CLINICAL STUDY PROTOCOL

Title:	**A Prospective, Multi-Center All Comers Study of a Novel Resorbable Mesh (Phasix™ Mesh) for Ventral or Incisional Hernia Repair**
Protocol Number:	**DVL-HE-015**
Study Type:	**Post-market, single-arm, observational, multi-center, prospective**
Date:	**August 21, 2014**
Version:	**Version 3.0**
Study Devices:	**Phasix™ Mesh**
Sponsor:	**Davol Inc.** **Subsidiary of C. R. Bard, Inc.** **100 Crossings Boulevard** **Warwick, RI 02886** **Phone: 1-800-556-6756**
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Protocol Signature Page

The Investigator agrees to conduct the clinical study, which is the subject of this protocol, in accordance with the Clinical Study Agreement, this protocol, all applicable laws and regulations, and the conditions of approval imposed by the reviewing Institutional Review Board.

Agreed to by (Investigator):

_____
Printed Name – Investigator

_____
Signature – Investigator

_____
Date

Protocol Abbreviations/Acronyms

Abbreviation/Acronym	Definition
AE	Adverse event
Bard	C. R. Bard, Inc.
BMI	Body Mass Index
CDC	US Centers for Disease Control and Prevention
CFR	Code of Federal Regulations
Cm	Centimeter
CT	Computed Tomography Scan
COPD	Chronic Obstructive Pulmonary Disease
CST	Component Separation Technique
CV	Curriculum vitae
eCRF	Electronic Case Report Form
e.g.	For Example
FDA	Food and Drug Administration
HIPAA	Health Insurance Portability and Accountability Act
HIV	Human Immunodeficiency Virus
Hrs	Hours
ICF	Informed Consent Form
i.e.	That Is
IRB	Institutional Review Board
IFU	Instructions For Use
LTF	Lost to Follow-Up
Mm	Millimeter
MRI	Magnetic Resonance Imaging
N	Sample Size
P4HB	poly-4-hydroxybutyrate
PE	Physical Exam
SAE	Serious Adverse Event
SF-12®	12-Item Short Form
SSI	Surgical Site Infection
VAC	Vacuum Assisted Closure system
VAS	Visual Analogue Scale

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1 INTRODUCTION

1.1 **Background**

With more than 2 million abdominal operations occurring annually in the United States (US) and up to 20% of those patients developing ventral incisional hernias, abdominal wall defects and incisional hernias represent a challenging surgical condition.[1, 2] Approximately 250,000 ventral hernia repairs are performed on a yearly basis.[3] There are several options for repair, including primary repair, mesh reinforcements, repair with relaxing incisions, and use of musculofascial flaps, utilizing both open and laparoscopic approaches.[2] However, there is no clear-cut consensus regarding the optimal hernia repair technique, particularly in complex hernia repair cases where patient co-morbidities exist and a high risk of infection is present.

Simple suture repair has been associated with a high risk of hernia recurrence, with reports ranging from 10% to 55%, and has been nearly abandoned for the repair of hernias which are greater than five centimeters (cm) in size.[4, 5, 6, 7] As a result, many ventral hernia repair procedures involve the use of a mesh material as a soft tissue reinforcement.

Synthetic mesh repair procedures, either open or laparoscopic, have been reported to lead to fewer recurrences compared to primary repairs.[8, 9, 10] Improved outcomes are believed to be related to reduced tension on the fascial edges and sutures when mesh is used in hernia repair procedures. However, complex cases and large abdominal wall defects continue to pose a challenge to surgeons. Factors such as patient co-morbidities, defect size, location, tissue viability and degree of contamination are included in a surgeon's assessment and decision-making process.[11] These large abdominal wall defects have been associated with recurrence rates of up to 46%.[12]

Despite the positive clinical impact of reducing hernia recurrence rates, the use of synthetic mesh has been associated with complications such as infection, adhesions, fistulae, and foreign body reactions including increased inflammation.[13]

Non-absorbable meshes can lead to complications related to the body's reaction to the persistent foreign mesh material resulting in foreign body sensations including discomfort and chronic pain, which is described by the International Association for the Study of Pain as pain lasting for 3 months or greater following hernia repair.[14, 15]

Ideally, an absorbable mesh would provide adequate structural support throughout the healing process and would be fully absorbed when the wound has completely healed, thereby potentially reducing the chances for complications associated with the persistence of non-absorbable mesh material.[16,17,18] The development of absorbable mesh products has faced challenges related to the rate of absorption with complications arising when the mesh product is absorbed too quickly. An absorbable mesh should retain its functional strength for a sufficient period of time to allow native cellular ingrowth tissue remodeling, maturation of collagen, and gradual shift of mechanical load.

Phasix™ Mesh is a commercially available medical device in the United States. It is a resorbable mesh prepared from poly-4-hydroxybutrate (P4HB) which has been studied for use as a biomaterial for a number of applications in medical devices and tissue engineering due to favorable mechanical properties, biocompatibility and desirable degradation times.[19, 20, 21] Using standard measures of mechanical strength (suture pull-out, tear and ball burst strength) Phasix™ Mesh is comparable in performance to traditional polypropylene mesh. Pre-clinical implantation studies indicate that the resorption of the Phasix™ Mesh fibers is minimal throughout the 12 week expected period of healing and up to ~26 weeks post-implantation. Resorption of the fibers is essentially complete in 12-18 months.[24]

A bridging hernia repair study in a porcine model demonstrated that Phasix™ Mesh could perform as a durable scaffold for soft tissue repair when spanning a surgical defect.[24] The results of the 52-week study showed that the repair site had three times greater mechanical repair strength, as compared to native abdominal wall. This persisted even after significant Phasix™ Mesh resorption (as measured by molecular weight). Only 10% of the strength of the repair site came from the Phasix™ Mesh at the 52 week timepoint. Phasix™ Mesh showed an initial mild-moderate host inflammatory response, that declined to mild over 52 weeks. Neovascularization (angiogenesis) and new collagen deposition were evident at 6, 12, 26 and 52 weeks, as histologically evaluated by a board-certified veterinary pathologist. In a 24-week rat study, histological analyses of the repair site demonstrated that some competitive meshes had a greater overall host inflammatory response, some had less of a response and one had a very similar response, to Phasix™ Mesh.[24] In the same study, histological analyses demonstrated similar variability on measures of host fibrotic response.

This post-approval clinical study is being conducted to evaluate the use of Phasix™ Mesh in primary ventral or incisional hernia repair. Patients who receive a Phasix™ Mesh implant will be followed for 24 months.

