unable to occur, alternative follow up may be utilized. Remote or phone follow-up, medical record review, or follow-up with other healthcare practitioner may be utilized for 1-month, 3-month, 12-month and 24-month visits.

Clinic Electronic Medical Records (EMR) or medical records from primary care physicians may be used to assess hernia recurrence/reoperation and adverse events. Assessments will take place by delegated study personnel via remote follow-up visit(s).

- Assessments will include:
- Hernia recurrence/reoperation
- Adverse events assessment
- The Carolinas Comfort Scale™ QOL questionnaire (MDT17051PDS Clinical Investigation Protocol, Section 17.2: Appendix B) may be answered over the phone/remote to study personnel as requested at 1-month, 12-month and 24-month follow-up intervals, exempting 3-month follow-up visit as per the Parietene™ DS Composite Mesh in Ventral Hernia Repair CIP v3.

If hernia or hernia reoccurrence is suspected, the subject will be instructed to return to the clinic or hospital for diagnosis by the surgeon through clinical assessment. This should be done at the discretion of the Principal Investigator.

Data collection from remote follow-up visits will be entered in the EMR and via Oracle Clinical Remote Data Capture (OC RDC).

10.6.1 Protocol Deviations and Remote Follow-up

If a subject is unable to attend an in-person follow-up visit and a remote follow-up visit occurs, it is expected that there will be a protocol deviation (PD). Follow-up procedures, such as physical examination, may not be able to be recorded.

For clinical protocol safety, the subjects should follow the general instruction of the Principal Investigator and hospital/clinic.

The following guidelines should be followed:

- In order to account for each deviation, all deviations need to be reported individually, according to the study protocol requirements.

- If any follow-up procedure is unable to be performed due to a remote visit due to COVID-19 Pandemic, it should be documented in OC RDC as follows:
    - In the field "what was the reason for deviation?" please enter "COVID-19 impact." This is the acceptable rationale during the COVID 19 pandemic.

10.6.2 Subject Compensation and Remote Follow-up

In the event of remote subject follow-up visits, subject may be compensated if such compensation is included in the institution's Clinical Study Agreement.

10.7 Randomization and Treatment Assignment

No randomization will occur throughout the course of this study.

10.7.1 Blinding

No blinding will occur throughout the course of this study.

10.8 Assessment of Efficacy

Hernia recurrence within 24 months post-operatively will be recorded in the eCRF and used to assess the efficacy of the Parietene™ DS Composite Mesh.

10.9 Assessment of Safety

All intra-operative and post-operative subject adverse events will be reported in the database. Adverse events will be reported to IRBs and regulatory authorities in accordance with the local IRB regulations and FDA regulations.

10.10 Recording Data

This study will utilize an electronic database and eCRFs. All data requested on the eCRFs 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 eCRFs. Changes to data previously submitted to the sponsor will require a new electronic signature by the Investigator to acknowledge/approve the changes.

10.11 Deviation Handling

No changes to the protocol will be permitted by the Investigator(s). The investigator(s) must notify Medtronic and the reviewing IRB of any deviation from the Investigational Plan when specific to the protection of the life or physical well-being of a subject in an emergency per local IRB regulations. The

deviation will be recorded in the eCRFs and such notice must be given as soon as possible, but in no event later than 5 working days after the emergency has occurred. Except in such an emergency, prior written approval by Medtronic is required for changes in or deviations from the Plan. If these changes or deviations affect the scientific soundness of the Investigational Plan or the rights, safety, or welfare of human subjects the IRB will also be notified. All other deviations will be reported per the site's IRB deviation policy. Should any deviations from the Investigational Plan occur, these will be reviewed by Medtronic for their clinical significance and compliance to the protocol. If the deviation is performed without written approval from all parties, the investigator may be terminated from the study.

10.12 Subject Exit, Withdrawal or Discontinuation

10.12.1 Enrolled

A subject is considered enrolled in the study when it is confirmed that the ICF is signed, subject meets all pre-operative inclusion criteria, subject meets no pre- or intra-operative exclusion criteria, and the subject has received Parietene™ DS composite intra-operatively. The subject must be followed for the full 24 months if the procedure was begun or completed with the study device. See section 8.2 for additional details.

10.12.2 Screen Failure

10.12.2.1 Prior to Surgery

Subjects who provide study consent, but then are determined to be ineligible prior to the procedure due to Pre-Operative inclusion or exclusion criteria will be considered a "screen failure prior to surgery" and will not require additional study follow-up visits. The reason for the screening failure will be clearly recorded on the applicable eCRFs and subjects who are considered a Screen Fail prior to surgery will be replaced.

10.12.2.2 During Surgery

Subjects who provide study consent and experience skin incision but then are determined to be ineligible during the procedure due to intra-operative exclusion criteria (i.e., Subject receives any mesh other than Parietene™ DS Composite Mesh or meet other exclusion criteria) will be considered "screen failed during surgery" and will be followed until discharge (no additional follow-up). Subjects who have not met eligibility and are considered a Screen Fail during surgery, will be replaced.

10.12.3 Study Exit

A study exit eCRF 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. 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 did not meet inclusion/exclusion criteria
- Subject was not implanted with a (investigational) device
- Subject did not provide consent <or data use protection authorization>
- Subject chooses to withdraw (e.g., consent withdrawal, relocation to another geographic location)
- Investigator deems withdrawal necessary (e.g., medically justified, inclusion/exclusion criteria not met, failure of subject to maintain adequate study compliance)

If discontinuation is because of safety or lack of effectiveness, the subject may be asked to be followed for collecting safety data outside the clinical investigation.

10.12.4 Withdrawal

The reason for study exit will be documented on the applicable eCRFs. In the event the subject withdraws consent during the study, the date of withdrawal will be documented. If the study Investigator(s) 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(s). Withdrawn subjects will be not replaced.

10.12.5 Lost to Follow-up (LTFU)

Subject (LTFU) should be avoided as much as possible, and investigators are urged to do their utmost best to maintain subject follow-up compliance.

Subjects are not considered lost to follow-up until the end of the study, before the database is locked.

As is the case before documenting a missed visit, the following should take place and be documented before considering them LTFU.

- Three (3) phone calls should be made to the subject. 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 documentation.

- In case a subject can no longer be found, the monitor shall check the appropriateness of the site's attempts to contact the subject.

Prior to final database lock, when all due diligence attempts to contact have been made, the subject is considered lost to follow-up. The Sponsor must be notified and the Exit eCRF must be completed.

11. Risks and Benefits

11.1 Potential Risks

Surgeons participating in this study are experienced with the known risks related to standard of care for hernia repair procedures. Risks associated with the use of Parietene™ DS composite include, but are not necessarily limited to: seroma, hematoma, recurrence, adhesions, bowel obstruction, fistula formation, infection, inflammation, acute and chronic pain, extrusion/erosion and/or allergic reaction to the components of the device.