1.2 **Rationale**

This study is intended to evaluate the use of Phasix™ Mesh for primary ventral, incisional and first-recurrent incisional hernia repair.

1.3 **Device Descriptions**

1.3.1 Phasix™ Mesh

The Phasix™ Mesh (Davol, Inc.) is a resorbable mesh prepared from P4HB. P4HB is produced from a naturally occurring monomer and is processed into monofilament fibers and knitted into a surgical mesh. Phasix™ Mesh degrades through a process of hydrolysis and a hydrolytic enzymatic digestive process. It was developed to minimize the variability of resorption rate (loss of mass) and strength and provide support throughout the expected period of healing.

Pre-clinical implantation studies indicate that the resorption of the Phasix™ fibers is minimal throughout the 12-week expected period of healing and up to about 26 weeks post implantation. Resorption of the fibers is essentially complete in 12 to 18 months.[24]

Phasix™ Mesh has been commercially available in the United States since 2012 and is indicated to reinforce soft tissue where weakness exists, such as the repair of hernia or other fascial defects that require reinforcement or bridging material to obtain the desired surgical result. Because Phasix™ Mesh is fully resorbable, it should not be used in repairs where permanent wound or organ support from the mesh is required. A full description of Phasix™ Mesh is included in the product's Instructions for Use (IFU) (Appendix 2).

2 STUDY OBJECTIVES

The objective of this single-arm observational study is to collect additional data on safety, performance, and effectiveness of Phasix™ Mesh in subjects requiring primary ventral or incisional hernia repair.

3 STUDY ENDPOINTS

3.1 Primary Endpoint:

Hernia Recurrence Rate

Hernia recurrence rates will be assessed by physical examination at each study visit through 24 months. A recurrent hernia will be defined as any hernia identified or confirmed by the investigator, during any study follow-up visit, in approximately the

same position as the hernia repaired in the study procedure. Potential hernias identified via incidental magnetic resonance imaging (MRI) or computed tomography (CT) scan will be evaluated by the operating surgeon for clinical significance and confirmation of hernia recurrence.

3.2 Secondary Endpoints:

1. Device related adverse event incidence
2. Quality of life assessments (Carolinas Comfort Scale® and SF-12® - 12-item short form health survey)
3. Surgical procedure time as measured from incision to closure (skin to skin)
4. Length of hospital stay post index surgical procedure
5. Number of study-related post-operative surgical procedures and admissions
6. Number of study-related post-operative visits unrelated to standard of care.
7. Incidence of Seroma.

4 STUDY DESIGN

This is a prospective, multi-center, single-arm, observational study designed to collect additional data on safety, performance and effectiveness of Phasix™ Mesh for primary ventral or incisional or first-recurrent hernia repair. Follow-up visits will be conducted at 1, 3, 6, 12, 18, and 24 months following surgery. See Section 6 for a detailed schedule of study visits and procedures.

5 STUDY POPULATION

5.1 **Number Of Subjects**

This study is projected to enroll up to 30 subjects at approximately 5 US sites.

5.2 **Eligibility Criteria**

5.2.1 Inclusion Criteria

The subject must meet all of the criteria listed below to be enrolled in the study:

1. Subject must be 18 years of age or older
2. Subject or subject's legally authorized representative must be willing to give written informed consent
3. Subject must be diagnosed with ventral or incisional hernia
4. Subject must be willing to undergo open ventral hernia repair and be able to undergo all other study procedures as outlined in this protocol.

5.2.2 Exclusion Criteria

The subject must be excluded from study enrollment if any of the following criteria are met:

Screening Exclusion Criteria:

1. Subject is an active smoker (if attempts to quit smoking within two weeks of surgery have failed and the patient is still an active smoker at the time of surgery).
2. Subject has had 4 or more previous hernia repairs.
3. Subject's body mass index (BMI) >40 kg/m^2.
4. Subject has peritonitis.
5. Subject is on or suspected to be placed on chemotherapy medications during any part of the study.
6. Chronic steroid use or immunosuppression drugs (> 6 months).
7. Subject has cirrhosis, and/or ascites.
8. Subject is American Society of Anesthesiology Class 4 or 5.
9. Subject is pregnant or planning to become pregnant during the course of the study.
10. Subject is known to be infected with human immunodeficiency virus (HIV).
11. Subject has a life expectancy of less than 2 years at the time of enrollment.
12. Subject has been treated with an investigational product in the past 30 days.
13. Subject is part of the site personnel directly involved with this study
14. Subject has a known allergy to tetracycline hydrochloride or kanamycin sulfate, the test device or its component materials.
15. Subject has any condition that in the opinion of the Investigator would preclude the use of the study device, or preclude the subject from completing the follow-up requirements.

Intra-operative Exclusion Criteria:

16. The fascia cannot be closed intraoperatively.
17. The use of surgical repair as a bridge.
18. Patient has a contraindication to placement of mesh.
19. Complete removal of existing mesh from a prior hernia repair (in the same affected area) is not possible.
20. Skin closure cannot be achieved intraoperatively.
21. Subject has an active or latent systemic infection

6 STUDY PROCEDURES

6.1 **Subject Screening and Baseline Evaluation**

Subjects with a diagnosis of a primary ventral or incisional hernia or up to 3 recurrent hernias requiring surgical repair to close the defect will be screened for potential eligibility against the study protocol inclusion and exclusion criteria, utilizing ordinary standard of care procedures (e.g. physical examination, blood work, medical evaluation) within 60 days of the date of consent. This may include a full anesthetic work-up customary for hernia repair procedures. Any other standard of care examination or evaluation within 60 days of the date

of consent may be considered baseline for study purposes. Prior medical records documenting these tests, examinations and evaluations may be used as the source documents for the baseline visit.

During the screening and recruitment process, the Investigator will be responsible for describing the nature of the clinical study, verifying that the eligibility criteria have been met, and obtaining informed consent. Written informed consent and a Health Insurance Portability and Accountability Act (HIPAA) waiver must be obtained prior to performance of any protocol specific procedures.

The following screening/baseline procedures will be conducted and documented.

6.1.1 Informed Consent

The investigator will explain the study to the subject, answer all of the subject's questions, and obtain written informed consent in a language in which the subject is fluent before the collection of any study data or performance of any study procedures.

The subject (or subject's legally authorized representative) must be willing and able to sign and date the informed consent form (ICF) prior to the collection of study data or performance of any study procedures. The original, signed informed consent will be retained with the subjects' records and a copy provided to the subject.

6.1.2 Enrollment

Subjects who sign the informed consent and receive Phasix™ Mesh as a part of this study will be considered enrolled in the study.