The instructions for use (IFU) and training will guide surgeons on proper use of the device. Surgeons will undergo training on the device prior to participation in the study.

As with any device, there is always a risk of a rare or previously unknown side effect developing from the treatment or use of the device. Overall, the residual risk for Parietene™ DS Composite Mesh was deemed acceptable.

11.2 Potential Benefits

The information obtained from this study will be used to confirm the safety and performance of Parietene™ DS Composite Mesh in ventral hernia repair. This information may lead to findings that may or may not result in a reduction of adverse events for future subjects.

11.3 Risk Minimization

Parietene™ DS Composite Mesh was 510(k) Cleared by the FDA (USA) in June 2017. Consequently, Parietene™ DS Composite 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 Parietene™ DS Composite Mesh and concurrent medical interventions.

12. Adverse Events and Device Deficiencies

All information will be collected throughout the study duration, starting at the time of signing the Informed Consent. Reporting of these events to Medtronic will be occur on an AE eCRF. Each event must

be reported separately. Documented pre-existing conditions will not be considered AEs unless the nature or severity of the condition has worsened. For AEs that require immediate reporting (Table 2), initial reporting may be done by phone, fax, or on the CRF completing as much information as possible. The completed AE eCRF must be submitted to Medtronic as soon as possible. Any indication/treatment associated with the treatment of an AE must be reported.

12.1 Adverse Events

Potential Adverse Events associated with the use of Parietene™ DS composite in ventral hernia repair could include but are not limited to; seroma, hematoma, recurrence, adhesions, bowel obstruction, fistula formation, infection, inflammation, acute and chronic pain, extrusion/erosion and/or allergic reaction to the components of the device. In regard to pain, the following definitions will be used for this study:

- Acute pain (pain that resolves within three months of surgery)
- Chronic pain (pain that lasts more than three months after surgery)

For study purposes, the following occurrences are considered to be unavoidable adverse events as they are expected observations following surgical procedures (primarily associated with anesthesia) and will not be considered reportable AEs, as long as the event is not associated with significant sequelae, does not prolong hospitalization, and responds to standard medical therapy:

- Post-Operative transient nausea determined to be procedure related within the first 24 post-operative hours.
- Post-Operative transient emesis determined to be procedure related within the first 24 post-operative hours.
- Post-Operative constipation determined to be procedure and/or medication related for the duration of medication administration for management of pain.
- Post-Operative pain that the Investigator considers common and within normal limits for the procedure and is well-managed with medication.

All Adverse Events and Device Deficiencies will be collected and documented in the eCRF starting at the time of enrollment for all subjects, up to and including 24 months follow-up and monitored until resolved if possible.

For Adverse Events that require immediate reporting initial reporting may be done by phone, fax, e-mail or on the eCRF, completing as much information as is available. The original fully completed Adverse Event eCRF must be submitted to Medtronic as soon as possible. In addition, Investigators are obligated to report Adverse Events in accordance with the requirements of their IRB.

12.2 Device Deficiency

Device deficiencies (DD) information will be collected throughout the duration of the study and required to be reported to Medtronic. If there is an adverse event that results from a device deficiency, that specific event would be recorded on the appropriate Adverse Event eCRF and Device Deficiency eCRFs. If the device deficiency did not lead to an adverse event but could have led to a serious adverse device effect (i.e., if suitable action had not been taken, if intervention had been made, or if the circumstances had been less fortunate) it requires immediate reporting. Device deficiencies that did not lead to an AE should be reported on the Device Deficiency eCRF (one for each device deficiency).

In the event of a device deficiency, the device should be returned to Medtronic for analysis, if possible. Instructions for returning the study device will be provided. Device deficiencies should also be documented in the subject's medical record.

12.3 Definitions and Classifications

All definitions are provided in Table 1: Adverse Event and Device Deficiency Definitions.

Table 1: Adverse Event and Device Deficiency Definitions

Event Type	Definition
Adverse Event (AE)	Any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device. *NOTE 1: This definition includes events related to the investigational medical device and the procedures involved.* *NOTE 2: For users or other persons, this definition is restricted to events related to investigational medical devices.*
Serious Adverse Event (SAE)	A serious adverse event (SAE) that has: a) led to death, b) led to a serious deterioration in the health of the subject, resulting in 1) resulted in a life-threatening illness or injury, or 2) resulted in a permanent impairment of a body structure or a body function, or 3) in-patient or prolonged hospitalization, or 4) medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function, c) led to fetal distress, fetal death or a congenital abnormality or birth defect.[10,11] *NOTE: Planned hospitalization for a pre-existing condition, or a procedure required by the clinical investigational plan, without serious deterioration in health, is not considered a SAE.*
Adverse Device Effect (ADE)	An Adverse Device Effect related to the use of an investigational medical device.

Table 1: Adverse Event and Device Deficiency Definitions

Event Type	Definition
	NOTE 1: This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device.[10] *NOTE 2: : This definition includes any event resulting from use error or from intentional misuse of the investigational medical device*
Serious Adverse Device Effect (SADE)	A Serious Adverse Device Effect is an adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event
Unavoidable Adverse Event	An Unavoidable Adverse Event inherent to a surgical procedure that is expected to occur in all subjects for a projected duration according to the Investigator's opinion.
Device Deficiency	Inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety, or performance. *NOTE: Device deficiencies include malfunctions, use errors, and inadequate labeling.*

12.4 Evaluation and Documentation of Adverse Events and Device Deficiencies

Investigators are required to evaluate and document in the subject's medical records all adverse events and device deficiencies (per the definitions in Table 1: Adverse Event and Device Deficiency Definitions) observed in study subjects from the time they are enrolled until they are exited from the study.

12.5 Adverse Event and Device Deficiency Classification

All AEs and DDs will be reviewed by a Medtronic representative. AEs will be classified according to the definitions provided (Table 2: Adverse Event Classification Responsibilities).

Upon receipt of an AE, a Medtronic representative will review the AE/DD for completeness and accuracy and when necessary will request clarification and/or additional information from the Investigator. Medtronic will utilize MedDRA for Regulatory Activities, to assign a MedDRA term for each AE based on the information provided by the investigator.

AEs and DDs will be classified according to the standard definitions as outlined in the table below:

Table 2: Adverse Event Classification Responsibilities

What is classified?	Who classifies?	Classification Parameters
Relatedness	Investigator	Study Device, Study Procedure
	Sponsor	Study Device, Study Procedure
Seriousness	Investigator	SAE, DD with SADE potential
	Sponsor	SAE, DD with SADE potential
Diagnosis	Investigator	Based on presenting signs and symptoms and other supporting data
	Sponsor	MedDRA term assigned based on the data provided by Investigator
Death Classification	Investigator	Sudden Cardiac, Non-sudden Cardiac, Non-Cardiac, Unknown

Severity will be defined according to the following criteria:

Mild	Awareness of event, but easily tolerated
Moderate	Discomfort enough to cause some interference with activities of daily living (ADL)
Severe	Incapacitating, with an inability to perform ADL

An AE can be classified as severe and not deemed an SAE. Similarly, an SAE is not automatically severe in nature. These assessments are made by the site Principal Investigator.