6.1.3 Eligibility

The subject's eligibility for study enrollment will be reviewed and documented on the appropriate eCRF. At the time of screening, a related progress note must be entered in the source documentation to indicate that all eligibility criteria were reviewed and screening results noted. Final eligibility will be determined intraoperatively.

Subjects who fail to meet eligibility criteria should be considered screen failures and treated according to the Investigator's standard of care. Data are to be collected for screen failure subjects from the time the ICF is signed until the subject is deemed a failure. At a minimum, subject demographics and the reason for failure must be collected; adverse events (AEs) will also be collected and followed through satisfactory resolution or stabilization.

6.1.4 Assignment of Subject Screening Number

A unique identification number will be given to study subjects. Subject numbers will be assigned in a sequential order. The subject number will consist of six digits. The first three digits will designate the study site. The last three digits will designate the subject by number in sequential order at each study site.

6.1.5 Blinding

The study is an open-label study with a single treatment condition. Subjects and investigator (and surgeon) will be not be blinded to the study treatment.

6.1.6 Demographics and Medical History

The subject's medical history and demographic information will be documented on the appropriate eCRF. Demographic information will include gender, date of birth, race and ethnicity.

6.1.7 Physical Examination

A standard physical exam, appropriate to subjects about to undergo abdominal surgery, will be performed by the physician. Height and weight measurements will be recorded to allow for the calculation of BMI. The subject's ability to participate and meet the follow-up requirements will be established.

6.1.8 Concomitant Pain Medication Usage

Prescription and over the counter (OTC) pain medication must be recorded in the source documentation and in the eCRF. The condition/s necessitating the pain medication will be recorded. All current pain medication will be captured at baseline, 12 months, and 24 months.

6.1.9 Patient Reported Outcome Assessments

Subjects will complete the Carolinas Comfort Scale® and SF-12® to measure discomfort and quality of life.

6.2 **Surgical Procedure**

6.2.1 General Procedures

All subjects will undergo an open ventral repair of hernias. All intraoperative eligibility criteria should be verified. Defect closure, defined as both fascial and skin closure, must be confirmed.

The surgical technique will require retro-rectus or onlay placement (using absorbable suture) with or without Component Separation Technique (CST). Subjects will be administered antibiotics according to hospital protocol.

Subjects are prepared to undergo hernia repair following the instructions supplied by the Sponsor. The IFU for Phasix™ Mesh device is presented in Appendix 2.

Phasix™ Mesh will be placed in the retro-rectus or onlay space with absorbable mesh fixation. The peritoneum should remain posterior to the mesh upon completion of mesh placement. Phasix™ Mesh may be cut to shape or size desired for each specific application. To prevent recurrence when repairing hernias, a mesh larger than the defect is required to ensure adequate coverage. The mesh is to be positioned so its edges extend beyond the margins of the defect by at least 5 cm. It is recommended that fixation be placed at approximately 5 to 6 cm intervals (6 to 12 resorbable sutures) around the periphery of the mesh. The edges are then fixated to assure proper closure under correct tension.

The procedure may include CST to obtain site closure. All incisions will be closed with staples and/or sutures and wounds will be dressed with sterile occlusive dressings.

6.2.2 Component Separation Technique Surgery

Prophylactic antibiotics will be administered according to hospital protocol. If a prior hernia repair utilizing mesh is in the affected area, complete removal of any mesh remaining is required. Once all of the dissection is performed and all of the hernia has been exposed, the largest vertical and transverse dimensions should be recorded.

If the CST is utilized, the surgical technique will be a modification of the "component separation technique" by Ramirez et al. with the graft being implanted into the tissue plane of the surgeon's preference, according to the following: Separation of components may be done via open, posterior or endoscopic/minimally invasive technique as described below.[8, 26]

6.2.2.1 Open Technique

After entering the abdominal cavity, adhesiolysis is performed to dissect free any intra-abdominal contents from the abdominal wall. The skin and subcutaneous fat are dissected free from the anterior sheath of the rectus abdominal muscle and the external oblique muscle. The external oblique is separated through the aponeurosis approximately 1-3 cm from the edge of the rectus, or through the muscle. If the hernia is subxiphoid in position, release must be done above the rib cage and come across the rectus sheath and muscle at the level of where the pectoralis meets the rectus. The external oblique muscle is separated from the internal oblique muscle, as far laterally as possible (aiming to the anterior axillary line), above and below the hernia by approximately 5 cm.

6.2.2.2 Posterior Technique

Posterior component separation with transversus abdominis release (TAR): Starting in the upper third of the abdomen, about 0.5 cm medial to the anterior/posterior rectus sheath junction (linea semilunaris), the posterior rectus sheath is incised to expose the underlying transversus abdominis muscle. The muscle is then divided along its entire medial edge using electrocautery. The use of a right-angled dissector significantly facilitates this release and minimizes injury to the underlying transversalis fascia and peritoneum. Transection of the medial edge of the transversus abdominis muscle allows for entrance to the space between the transversalis fascia and the lateral edge of the divided transversus abdominis muscle. The retromuscular space is bluntly developed further laterally to as far as the lateral border of the psoas muscle to allow for a reinforcement of a visceral sac with a large mesh. Also, if needed, this dissection may be extended superiorly above the costal margin and inferiorly to expose both myopectineal orifices.

6.2.2.3 Endoscopic/Minimally Invasive Technique

Make a 2 cm incision in the upper abdomen in a location that is convenient for release (such as directly over the costal margin at the level of the mid clavicular line, or at the tip of the 11th rib). Please note: this incision may occasionally need to be placed further lateral to ensure the incision is lateral to the linea semilunaris. Dissect down to the level of the external oblique muscle. Separate the external oblique muscular fibers (this allows for visualization of the underlying internal oblique aponeurosis below). Advance a balloon dissector between the internal and external oblique muscle down to the level of the inguinal ligament. Insufflate the balloon under endoscopic visualization. Remove the dissecting balloon and replace with a trocar (first port). Infuse the lateral abdominal cavity with gas, such as carbon dioxide. Place a second port into the lateral abdominal cavity to allow for dissection. A third port may be used to facilitate easier access to parts of the anatomy. If performing a minimally invasive technique multiple incisions may be used to visualize and release the external oblique under direct visualization. Use cautery or alternatively ultrasonic dissection to divide the external oblique muscle from the costal margin down to the inguinal ligament. Please note: extending the dissection to the level of Scarpa's fascia results in even greater abdominal wall advancement. This technique is generally performed bilaterally.