12.5.1 Adverse Event Relationship Classifications

Causality assessments define the relationship between the use of the medical device (including the medical-surgical procedure) and the occurrence of each adverse event. 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 for procedure and device. The sponsor and the investigator(s) will use the following definitions to assess the relationship of the adverse event to the investigational medical device and procedures:

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

1. the event is not a known side effect of the product category the device belongs to or of similar devices and procedures
2. the event has no temporal relationship with the use of the device or the procedures;
3. the serious event does not follow a known response pattern to the medical device (if the response pattern is previously known) and is biologically implausible;
4. the discontinuation of medical device application or the reduction of the level of activation/exposure - when clinically feasible – and reintroduction of its use (or increase of the level of activation/exposure), do not impact on the serious event;

5. the event involves a body-site or an organ not expected to be affected by the device or procedure;
6. the serious event can be attributed to another cause (e.g., an underlying or concurrent illness/ clinical condition, an effect of another device, drug, treatment or other risk factors);
7. the event does not depend on a false result given by the device used for diagnosis, when applicable;
8. harms to the subject are not clearly due to use error;
9. In order to establish the non-relatedness, not all the criteria listed above might be met at the same time, depending on the type of device/procedures and the serious event.

Unlikely: the relationship with the use of the device seems not relevant and/or the event can be reasonably explained by another cause, but additional information may be obtained.

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

Probable: the relationship with the use of the device seems relevant and/or the event cannot be reasonably explained by another cause, but additional information may be obtained.

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

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

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

The Sponsor and the Investigator(s) will distinguish between the adverse events related to the device and those related to the procedures (any procedure specific to the clinical investigation). An adverse event can be related both to procedures and the device. Complications of procedures are considered not related if the said procedures would have been applied to the subjects also in the absence of device use/application.

In some 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 Investigator(s) will make the maximum effort to define and categorize the event and avoid these situations.

12.6 Adverse Event and Device Deficiency Reporting Requirements

Investigators are obligated to report applicable adverse events to the study sponsor and in accordance with reporting requirements of their IRB.

Events will be reviewed by the sponsor to determine any reporting obligations to IRBs and regulatory authorities.

SAEs need to be reported to the sponsor within 24 hours of becoming aware.

Assessment of the occurrence of an AE will be based on changes in the subject's physical examination, laboratory results and/or signs and symptoms. Adverse events will be monitored until a subject completes the study, or 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 an AE eCRF and applicable source documentation. 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). For subjects who are screen failure during surgery (Section 10.12.2.2) AEs will be recorded at time of enrollment until discharge. For other subjects, AEs occurring at time of enrollment 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 pre-existing condition found at the time of screening, unless the condition has worsened since enrollment.

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

All AEs observed during the course of this study, regardless of severity, seriousness, or relationship to the device and procedure will be recorded on the appropriate AE eCRF.

12.7 Study Contact Information

Questions regarding safety or medical procedures should be directed to Medtronic. All other questions including emergency contact for reporting serious adverse events and serious adverse device effects should be directed to Medtronic Surgical Innovations (Formerly MITG Surgical Innovations), Clinical Research. Sponsor contact information is subject to change and will be maintained in a document separate from the clinical investigation plan. Sponsor contact information available to sites upon request.

12.8 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.

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

13. Data Review Committees

13.1 Independent Medical Monitor

Medtronic will utilize an Independent Medical Monitor to provide an independent adjudication of pre-specified adverse events in support of protocol defined endpoint data. The Independent Medical Monitor will be a surgeon in the field of hernia surgery, who is board certified/board eligible, qualified by education and training, and relevant experience appropriate to the use of the product and associated procedures that is not affiliated with an investigative center. The Independent Medical Monitor will contribute to safety aspects of the clinical study and will review any potential adverse events collected related to the procedure/product, and all SAEs as determined by sponsors or sites.

The Independent Medical Monitor will be blinded to the investigational sites.

14. Statistical Design and Methods

14.1 Statistical Test Methods & Analysis Populations

Statistical analysis consists mainly of a descriptive analysis, and will be performed on:

- the Full Analysis Set (FAS, including any subject enrolled and receiving study device) representing the primary analysis population,
- the Per Protocol Analysis Set [PPAS, a subset of the FAS of subjects who meet the primary endpoint (12-month assessment) and who did not deviate (major) from the protocol], as confirmatory analysis and,
- the Safety Analysis Set (any subject with skin incision including those who are 'screen failure during surgery') for safety and efficacy analysis

Continuous variables will be summarized using counts, means, standard deviations, medians, minimum and maximum. Categorical variables will be summarized using frequencies and percentages.

Time to events analyses using Kaplan Meier estimates and curve will be performed for time to recurrence or to adverse event occurrence

Changes to the planned statistical analysis as defined in the protocol will be documented in the statistical analysis plan and clinical study report.

Statistical analysis will be performed using SAS version 9.4 and Minitab® Version 15.0.

For the purposes of study analysis and statistics adverse event will be defined as procedure related adverse events and adverse device effects.

14.2 Interim Analysis

Preliminary analysis will be conducted in the study when 30 enrolled subjects complete the 3-month follow-up time-point. The objective is to confirm safety of the product at 3 months. This 3-month time-point is consistent with the wound healing period and the Parietene™ DS Composite Mesh film degradation profile (completely degraded by bulk hydrolysis in less than 15 weeks). This interim analysis is driven by regulatory needs, to support CE marking submission.

Through analysis of clinical data available on a predicate device (Proceed™ surgical mesh) and similar Medtronic composite meshes (Parietene™ Composite Mesh, Parietex™ Composite Mesh) used in ventral hernia repair (primary and incisional) by open or laparoscopic approach assessed during short-term post-surgery report the following adverse event rates:

- 10.6% on the equivalent, Proceed™ surgical mesh used in laparoscopic ventral hernia repair at 3- 6 weeks follow-up (9),
- 14.3% on Parietene™ Composite mesh used in laparoscopic ventral hernia repair at 10 weeks follow-up (range 6-25 weeks) (10),
- To 25%, on Parietex™ Composite mesh used in laparoscopic and open ventral hernia repair after 2 months follow-up with a population of 30 subjects (11), we obtain the following binomial probabilities to observe one or more event(s):

Based on these studies, adverse event rates were estimated to range between 11% and 25% and used to generate binomial probabilities to observe at least 1 or 2 AEs with a sample size of 30 subjects as shown in the table below.

N=30 subjects	**Hypothetic procedure related adverse event rate**					
prob. to observe:	11%	12%	14%	17%	20%	25%
≥ 1 AE	97.0%	97.8%	98.9%	99.6%	99.9%	100.0%
≥ 2 AEs	85.7%	89.0%	93.6%	97.3%	98.9%	99.8%

With an N=30 of enrolled and evaluable subjects at the time of interim analysis, and assuming an 11% adverse event rate, there is a 97% probability to observe at least 1 adverse event and an 85.7% probability to observe at least 2 adverse events. In addition, the probability to observe adverse events increases as the adverse event rate increases to a maximum of 100% and 99.8% for observation 1 and 2 adverse events respectively at an adverse event rate of 25%.

An additional interim analysis is planned to occur for completed 12-month follow-up visit data.

For the purpose of the interim analysis and in accordance with regulatory requirements all safety data will utilize MedDRA and are to be assessed using the potential risks identified and defined in Section 12.3. The seriousness and relation of the adverse event to the device and procedure is assessed first by the Principal Investigator of the site, and if applicable by the external Medical Monitor or Internal Medtronic Safety Representative. Reconciliation is made between these assessments and the most conservative assessment will be used.

14.3 Statistical Analysis Endpoints

14.3.1 Primary Endpoint

Incidence of hernia recurrence within 12 months will be calculated on the FAS subjects who reach the 12-month follow-up including any subject with hernia recurrence diagnosed within the 12-month period following surgery (even if the subject has withdrawn from the study before the 12-month assessment).

The primary endpoint will be summarized using count, percentage, and the corresponding 95% confidence interval. Sub-group analyses on primary endpoints will be performed according to study needs and will be described in the Statistical Analysis Plan and the Clinical Study Report.

14.3.2 Secondary Endpoints

- Incidence of ADEs intra-operatively will be calculated on the FAS subjects who reach the corresponding time point, including any subject experiencing hernia recurrence, AEs or ADE within the corresponding follow-up period.
- Incidence of hernia recurrences will be calculated on the FAS subjects who reach the corresponding time point.
- Time to hernia recurrence, as well as time to AE occurrence analyses will be run using Kaplan Meier estimate and curve.
- Subject quality of life (QoL) questionnaires will be evaluated using the Carolinas Comfort Scale™ (Appendix B), and statistical analysis will follow the corresponding analysis guideline.
- Length of hospital stay will be summarized using count, mean, standard deviation, median, minimum, and maximum.

Subgroup analyses on secondary endpoints will be performed according to study needs and will be described in the statistical analysis plan and the clinical study report.

14.4 Safety Assessment

Most of the safety endpoints are part of secondary endpoints and method of evaluation are described above.

Incidence of Adverse device effect, as well as SAEs, and SADEs will be calculated on the Full Analysis Set, Safety Analysis Set and Per protocol Analysis Set and summarized by counts and percentages.

Listings of AEs will be generated including event description, severity and seriousness, relation to procedure, relation to the device and outcome.

In the case that a subject becomes pregnant postoperatively, a deviation will be submitted, and they will be followed for safety assessment. They will not be included in the primary or secondary endpoint analyses.

14.5 Sample Size Determination

Sample size has been determined based on an acceptable level of accuracy for the estimated rate of hernia recurrence at 12 months (primary endpoint).

Previous studies of the predicate device (Proceed™ Surgical mesh) with similar study indications, population, and design (prospective study with a long-term follow-up with more than 100 subjects), have reported the incidence of recurrence at 12 months to range from 3.5% to 5.2%. (8, 9).

95% confidence intervals obtained from incidence rates between 3.5% and 5.2% with N=100 subjects are shown below. Precision of the recurrence rates range from ± 3.6% to ± 4.4% as the recurrence rate increases.

	Recurrence rate at 12-month (1 year)			
	3.5%	**4.0%**	**4.5%**	**5.2%**
N	100	100	100	100
95% CI	[0.0 % - 7.1 %]	[0.2% - 6.7%]	[0.4% - 8.6%]	[0.8% - 9.6%]
accuracy (+/-)	3.6%	3.8%	4.1%	4.4%

Anticipating an attrition rate of 20% at 12 months, 125 subjects will be enrolled for this study.

14.6 Handling of Missing Data

No data imputation will be performed for missing data unless otherwise noted in statistical analysis plan. All practical monitoring and follow-up steps will be taken to ensure complete and accurate data collection.

15. Ethics

15.1 Statement(s) of Compliance

This clinical investigation will be conducted in accordance with the protocol, with the ethical principles that have their origin in the Declaration of Helsinki, Good Clinical Practice guideline and any regional or national regulations such as FDA regulations (US), as appropriate. All principles of the Declaration of

Helsinki have been implemented in this clinical study by means of the subject informed consent process, IRB approval, clinical study training, clinical study registration, publication policy.

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

- 21 CFR Part 11 (Electronic Records, Electronic Signatures)
- 21 CFR Part 50 (Protection of Human Subjects)
- 21 CFR Part 54 (Financial Disclosure by Clinical Investigators)
- 21 CFR Part 56 (IRBs)
- 21 CFR Part 803 (Medical Device Reporting)
- The CTA
- Procedures described within this CIP
- Local EC Requirements

The clinical investigation will not begin until all necessary approvals/favorable opinions are obtained from the appropriate IRB. Should an IRB impose any additional requirements, they will be followed.

Information regarding the study and study data will be made available via publication on clinicaltrials.gov. Additionally, the results of this study will be offered for publication at the conclusion of the study, if participating investigator(s) believe the data warrants publication in an appropriate journal.

16. Study Administration

16.1 Monitoring

Site visits will be conducted by authorized Medtronic representative(s) to qualify potential sites, conduct site initiation, ensure compliance, assess informed consent process, conduct interim monitoring visits to monitor study data, subjects' medical records, eCRFs, device accountability, device use and storage, IRB submissions, regulatory binder in accordance with current protocol, ICH, GCPs and the respective local and national regulations and guidelines (if applicable) as well as close-out site activities. The Study Investigator(s) and the investigating site will permit authorized clinical research personnel from Medtronic or contracted by Medtronic to review completed eCRFs, IRB decisions, and Investigator and clinical site records at regular intervals throughout the study as well as permit study-related monitoring, audits, IRB review, and regulatory inspection(s) by providing direct access to source data/documents per the monitoring plan. Additionally, subject charts and clinical records will be requested and reviewed so that protocol adherence and source documentation can be verified. In instances where data protection regulations prohibit the direct examination of hospital records by the

study Sponsor or designee(s), the Investigator(s) will cooperate in a system of source data verification with the Sponsor. Monitoring may be performed with in person visits or remotely, when applicable.

To ensure the rights, safety, and welfare of study subjects are being maintained, the monitor will maintain assurance that all study staff are trained on the study protocol and use of the study devices. If the monitor discovers that an investigator is not complying with the signed Investigator Agreement, the

investigational plan, applicable laws, or any conditions of approval imposed by the reviewing IRB, the monitor will report to the Sponsor and take such steps necessary to promptly secure compliance. If compliance cannot be secured, device shipments to the investigator may be discontinued and the investigator's participation in the investigation terminated. The monitor shall also require such an investigator to dispose of or return the device, unless this action would jeopardize the rights, safety, or welfare of a subject.