6.2.2.4 Open or Endoscopic Technique

If necessary, resect/debride the edges of the rectus fascia to ensure apposition of healthy well-vascularized tissue as the midline is closed. Care must be taken not to damage the blood supply and the nerves that run between the internal oblique and transverse muscle and enter the rectus abdominal muscle at the posterior side.

Closure should be performed with permanent or long lasting sutures every 1-2 cm between sutures, for example with an interrupted Figure-8 closure or running stitch. The surgeon should make every effort to close the fascial edges including the use of the component separation technique. If the fascia cannot be closed, the peritoneum of the hernia sac should

have been preserved so that this can be closed over the Phasix™ to provide vascularized tissue.

If a previous scar of skin is present, the scar should be excised. The fascial and subcutaneous layer should be closed with sutures. The skin should be closed with staples and/or sutures. When skin closure can't be achieved, a wound vac can be used.

6.2.3 Postoperative Care

Subjects will be discharged and postoperatively managed according to standard of care practices, determined by their physician/Investigator.

If for any reason the mesh is removed and a mesh infection is suspected, routine culture, at the site of the wound, area of contamination, or potential contamination, obtained via each site's normal protocol, should be obtained to determine cell count and type (i.e., yeast, gram positive or gram negative bacteria, or other). If genus and species of the culture are identified as part of the routine practice at the site, that information should be recorded.

6.2.4 Surgical Details

Surgical details will be recorded and entered in the appropriate source documentation and eCRF(s). Details will include but may not be limited to procedure date, start/stop times, procedure related complications, and AEs.

6.3 **Subject Follow-up**

6.3.1 Subjects Not Implanted and Surgical Repair Failures

Subjects who are enrolled but do not have the test device placed or meet intraoperative eligibility criteria should be considered a screen failure and treated per hospital standard of care. Screen failure subjects who experience a protocol defined AE will be followed through satisfactory resolution or stabilization of the event.

Reason for failure of the surgical repair procedure, as well as all information outlined in Section 6.2.3 must be recorded in the source documentation. Reasons for failure include, but are not limited to, inability to re-approximate the fascia, excessive tension on the midline incision, bowel perforation, intra-abdominal pressure too high, or staged procedure to eliminate active contamination.

6.3.2 Subjects Successfully Implanted

Subjects successfully implanted with Phasix™ Mesh will be followed as per the protocol defined follow-up procedures (see Table of Study Events).

6.3.3 Assessments

Subjects should report to their respective study site for follow-up visits at the following times:

- 1 month assessment: Day 30 ± 7 days post device placement
- 3 month assessment: Day 90 ± 30 days post device placement
- 6 month assessment: Day 180 ± 30 days post device placement
- 12 month assessment: Day 365 ± 30 days post device placement
- 18 month assessment: Day 545 ± 30 days post device placement
- 24 month assessment: Day 730 ± 30 days post device placement

At each study visit, the following procedures will be completed and these data recorded in source documentation and on the eCRF:

- Physical exam to check for hernia recurrence and surgical complications.
  Note: If the subject undergoes imaging for any reason and a recurrent hernia is identified, it must be recorded.
- Carolinas Comfort Scale®
- SF-12®
- Concomitant pain medication usage (all pain medication will be captured at baseline. Hernia associated pain medication only will be captured at 12 and 24 months)
- Assessment of AEs/complications

6.3.4 Unscheduled Visits

If the subject has an evaluation related to the abdomen or abdominal organs at any time during the study follow-up period, the subject will undergo unscheduled visit study procedures (see Table of Study Events).

6.4 TABLE OF STUDY EVENTS

Study Procedure	Screening and Baseline Period	Surgery	1 Month Visit	3 Month Visit	6 Month Visit	12 Month Visit	18 Month Visit	24 Month Visit	Unscheduled Visit/Early Termination
Visit Window (days)	**Within 60 days of consent**	**0**	**30 ± 7**	**90 ± 30**	**180 ± 30**	**365 ± 30**	**545 ± 30**	**730 ± 30**	**--**
Describe study to potential subject	**X**								
Obtain informed consent	**X**								
Verify eligibility criteria	**X**	**X**							
Collect demographics and medical history	**X**								
Conduct physical examination	**X**		**X**	**X**	**X**	**X**	**X**	**X**	**X**
Placement Procedure of Device		**X**[1]							
Carolinas Comfort Scale®	**X**		**X**	**X**	**X**	**X**	**X**	**X**	**X**
SF-12®	**X**		**X**	**X**	**X**	**X**	**X**	**X**	**X**
Collect adverse events/ complications		**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**
Collect pain medication usage	**X**					**X**		**X**	

[1] See Section 6.2 for surgical procedure details

6.5 **Withdrawal and/or Early Termination**

Subjects will be informed that they have the right to withdraw from the study at any time, without affecting their future care. Subjects may also be discontinued from the study, if the Investigator determines it is in the best interest of the subject.

Additionally, subjects may be discontinued for reasons including, but not limited to the following:

- Consent is withdrawn
- Lost to follow-up (LTF)
- Death
- Investigator withdrawal of subject
- Sponsor's decision
- Other

A subject is considered LTF if the investigational site personnel are unable to locate the subject despite two documented attempts to notify the subject via telephone and a third attempt by certified mail.

A subject is considered an Early Termination (ET), if discontinuation occurs after successful implant of the test device. The site should attempt to bring the subject back to complete all ET visit study procedures (see Table of Study Events).

Once a subject discontinues from the study, the Investigator must complete a Study Completion eCRF and the reason for subject discontinuation must be fully documented.

7 STATISTICAL METHODS

This section describes the planned statistical analyses for this study. A detailed Statistical Analysis Plan (SAP) will be completed and placed on file prior to database lock. The SAP will contain a comprehensive explanation of the methodology used in the statistical analyses described below.

7.1 **Study Hypothesis**

There is no formal statistical hypothesis for this observational post-market study. The study will follow eligible patients implanted with the Phasix™ Mesh for hernia repair in order to assess long-term recurrence rates.

7.2 **Sample Size Considerations**

This study is projected to enroll up to 30 subjects at approximately 4 sites. The sample size of 30 subjects is based on potential adequacy of data to meet the study objectives. It is not based on any statistical consideration.

7.3 **Data Analysis**

The Intent-to-treat (ITT) population consists of all enrolled subjects who have signed the Informed Consent Form. The modified ITT (mITT) population is defined as those subjects in the ITT population in whom Phasix™ Mesh has been implanted. All analyses will be primarily based on the mITT population.