16.2 Data Management

Data review will be performed to identify possible data discrepancies. Manual and/or automatic queries will be created in the Oracle® Remote Data Capture (RDC) system and will be issued to the site for appropriate response. The site staff will be responsible for resolving all queries in the database. Adverse Events will be coded per Medical Dictionary for Regulatory Activities (MedDRA).

This study will be using a 21 CFR Part 11 compliant electronic data capture system. All system level validation documentation is retained within the Medtronic Information Systems group.

16.3 Direct Access to Source Data/Documents

Investigator(s)/institution(s) will permit study-related monitoring, audits, IRB review, and regulatory inspection(s), and provide direct access to source data/documents as per local policies and regulations.

16.4 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 eCRFs, 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, IRBs, 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 subject list to enable subjects' records to be identified.

16.5 Liability

Medtronic 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 IRB.

16.6 Clinical Investigation Plan (CIP) / Protocol Amendments

A CIP/Protocol amendment will be prepared when there are revisions that are significant changes or corrections, or modifications that impact subject safety, ethical conduct, data integrity or study design. CIP/Protocol amendments must undergo review and approval by the sponsor, IRB, and any appropriate regulatory authority, and will be logged in the document version history (Section 18). IRB approval, regulatory authority approval (if applicable), site training and a new Acknowledgement form will be signed and returned before any new enrollment takes place.

16.7 Record Retention

The investigator(s) 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 IRB, 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, must be kept for a period of no less than 24 months after the latter of the following two dates: the date on which this investigation is terminated or completed. 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. All data and documents should be made available if requested by relevant authorities.

16.8 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 investigator(s) provided that such publication or use is in accordance with this protocol, the Medtronic Publication and Authorship Policy, and the Clinical Investigation Agreement. Investigator(s) 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).

16.9 Suspension or Early Termination

Medtronic or appropriate regulatory authorities reserve the right to suspend or discontinue the study at any stage, with 60 days written notice to all investigators, all institutions, all reviewing IRBs, all subjects and subjects' personal physicians and any applicable regulatory agencies. Similarly, investigator(s) may withdraw from the study at any time, subject to providing written notification to Medtronic 60 days prior to the date they intend to withdraw. However, Medtronic and investigator(s) will be bound by their obligation to complete the follow-up of subjects already enrolled in the study. The subjects must be followed according to the clinical protocol, and information obtained during subject follow-up shall be reported to Medtronic on the appropriate eCRF. Either Medtronic or the investigator may also terminate the agreement if the other breaches the terms or conditions of the agreement and fails to address the breach within 30 days after receiving written notice. Furthermore, the institution may immediately terminate the study for concerns related to Study Subject health and safety.

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18. Appendices

18.1 APPENDIX A: List of Investigators and Institutions

Investigational Site information including addresses, contact information, Principal Investigators, their respective IRBs 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.

18.2 APPENDIX B: Carolinas Comfort Scale™

Carolinas Comfort Scale ™

NOT FOR USE WITHOUT SCORING ALGORITHM AND LICENSE AGREEMENT

Carolinas Medical Center

Division of Gastrointestinal and Minimally Invasive Surgery

Name: _____

Date of Survey: _____

0 = No symptoms
1 = Mild but not bothersome symptoms
2 = Mild and bothersome symptoms
3 = Moderate and/or daily symptoms
4 = Severe symptoms
5 = Disabling symptoms

A. Preoperative assessment:

Please answer ALL questions for each of the 8 activities.
Use N/A if an activity was not performed.

1. While lying down, do you have							
b) pain	0	1	2	3	4	5	N/A
2. While bending over, do you have							
b) pain	0	1	2	3	4	5	N/A
c) movement limitations	0	1	2	3	4	5	N/A
3. While sitting up, do you have							
b) pain	0	1	2	3	4	5	N/A
c) movement limitations	0	1	2	3	4	5	N/A
4. While performing activities of daily living (i.e. getting out of bed, bathing, getting dressed), do you have							
b) pain	0	1	2	3	4	5	N/A
c) movement limitations	0	1	2	3	4	5	N/A
5. When coughing or deep breathing, do you have							
b) pain	0	1	2	3	4	5	N/A
c) movement limitations	0	1	2	3	4	5	N/A
6. While walking, do you have							
b) pain	0	1	2	3	4	5	N/A
c) movement limitations	0	1	2	3	4	5	N/A
7. When walking up the stairs, do you have							
b) pain	0	1	2	3	4	5	N/A
c) movement limitations	0	1	2	3	4	5	N/A
8. While exercising, do you have							
b) pain	0	1	2	3	4	5	N/A
c) movement limitations	0	1	2	3	4	5	N/A

Carolinas Comfort Scale ™

NOT FOR USE WITHOUT SCORING ALGORITHM AND LICENSE AGREEMENT

Carolinas Medical Center

Division of Gastrointestinal and Minimally Invasive Surgery

Name: _____

Date of Surgery: _____

Date of Survey: _____

0= No Symptoms
1= Mild but not bothersome symptoms
2= Mild and bothersome symptoms
3= Moderate and/or daily symptoms
4 = Severe symptoms
5= Disabling symptoms

B. Post-operative assessment:

Please answer ALL questions for each of the 8 activities.

Use N/A if an activity was not performed.

1. While lying down, do you have							
a) sensation of mesh	0	1	2	3	4	5	N/A
b) pain	0	1	2	3	4	5	N/A
2. While bending over, do you have							
a) sensation of mesh	0	1	2	3	4	5	N/A
b) pain	0	1	2	3	4	5	N/A
c) movement limitations	0	1	2	3	4	5	N/A
3. While sitting up, do you have							
a) sensation of mesh	0	1	2	3	4	5	N/A
b) pain	0	1	2	3	4	5	N/A
c) movement limitations	0	1	2	3	4	5	N/A
4. While performing activities of daily living (i.e. getting out of bed, bathing, getting dressed), **do you have**							
a) sensation of mesh	0	1	2	3	4	5	N/A
b) pain	0	1	2	3	4	5	N/A
c) movement limitations	0	1	2	3	4	5	N/A
5. When coughing or deep breathing, do you have							
a) sensation of mesh	0	1	2	3	4	5	N/A
b) pain	0	1	2	3	4	5	N/A
c) movement limitations	0	1	2	3	4	5	N/A
6. While walking, do you have							
a) sensation of mesh	0	1	2	3	4	5	N/A
b) pain	0	1	2	3	4	5	N/A
c) movement limitations	0	1	2	3	4	5	N/A
7. When walking up the stairs, do you have							
a) sensation of mesh	0	1	2	3	4	5	N/A
b) pain	0	1	2	3	4	5	N/A
c) movement limitations	0	1	2	3	4	5	N/A
8. While exercising, do you have							
a) sensation of mesh	0	1	2	3	4	5	N/A
b) pain	0	1	2	3	4	5	N/A
c) movement limitations	0	1	2	3	4	5	N/A

18.3 APPENDIX C: Centers for Disease Control (CDC) Wound Class

CDC Wound Class (January 2017)	Definition:
1	**Clean:** An uninfected operative wound in which no inflammation is encountered and the respiratory, alimentary, genital, or uninfected urinary tracts are not entered. In addition, clean wounds are primarily closed and, if necessary, drained with closed drainage. Operative incisional wounds that follow nonpenetrating (blunt) trauma should be included in this category if they meet the criteria.
2	**Clean-Contaminated:** Operative wounds in which the respiratory, alimentary, genital, or urinary tracts are entered under controlled conditions and without unusual contamination. Specifically, operations involving the biliary tract, appendix, vagina, and oropharynx are included in this category, provided no evidence of infection or major break in technique is encountered.
3	**Contaminated:** Open, fresh, accidental wounds. In addition, operations with major breaks in sterile technique (e.g., open cardiac massage) or gross spillage from the gastrointestinal tract, and incisions in which acute, nonpurulent inflammation is encountered including necrotic tissue without evidence of purulent drainage (e.g., dry gangrene) are included in this category.
4	**Dirty or Infected:** Includes old traumatic wounds with retained devitalized tissue and those that involve existing clinical infection or perforated viscera. This definition suggests that the organisms causing postoperative infection were present in the operative field before the operation.

18.4 APPENDIX D: Parietene™ DS Composite Mesh Instructions for Use

COVIDIEN

Parietene™ DS
Composite Mesh

(99)7500179

PT00079601

en

BEFORE USING PRODUCT, READ THE FOLLOWING INFORMATION THOROUGHLY.

IMPORTANT!
This booklet is designed to assist in using this product. It is not a reference to surgical techniques. This device was designed, tested and manufactured for single patient use only. Reuse and/or reprocessing and /or re-sterilization of this device may lead to its failure, subsequent patient injury and may create the risk of contamination and patient infection. Do not reuse, reprocess or re-sterilize this device.

DESCRIPTION
Parietene™ DS composite mesh is designed to be placed in an intraperitoneal site by a laparoscopic or open approach. The mesh is composed of a permanent macroporous polypropylene textile on one side and a fully absorbable synthetic film on the other side. The film is adhered to the textile using a binding agent localized on the textile fibers. A violet marking is positioned on the mesh to help center and orient the mesh. Non-absorbable pre-placed sutures are tied to the mesh.

- The macroporous textile is knitted from a permanent monofilament polypropylene yarn.
- The synthetic film is made out of absorbable synthetic copolymer of glycolide, caprolactone, trimethylene carbonate, and lactide.
- The binding agent and the violet marking are made out of absorbable polycaprolactone. The "D&C Violet No. 2" dye is used for the marking.
- The pre-placed sutures are made out of an isotactic crystalline stereoisomer of polypropylene (a synthetic linear polyolefin) and polyethylene. The Copper Phthalocyanine Blue is used to color the sutures.

The permanent macroporous textile is designed to be placed over the abdominal wall to ensure long term reinforcement of soft tissues, while the continuous absorbable film is designed to minimize tissue attachment to the mesh in case of direct contact with the viscera and is essentially degraded within 105 days by hydrolysis.

INDICATIONS
Parietene™ DS composite mesh is intended for the reinforcement of abdominal wall soft tissue where a weakness exists. It is indicated for the repair of ventral hernias.

CONTRAINDICATIONS
- As the mesh will not stretch to accommodate growth, its use is not appropriate in patients in a period of growth.
- Any foreign material may potentiate or prolong infection in the presence of bacterial contamination, and as such, the use of this mesh is not appropriate in a contaminated or infected site. Furthermore, this product should be used with the understanding that infection may require removal of the mesh.

POSSIBLE COMPLICATIONS
The possible complications associated with the use of the mesh are: seroma, hematoma, recurrence, adhesions, bowel obstruction, fistula formation, infection, inflammation, acute and chronic pain, extrusion/erosion and/or allergic reaction to the components of the product.
It is important that patients are given complete information regarding possible complications.

WARNINGS
1. Do not use the device past the labeled expiration date.
2. The device is provided in a single sterile package and intended for single use only. Upon receipt of shipment, ensure that the packaging is not open or damaged and retains its sealed integrity. Do not use the device if the package is opened or damaged or if the integrity of the packaging appears compromised.

NOTE: The package contains a circular desiccant tab. It is neither intended to be used in combination with the device nor during the surgery.

3. Parietene™ DS composite mesh is not designed for "bridging" repair technique with the mesh placed in an "inlay" position. The "inlay" repair technique is defined as cutting mesh to the size of the defect, positioning the mesh in the abdominal wall defect and then suturing the edges of the mesh to the edges of the defect. In any case, every effort should be made to close the defect.
4. Parietene™ DS composite mesh is not intended for repair of pelvic organ prolapse and treatment of stress urinary incontinence.
5. The effectiveness and safety related to the use of this device in pregnant women have not been established. For women planning future pregnancies, the surgeon should be aware that this product will not stretch significantly as the patient grows.
6. To avoid injury, exercise caution when fixating the mesh in the presence of nerves and/or vessels.
7. When trimming, the central marking may no longer be centered.
8. The pre-placed sutures are necessary to guarantee sides differentiation when deploying the mesh. If it is required to trim the device, ensure that the pre-placed sutures remain on the device.
9. If the pre-placed sutures are not used for transparietal fixation, do not remove them until the placement of the mesh is secured.
10. Do not force the mesh through the trocar. Inappropriate insertion may lead to textile and/or film damage. The meshes equal or larger than 35 x 30 cm are not designed for laparoscopic use.

PRECAUTIONS
1. Users should be familiar with surgical procedures and techniques involving the use of surgical mesh before employing this device.
2. This device should only be used by experienced practitioners who do so under their own responsibility.

OPERATING STEPS
1. Parietene™ DS composite mesh can be trimmed to the desired size.

CAUTION: The pre-placed sutures are necessary to guarantee sides differentiation when deploying the mesh. If it is required to trim the device, ensure that the pre-placed sutures remain on the device. When trimming, the central marking may no longer be centered.

2. Should it be used in a laparoscopic approach, Parietene™ DS composite mesh can be rolled on either side (film side or textile side) without damaging the device.

To facilitate mesh deployment within the abdominal cavity, it is suggested to roll the Parietene™ DS composite mesh with the film inside.
It is recommended to introduce a mesh of size up to 20 x 15 cm in a trocar with minimum internal diameter of 10 mm, a mesh of size up to 30 x 20 cm in a trocar with minimum internal diameter of 12 mm. Mesh insertion capability may vary depending on rolled mesh size and graspers/trocars used.