Demographics and baseline characteristics will be summarized using the ITT population. Summary statistics for categorical variables will include frequency counts and percentages and for continuous variables mean, standard deviation, minimum, median and maximum.

The primary endpoints of hernia recurrence rate and surgical site infection rate will be reported by visit along with their 95% confidence intervals based on the mITT population. The calculation of rates at each time point will be based on available data at the time point. Missing data will not be imputed. Additionally, a Kaplan-Meier survival analysis will be performed.

The secondary endpoints of Carolinas Comfort Scale and SF-12® will be summarized based on the mITT population with mean, standard deviation, minimum, median and maximum presented by visit. Other secondary endpoints will be summarized as appropriate.

A Per-Protocol (PP) population may be created if there are subjects who have any major protocol violations. The PP population will consist of any subjects in the MITT population who do not have any major protocol violations. The protocol violations that are considered to have a “major” grade will be defined a priori in the analysis plan.

Subjects who do not have Phasix™ Mesh implanted will have their AEs summarized separately and their outcome data will not be collected or analyzed.

Exploratory analyses on subpopulations may be performed.

8 ADVERSE EVENTS

The Investigator is responsible for the detection and documentation of events meeting the criteria and definition of an AE or SAE, as provided in this protocol. All AEs that occur during the study should be treated with established standards of care that will protect the life and health of the study subjects.

Adverse events will be collected from the time of enrollment through the end of study participation (either study completion or early discontinuation) and will be documented on the medical record or source document and on study eCRFs. Events with an onset prior to enrollment should be reported in the subject's medical history.

8.1 **Definition of Adverse Events**

In this study, an AE is defined as any undesirable clinical event occurring in the abdominal space including the lower abdominal, inguinal and pubic regions (including the skin), as well as any other undesirable clinical events judged to be related to the study device or surgical procedure regardless of anatomical region.

Abnormal laboratory results are not to be considered AEs unless the results are accompanied by clinical signs or symptoms. A pre-existing condition should not be reported as an AE unless there has been a substantial increase in severity or frequency of the condition (worsening of the underlying disease), which has not been attributed to natural history. Pre-existing conditions should be considered as part of the subject's medical history. Exacerbation of an existing condition should be reported as an AE, if the event meets the protocol definition of an AE.

The Investigator will assess the relationship of an AE to the study device or procedure as described in Section 8.5.

8.2 **Definition of Serious Adverse Events**

An event will be classified as a serious adverse event (SAE) if it meets the definition of serious injury in the Medical Device Reporting Regulation [21 CFR 803.3] as listed below:

- results in, or contributes to, a death or serious injury;
- is life-threatening (i.e., the subject was at risk of death at the time of the event);
- requires in subject hospitalization or prolongation of existing hospitalization;
- results in persistent disability or incapacity (i.e., permanent impairment of a body function or permanent damage to a body structure);
- necessitates medical or surgical intervention to prevent one of the outcomes listed above in this definition (i.e., to preclude permanent impairment of a body function or permanent damage to a body structure)

NOTE: The term serious is not synonymous with severity, which may be used to describe the intensity of an event experienced by the subject.

8.3 **Relationship of Adverse Event to Device/Procedure**

Assess each AE for its relationship to the device (Phasix™ Mesh) or surgical procedures as follows:

- Device: This category should be restricted to AEs directly attributable to devices used as part of the study procedure.
- Procedure: This category should be restricted to AEs directly attributable to the study device surgical procedure.

Use the following categories for assigning the certainty of the relatedness:

- Definitely Related: An AE is definitely related if it is obvious, certain or there is little doubt regarding the relationship.
- Possibly Related: An AE is possibly related if it is capable of being related but relatively unlikely.
- Not Related: An AE is not related if it is determined that there is no plausible association.

8.4 **Severity of Adverse Events**

Each AE should be assessed for its severity, or the intensity of an event, experienced by the subject.

- Mild: Awareness of a sign or symptom that does not interfere with the subject's activity or is transient and is resolved without treatment or sequelae.
- Moderate: May interfere with the subject's activity and require additional intervention and/or treatment, and may have additional sequelae.
- Severe: Significant discomfort to the subject and/or interferes with the subject's activity. Additional intervention and/or treatment are necessary. Additional sequelae occur. Severe is used to describe the intensity of an event experienced by the subject.

8.5 **Reporting of Adverse Events**

If an AE occurs, all sections of the appropriate eCRF must be completed.

All Investigator-judged device- or procedure-related AEs that occur (whether serious or not) must be reported to Davol Inc. Field Assurance using the contact information provided in Section 9, within 24 hours of becoming aware of the event.

Additionally, all SAEs (whether device- or procedure-related or not) must be reported to the Sponsor within 24 hours of becoming aware of the event.

It is the responsibility of the Investigator to inform the Institutional Review Board (IRB) of AEs according to IRB requirements. The Sponsor will report to the Food and Drug Administration (FDA) as appropriate after becoming aware of a reportable event.

9 MECHANICAL FAILURES, MALFUNCTIONS AND DEFECTS

The Investigator will record if the surgical mesh device used in the study procedure failed to meet its performance specifications whether due to mechanical failure, malfunction or defects. This applies to: devices used in the subject, devices in which the package was opened but the device was not used for implantation in the subject, or devices with which implantation was attempted, but the device did not remain (was not used) in the subject.

A recurrence (unless it is in a different location than the study hernia) is considered a device failure if the recurrence is clearly device related, and not procedure related or an issue of patient mismanagement (e.g., use of a Vacuum Assisted Closure (VAC) system for too long; mesh used was too small to adequately cover the defect), as determined by the Investigator.

All mechanical failures, malfunctions, missing components, foreign matter inclusion or any other defects of the study device or any components of the device kit that do not perform to specifications must be promptly reported to the Davol Field Assurance Department:

Telephone: 800-556-6756
Email: davol.fieldassurance@crbard.com

The event must also be documented on the Device Failure eCRF and the malfunctioning device promptly returned to the manufacturer.

10 CASE REPORT FORMS

The Investigator is responsible for ensuring the accuracy and completeness of all study documentation. All clinical study data will be recorded in the eCRFs provided to the investigational site.

11 RISK/BENEFIT ANALYSIS

Subjects participating in this study will require hernia repair surgery as part of their standard of care. The device utilized in this study is commercially available, has 510(k) clearance from the US FDA and will be used in accordance with the indications in labeling which are in effect during the study period. This study will not pose any additional potential risk to the

health, safety, or welfare of the subject. The risks associated with hernia repair and Phasix™ Mesh are described in full in the IFUs (Appendix 2).