CAUTION: Do not force the mesh through the trocar. Inappropriate insertion may lead to textile and/or film damage. The meshes equal or larger than 35 x 30 cm are not designed for laparoscopic use.

3. The textile side (the porous side) should be placed against the abdominal wall for tissue integration, while the film side (the smooth side) should be facing the viscera to minimize tissue attachment.
4. The pre-placed sutures are positioned on the textile side to help with the mesh handling once it is unrolled in the abdominal cavity. These yarns allow to easily pinpoint the mesh textile side. They can be used for the transparietal fixation of the mesh.

CAUTION: If the pre-placed sutures are not used for transparietal fixation, do not remove them until the placement of the mesh is secured.

5. The device should be centered on the defect. The central marking is designed to help centering. Use the violet dots on the mesh to facilitate its placement and orientation.
6. The choice of mesh size is determined by the surgeon. The edge of the mesh should be at least 3 cm over the edges of the defect(s).

NOTE: The distance between two violet dots is approximately 2.5 cm.

7. The technique used to anchor the mesh (suture and/or tack) is left up to the practitioner.

If the pre-placed sutures are used for transparietal fixation, it has to be combined with standard fixation means (suture and/or tack) to guarantee a secured mesh fixation. It is suggested to fixate the mesh to the abdominal wall at a distance of approximately 1 cm from the edge of the mesh. A moderate and equal tension should be applied in all directions for fixation in order to account for wound shrinkage during the healing process and to prevent damage to the mesh.

STORAGE
It is recommended that the Parietene™ DS composite mesh be stored at room temperature.

TRACEABILITY
A traceability label is supplied with every device which identifies the type and lot number of the device. This label should be affixed to the patient's permanent medical record to clearly identify the device that was implanted.

fr

Renfort Composite

AVANT D'UTILISER CE PRODUIT, LIRE ATTENTIVEMENT LES INFORMATIONS CI-DESSOUS.

IMPORTANT !
Cette notice est destinée à faciliter l'utilisation de ce produit. Elle ne constitue pas une référence en matière de techniques chirurgicales. Ce dispositif a été conçu, testé et fabriqué pour un usage chez un seul patient. Sa réutilisation et/ou son retraitement et/ou sa restérilisation peuvent provoquer un dysfonctionnement, des blessures chez le patient et entrainer un risque de contamination et d'infection du patient. Ne pas réutiliser, retraiter ou restériliser ce dispositif.

DESCRIPTION
Le renfort Parietene™ DS Composite est conçu pour une utilisation intrapéritonéale et pour une approche par voie ouverte ou coelioscopique. Le renfort est constitué d'un textile macroporeux non-résorbable en polypropylène sur une face et d'un film synthétique entièrement résorbable sur l'autre face. Le film adhère au textile par l'intermédiaire d'un adhésif déposé sur les fibres textiles. Un marquage violet est présent pour aider à centrer et orienter le renfort. Des fils de suture pré-placés, non résorbables, sont accrochés au renfort.

- Le textile macroporeux est tricoté à partir d'un monofilament permanent de polypropylène.
- Le film synthétique est composé d'un copolymère synthétique résorbable constitué de glycolide, de caprolactone, de carbonate de triméthylène et de lactide.
- L'adhésif et le marquage violet sont constitués de polycaprolactone résorbable. Le colorant « D&C Violet N°2 » est utilisé pour le marquage.
- Les sutures sont composées d'un stéréoisomère cristallin isotatique de polypropylène (une polyoléfine linéaire synthétique) et de polyéthylène. Le bleu de phtalocyanine de cuivre est utilisé pour colorer les sutures.

Le textile permanent macroporeux est conçu pour être positionné sur la paroi abdominale afin d'assurer le renforcement à long terme des tissus mous, alors que le film résorbable continu est conçu pour minimiser les adhérences en cas de contact avec les viscères et est essentiellement dégradé en 105 jours par hydrolyse.

INDICATIONS
Le renfort Parietene™ DS composite est utilisé pour le renforcement des tissus mous en cas de faiblesse de la paroi abdominale. Il est indiqué pour la réparation des hernies ventrales.

CONTRE-INDICATIONS
- Comme le renfort ne s'allongera pas avec la croissance, son utilisation n'est pas appropriée chez les patients en période de croissance.
- Tout matériau étranger est susceptible de provoquer ou de prolonger une infection en présence d'une contamination bactérienne et, de ce fait, l'utilisation de ce renfort peut ne pas convenir en cas d'intervention en site infecté ou contaminé. De plus, ce produit doit être utilisé en sachant que l'infection peut nécessiter le retrait du renfort.

COMPLICATIONS EVENTUELLES
Les éventuelles complications associées à l'utilisation du renfort sont : sérome, hématome, récidive, adhérence, occlusion intestinale, formation de fistules, infection, inflammation, douleur aiguë et chronique, extrusion/érosion et/ou réactions allergiques aux constituants du produit.
Il est important d'informer le patient de l'ensemble des complications éventuelles.

AVERTISSEMENTS
1. Ne pas utiliser le dispositif au-delà de la date d'expiration figurant sur l'étiquette.
2. Le dispositif est livré sous un simple emballage stérile et est destiné à un usage unique. A réception du dispositif, s'assurer que le conditionnement n'a été ni ouvert ni endommagé et conserve intégre son scellage. Ne pas utiliser le dispositif si l'emballage est ouvert ou endommagé ou présente un défaut d'intégrité pouvant compromettre la stérilité.

NOTE : L'emballage contient un dessicant circulaire. Il ne doit être ni utilisé en combinaison avec le dispositif, ni lors de la chirurgie.

3. Le renfort Parietene™ DS composite n'est pas conçu pour la technique de réparation par « bridging » lorsque le renfort est placé en position "Inlay". Cette technique dite « Inlay » est définie par un découpage du renfort aux dimensions du défaut, par un positionnement du renfort au niveau de la paroi abdominale au sein même du défaut et par la suture des bords du renfort aux bords du défaut. Dans tous les cas, un effort particulier doit être fait pour fermer le défaut.
4. Le renfort Parietene™ DS composite n'est pas destiné au traitement des prolapsus des organes pelviens et des incontinences urinaires d'effort.
5. Efficacité et la sécurité relatives à l'utilisation de ce dispositif chez la femme enceinte n'ont pas été établies. Pour les femmes en âge de mener une grossesse, le chirurgien doit être attentif au fait que le dispositif ne s'allongera pas de manière significative lors de la croissance survenant lors de la grossesse.
6. Pour prévenir toute blessure, une attention particulière est requise lors de la fixation du renfort en présence de nerfs et/ou de vaisseaux.
7. En cas de découpe du renfort, le marquage central peut ne plus être centré.
8. Les fils de suture pré-placés sont nécessaires pour garantir la différenciation des faces au moment du déploiement du renfort. En cas de découpe du dispositif, s'assurer que les fils de suture pré-placés restent positionnés sur le dispositif.
9. Si les fils de suture pré-placés ne sont pas utilisés pour une fixation transpariétale, ne pas les retirer avant d'avoir sécurisé le placement du renfort.
10. Ne pas forcer lors de l'insertion du renfort dans le trocart. Une insertion inappropriée peut conduire à un endommagement du textile et/ou du film. Les renforts de dimensions égales ou supérieures à 35 x 30 cm ne sont pas conçus pour une utilisation coelioscopique.