There is no immediate benefit to the subject for participation in this study. Collection and analysis of the data generated in this study may be of benefit to future subjects who require hernia repair.

12 ADMINISTRATIVE REQUIREMENTS

This study will be conducted in accordance with the Declaration of Helsinki, HIPAA requirements, Good Clinical Practices (GCP), and applicable FDA regulations (21 CFR parts 50, 54, 56 and will be exempt from the requirements of 21 CFR part 812, as per 21 CFR part 812.2(c)(2), as the device has been cleared by the FDA for commerce and will be used as per the IFU).

12.1 **Publication Policy**

At the conclusion of the study, a multi-center article may be prepared for publication in a scientific journal. The publication of the principal results from any single-center experience within the study is not allowed until the preparation and publication of the multi-center results. Exceptions to this rule require the prior approval of Davol. The analysis of other pre-specified and non-pre-specified endpoints will be performed by Davol or its designee. Such analyses, as well as other proposed investigations will require the approval of Davol. Davol anticipates the possibility of secondary manuscripts with principal authorship. For purposes of timely abstract presentation and publication, such secondary publications will be delegated to the appropriate principal authors, and final analyses and manuscript review for all multi-center data will require the approval of Davol.

12.2 **Investigator Selection**

The Investigator must be of good standing as an Investigator and knowledgeable in relevant areas of clinical research to ensure adherence to the requirements of the protocol, including the protection of human subjects. Other site personnel must have appropriate research experience and infrastructure to ensure adherence to the protocol and enrollment of sufficient numbers of evaluable subjects. The curriculum vitae (CV) of the Investigator will be maintained in the Sponsor files as documentation of previous medical training, and federal databases will be searched to ensure that the Investigator and/or the site are not prohibited from engaging in federally Sponsored clinical research. The Principal Investigator will sign the signature page of this protocol, agreeing to comply with all applicable government regulations and the requirements of this study.

12.3 **Regulatory and Ethical Considerations**

12.3.1 Institutional Review Board Approval

Before commencement of the study, the Investigator must provide Sponsor with written documentation of IRB approval. This approval must refer to the ICF and the study by both the title and the protocol number assigned by Sponsor. The Investigator, if a member of the IRB, is not to participate in the approval decision for this study. This non-participation should be noted in the approval letter.

The IRB must give written renewal of the original approval at least annually to continue the study. A copy of the written renewal must be provided to Sponsor.

12.3.2 Informed Consent and HIPAA Authorization

Prior to the procedure, the Investigator (or designee) must explain to each subject (or the subject's legally authorized representative) in layman's terms, the nature of the study, its purpose, expected duration, and the benefits and risks of study participation. Also, subjects will be informed of uses and disclosures of their medical information for research purposes and their rights to access information about them. The subjects must be informed of their rights to withdraw from the study at any time for any reason without sanction, penalty, or loss of benefits to which they are otherwise entitled, and that withdrawal from the study will not jeopardize their future medical care. After this explanation and before entering the study, the subject (or legally authorized representative) must voluntarily sign and date the IRB-approved ICF and HIPAA Consent Form in accordance with 21 CFR Parts 50 and 56. The subject will receive a copy of their ICF and HIPAA Consent Form.

12.3.3 Confidentiality

All information and data sent to Davol, Inc. or an authorized designee concerning subjects or their participation in the study will be considered confidential. All data used in the analysis and reporting of this study will be used in a manner without identifiable reference to the subject. The Investigator consents to visits by personnel of Davol, Inc. and its affiliates or designees, as well as, FDA representatives.

12.4 **Protocol Adherence and Deviations**

The study will be conducted as described in this protocol. Investigators are not permitted to deviate from this protocol except to protect patient rights, safety or well-being. Any deviations from this protocol must be documented by the Investigator. If an emergency situation arises in which the rights, safety and well-being of a subject may require immediate alternative intervention, the Investigator should act in the best interest of the subject. Sponsor and the site's IRB must be notified immediately if this occurs. This should be followed with written confirmation that describes the emergency action and outcomes, to

Sponsor and per IRB reporting requirements. Protocol deviations will be reviewed during routine monitoring visits. Investigators will be required to identify preventive and corrective actions to prevent further deviations. An Investigator may be disqualified from the study for repeated and/or egregious protocol deviations.

This protocol may be amended as necessary by the Sponsor. Any protocol amendments will be documented via an incremented version of this protocol (with relevant revision history) and a "was/is" comparison table to highlight the protocol changes. Amendments to the protocol must undergo the same approval process by the Sponsor, Investigators, IRBs and regulatory authorities as the original protocol.

12.5 **Device Accountability**

The study device may only be used for treated subjects in this study under the supervision of the Investigator and under the terms of this protocol. The Investigator may not provide the devices to any unauthorized person. The Investigator will also ensure that the device components are stored under the conditions outlined in the IFU and maintained under secure storage. Device accountability records will be maintained and will include:

- Product code
- Lot number
- Serial number
- Receipt dates
- Dates and quantities dispensed including subject number and initials, if applicable
- Return date to Bard (if any). Any study devices that have failed or malfunctioned should be returned to Bard. Any used study devices that have malfunctioned should be placed in a biohazard bag, labeled "Biohazard", and returned to Bard. Please refer to the site regulatory binder for return instructions.

Bard will supply the Investigator with an adequate number of study devices for completion of the study. Study devices may not be re-sterilized or reused. Device Accountability shall be completed in accordance with 21 CFR Parts 812.3, 812.100, 812.110, and 812.140.

12.6 **Data Collection**

The Investigator is responsible for completely and accurately recording study data in the appropriate sections of the eCRFs provided by Sponsor. The eCRFs must be signed by the Investigator or by his/her documented designee.

The Investigator is also responsible for making source documents and forms readily available for a thorough review by the study monitor at each monitoring visit. The monitor will ensure the accuracy of data recording at each investigational site by comparison to supporting source documents during periodic site visits. Adherence to proper recording of information as well as assuring that corrections are being made will also be addressed during these periodic visits.

12.7 **Subject Compensation**

To compensate subjects for their time and participation, they may receive stipends upon completion of each of the protocol specified study visits. If the subject does not complete a visit, they will not be compensated for that visit.

12.8 **Communications With The Sponsor**

Although the Investigator and his/her staff may have contact with other key individuals at the Sponsor throughout the course of the study, all communications regarding conduct of the study must be channeled through the Sponsor's clinical affairs personnel or their designees.

12.9 **Required Documentation**

An Investigator may not screen or enroll subjects until authorized to do so by the Sponsor. At a minimum, the following documentation must be received by the Sponsor prior to study commencement:

- CVs and medical licenses for the principal Investigator and sub-Investigators;
- Signed Clinical Study Agreement;
- Signed Nondisclosure Agreement;
- Signed "Protocol Signature Page" (page ii of this protocol);
- Study Personnel Identification List;
- Written approval from the IRB of both the protocol and ICF;
- Signed Financial Disclosure Statement; and
- IRB Assurance of Compliance Form or equivalent.

13 SITE MONITORING

The study monitors are designated as agents of the Sponsor and are assigned to oversee the conduct and progress of the study and to be the principal communication link between the Sponsor and the Investigator.

The study monitors will be involved in Investigator selection and training, assurance of IRB approvals, and periodic on-site inspection and monitoring of sites and records, to ensure continued compliance with the protocol and adequacy of the Investigator and the facility to carry out the study. In addition, the monitor will verify that the device is being used in accordance with the protocol instructions.

The site may also be subject to a quality assurance audit by personnel of the Sponsor as well as by FDA representatives.

The monitor will perform several types of site visits during the course of the study. In all cases, the study monitor will provide a written summary of the visit, including necessary follow-up items, to the Investigator and Sponsor.

It is important that the Investigator(s) and the relevant site personnel are available during the monitoring visits, and possible audit, and that sufficient time is devoted to the process.

13.1 **Study Initiation Visit**

Before the study begins, the study monitor will visit the site. The purpose of this visit is to review with the Investigator and staff the provisions and proper conduct of the clinical evaluation. This includes a detailed review of the protocol and eCRFs with instructions as to their completion, as well as reviewing regulations pertaining to the conduct of the clinical study. Arrangement for timely and accurate reporting of clinical data and relevant medical events will be established as well as ensuring safe and secure storage for the study devices.

The study monitor will:

- Confirm that the ICF to be used is the one approved by the IRB;
- Verify that all necessary documents are on file at the site; and
- Confirm that there are provisions to continue and maintain all documents and records throughout the study as required by GCP regulations.

13.2 **Ongoing Monitoring Visits**

The study monitor will maintain personal contact with the Investigator and staff throughout the study by telephone, e-mail, fax, mail, and on-site visits. On-site monitoring will begin after the first subjects are enrolled and continue until the study is completed. The monitoring will assure continued protocol compliance, adequate subject enrollment, accurate data reporting (including the comparison of eCRFs with subject records), device accountability (if required), and continued IRB acceptance of the study. The study monitor will evaluate and summarize the results of each visit in written reports, identifying any ongoing data problems with any study site and specifying recommendations for resolution of noted deficiencies. A formal monitoring plan will describe the planned extent of source data verification.

13.3 **Final Monitoring Visit**

At the completion of the study, the study monitor will conduct a final on-site visit. The purpose of this visit is to collect all outstanding study data documents, confirm that the Investigator's files are accurate and complete, review the record retention requirements with the Investigator, provide the return of unused devices (if required) to the sponsor, review records which account for device shipment (if required), and assure that all applicable requirements for closure of the study are met. The actions and observations made at this visit will be recorded and filed.

14 TERMINATION OF STUDY

Sponsor reserves the right to suspend enrollment or terminate the study at any time as set forth in the Clinical Study Agreement. Written notice will be submitted to the Investigator in advance of such termination.

Sponsor may suspend enrollment or terminate the study at a specific site for reasons including, but not limited to, inadequate data collection, low subject enrollment rate, achievement of the total enrollment, or non-compliance with the protocol or other clinical research requirements.

15 REPORTING REQUIREMENTS

The Investigator must promptly report to Sponsor any withdrawal of IRB approval at the site. Additional reporting requirements of the Investigator include:

- Reporting all ICF violations to the IRB
- Reporting all unanticipated problems, whether AEs or not
- Reporting all device-related AEs to Davol Field Assurance Department

As well as any additional requirements per the local IRB.

16 RECORD RETENTION

The investigator shall retain all study records for a period of 2 years after the investigation is terminated or completed, or until the records are no longer required as determined by the Sponsor. The investigator may withdraw from the responsibility to maintain records for the period required and transfer custody of the records to any other person who will accept responsibility for retaining them with pre-approval. Notice of a transfer shall be given to the Sponsor not later than 10 working days after transfer occurs.

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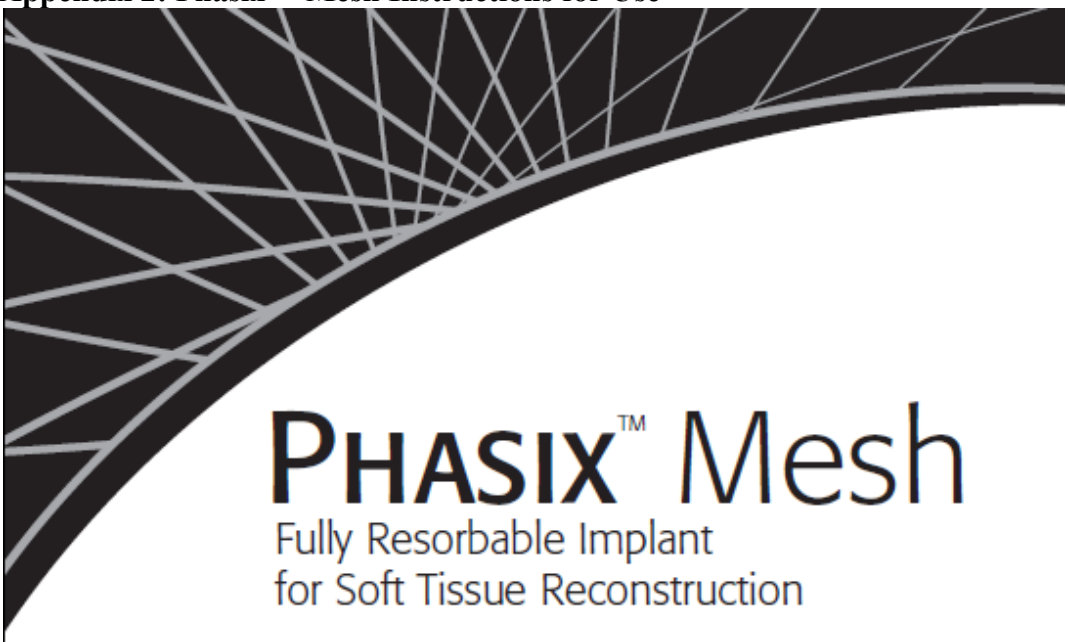
18 APPENDICES