PRECAUTIONS D'EMPLOI
1. Les utilisateurs doivent être familiers des procédures et techniques chirurgicales impliquant l'utilisation de renforts chirurgicaux avant d'utiliser le dispositif.
2. Ce dispositif est réservé aux praticiens spécialistes qui l'utilisent sous leur seule responsabilité.

MODE D'EMPLOI
1. Le renfort Parietene™ DS composite peut être découpé à la taille désirée.

ATTENTION : Les fils de suture pré-placés sont nécessaires pour garantir la différenciation des faces au moment du déploiement du renfort. En cas de découpe du dispositif, s'assurer que les fils de suture pré-placés restent positionnés sur le dispositif. En cas de découpe du renfort, le marquage central peut ne plus être centré.

2. En cas d'utilisation par voie coelioscopique, le renfort Parietene™ DS composite peut être roulé dans les deux sens (côté film ou côté textile) sans endommager le dispositif.

Pour faciliter son déploiement dans la cavité abdominale, il est suggéré de rouler le renfort Parietene™ DS composite avec le film à l'intérieur.
Pour des renforts de taille allant jusqu'à 20 x 15 cm, il est recommandé d'utiliser un trocart de diamètre interne d'au moins 10mm. Pour des renforts de taille allant jusqu'à 30 x 20 cm, il est recommandé d'utiliser un trocart de diamètre interne d'au moins 12mm. La facilité d'insertion du renfort peut varier selon sa taille après enroulement et les pinces/trocarts utilisés.

ATTENTION : Ne pas forcer lors de l'insertion du renfort dans le trocart. Une insertion inappropriée peut conduire à un endommagement du textile et/ou du film. Les renforts de dimensions égales ou supérieures à 35 x 30 cm ne sont pas conçus pour une utilisation coelioscopique.

3. La face textile (la face poreuse) doit être appliquée contre la paroi abdominale pour l'intégration tissulaire alors que la face film (la face lisse) doit être en regard des viscères pour minimiser les adhérences.
4. Les fils de couleur placés sur la face textile aident à la manipulation du renfort une fois déroulé dans la cavité abdominale. Ces fils permettent de repérer plus facilement la face textile du renfort. Ils peuvent servir à la fixation transpariétale du renfort.

ATTENTION : Si les fils de suture pré-placés ne sont pas utilisés pour une fixation transpariétale, ne pas les retirer avant d'avoir sécurisé le placement du renfort.

5. Le dispositif doit être centré sur l'orifice herniaire. Le marquage central a été conçu pour aider au centrage. Utiliser les points violets sur le renfort pour faciliter le placement et l'orientation de celui-ci.
6. Le choix de la taille du renfort est déterminé par le chirurgien. Le renfort doit déborder d'au moins 3 cm par rapport aux berges du ou des orifices herniaires.

NOTE : La distance entre deux points violets est approximativement de 2,5 cm.

7. La technique de fixation du renfort (suture et/ou agrafe) est laissée au choix du chirurgien. Si les fils de suture pré-placés sont utilisés pour une fixation transpariétale, ils doivent être combinés avec des moyens de fixation traditionnels (suture et/ou agrafes) pour sécuriser la fixation du renfort. Il est recommandé de placer les fixations à une distance d'environ 1 cm du bord du renfort. Une tension modérée et équivalente devrait être exercée dans toutes les directions afin de tenir compte de la rétraction de la plaie lors de la cicatrisation et pour éviter tout endommagement du renfort.

CONSERVATION

Il est recommandé de conserver le renfort Parietene™ DS composite à température ambiante.

TRACABILITE

Une étiquette de traçabilité, jointe à chaque dispositif, identifie le type et le numéro de lot du dispositif. Cette étiquette est destinée à être collée sur le dossier médical permanent du patient afin de clairement identifier le dispositif implanté.

Do not use if package is opened or damaged. / Ne pas utiliser en cas d'endommagement ou d'ouverture de l'emballage.

Rx ONLY

CAUTION: U.S. Federal law restricts this device to sale by or on the order of a physician. / MISE EN GARDE : La loi fédérale américaine restreint ce dispositif à la vente par un médecin ou sur prescription médicale.

STERILE EO | Single use | Do not resterilize | Caution, consult accompanying documents

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19. Version History

Version	Summary of Changes	Author(s)/Title
1.0	Not Applicable, New Document	Nicholas Paquette Senior Medical Writer
2.0	Amendment: -Cover page, header and section 1: Administrative change: updated document version number and date -Section3 and section 8.4: Exclusion criterion deleted: Procedure is a robotically assisted laparoscopic repair -Section 11.3: Administrative change: Updated study contact of Medical and Clinical Affairs representatives -Section 17.2: Administrative change: numbering of the questions of the Carolina Comfort scale pre-operative and post-operative assessments has been updated to correct the typo in the previous version of the CIP -Section 7.5.1: added "If barbed sutures are used for fixation, these sutures must have the specific indication for mesh fixation." -Section 9.1.3: added: "and barbed sutures may be used for mesh fixation only if these sutures are claiming such indication"	Marion Blanc Sr. Clinical Research Specialist
3.0	-Section 8.2: deleted: "No robotic procedures will be included as part of this study."	Marion Blanc Sr. Clinical Research Specialist
4.0	-Section 2: Adjusted glossary, removed Safety definitions as they are defined in the AE section of CIP, removed USADE/UADE as they are not required to be reported in post-market studies	Alyssa Sutch Sr. Clinical Research Specialist

	-Section 6.3: Clarified Steering Committee will only be comprised of site investigators -Section 10.6: Included verbiage allowing follow-up visits to be conducted remotely -Section 10.12.2.3: Added clarifying verbiage regarding Study Exit Visit -Section 10.12.2.5: Attempts made to contact patients that are considered LTFU will be monitored -Section 10.4.4: Clarified sites do not need prior written approval from Medtronic to complete a review of medical records should the patient be unwilling or unable to be seen by the investigator at the 12-month or 24-month follow-up visit -Section 12.1: Added table with Adverse Event Definitions -Section 12.3.1: Added clarifying verbiage regarding Device Deficiencies -Section 12.3: Updated Study Contact Information -Section 12.5: Added table that discusses Adverse Event Classification Responsibilities -Section 13.1: Safety Committee is not applicable for PPDS study -Section 15.1: Stated regulatory regulations -Section 18.2: Added Carolinas Comfort Scale -Minor administrative changes throughout	