Appendix 1: Principal Investigator Information

Yuri Novitsky, MD
Co-Director, Case Comprehensive Hernia Center
University Hospitals Case Medical Center
11100 Euclid Avenue
Cleveland, OH 44106

Phone: 216-286-6801
Fax: 216-844-2888
Email: yuri.novitsky@uhhospitals.org

Appendix 2: Phasix™ Mesh Instructions for Use



PHASIX™ Mesh

Fully Resorbable Implant
for Soft Tissue Reconstruction

INSTRUCTIONS FOR USE

Absorbable

Single Use

STERILE EO

℞ Only

Distributed by:
Davol Inc.
Subsidiary of C. R. Bard, Inc.
100 Crossings Boulevard
Warwick, RI 02886 USA
1-401-825-8300
1-800-556-6275

Medical Services & Support
Clinical Information Line
1-800-562-0027

Manufactured by:
Tepha, Inc.
99 Hayden Avenue, Suite 360
Lexington, MA 02421 USA

BARD
DAVOL INC.

PRODUCT DESCRIPTION

PHASIX™ Mesh is a resorbable mesh prepared from poly-4-hydroxybutyrate (P4HB). P4HB is produced from a naturally occurring monomer and is processed into monofilament fibers and knitted into a surgical mesh.

PHASIX™ Mesh degrades through a process of hydrolysis and a hydrolytic enzymatic digestive process. It has been developed to minimize the variability of resorption rate (loss of mass) and strength and provide support throughout the expected period of healing.

Pre-clinical implantation studies indicate that the resorption of the PHASIX™ fibers is minimal throughout the 12 week expected period of healing and up to about 26 weeks post implantation. Resorption of the fibers is essentially complete in 12 to 18 months.

INDICATIONS

PHASIX™ Mesh is indicated to reinforce soft tissue where weakness exists, such as the repair of hernia or other fascial defects that require the addition of a reinforcing or bridging material to obtain the desired surgical result.

CONTRAINDICATIONS

Because PHASIX™ Mesh is fully resorbable, it should not be used in repairs where permanent wound or organ support from the mesh is required.

WARNINGS

1. **Device manufacture involves exposure to tetracycline hydrochloride and kanamycin sulfate. The safety and product use for patients with hypersensitivities to these antibiotics is unknown. Use of this device in patients with known allergies to tetracycline hydrochloride or kanamycin sulfate should be avoided.**
2. **The safety and effectiveness of PHASIX™ Mesh in neural tissue and in cardiovascular tissue has not been evaluated or established.**
3. **The safety and effectiveness of PHASIX™ Mesh in pediatric use has not been evaluated or established.**
4. **The placement of PHASIX™ Mesh in direct contact with bowel or viscera is not recommended.**
5. **If an infection develops, treat the infection aggressively. Consideration should be given regarding the removal of the mesh. An unresolved infection may require removal of the device.**
6. **This device is supplied sterile. Inspect the device and packaging prior to use to be sure they are intact and undamaged.**
7. **This device is for single use only. Do not resterilize or reuse any portion of the PHASIX™ Mesh.**
8. **If unused prosthesis has been in contact with instruments or supplies used on a patient or contaminated with body fluids, discard with care to prevent risk of transmission of viral infections.**

PRECAUTIONS

1. Please read all instructions prior to use.
2. Only physicians qualified in the appropriate surgical techniques should use this device. Users should be familiar with strength and mesh size requirements. Improper selection, placement, positioning and fixation of the devices can cause subsequent undesirable results.

ADVERSE REACTIONS

In pre-clinical testing, PHASIX™ Mesh elicited a minimal tissue reaction characteristic of foreign body response to a substance. The tissue reaction resolved as the mesh was resorbed. Possible complications include infection, seroma, pain, mesh migration, wound dehiscence, hemorrhage, adhesions, hematoma, inflammation, extrusion and recurrence of the hernia or soft tissue defect.

DIRECTIONS FOR USE

PHASIX™ Mesh may be cut to shape or size desired for each specific application. To prevent recurrences when repairing hernias, a mesh larger than the defect is required to ensure adequate coverage. The mesh is to be positioned so its edges extend beyond the margins of the defect.

It is recommended that surgical fixation be placed ¼ to ½ inches (6 to 12mm) apart at a distance approximately ¼ inch (6mm) from the edge of the mesh. The edges are then fixated to assure proper closure under correct tension.

HOW SUPPLIED

PHASIX™ Mesh is available in single packets as a sterile, undyed fabric mesh in single sheet sizes of varying widths and lengths.

STORAGE

Store at room temperature. Avoid prolonged exposure to elevated temperatures. The indicator should be white or light grey. If the indicator is black on the box, check the indicator on the foil pouch. If the indicator is black on the foil pouch, do not use the product.

TRACEABILITY

A traceability label that identifies the type, size, expiration date and lot number of the device is attached to every package. This label should be affixed to the patient's permanent medical record to clearly identify the device that was implanted.

Appendix 3: Surgical Site Infection Classification[27]

Superficial Incisional Surgical Site Infections (SSI)
Infection occurs within 30 days after the operation
and
Infection involves only the skin or subcutaneous tissue around the incision and at least one of the following:

1. Purulent drainage with or without laboratory confirmation, from the superficial incision.
2. Organisms isolated from an aseptically obtained culture of fluid or tissue from the superficial incision.
3. At least one of the following signs or symptoms of infection: pain or tenderness, localized swelling, redness or heat and superficial incision is deliberately opened by a surgeon, unless the culture is negative.
4. Diagnosis of superficial incisional SSI by the surgeon or attending physician.

NOTE: Do not report the following as SSI:

1. Stitch abscesses (minimal inflammation and discharge confined to the points of suture penetration)
2. Infection of the episiotomy or neonatal circumcision sites
3. Infected burn wound.
4. Incisional SSI that extends into the fascial and muscle layers (see definition for Deep Incisional Surgical Site Infections below).

Note: Specific criteria are used for identifying infected episiotomy and circumcision sites and burn wounds.

Deep Incisional SSI
Infection occurs within 30 days after the operation if no implant is left in place or within one year if implant is in place and the infection appears to be related to the operation;
and
Infection involves deep soft tissues (e.g., fascia and muscle layers) of the incision and at least one of the following:

1. Purulent drainage from the deep incision but not from the organ/space of the surgical site.
2. A deep incision spontaneously dehisces or is deliberately opened by a surgeon when the patient has at least one of the following signs: fever (>38°C), localized pain or tenderness unless the culture is negative.
3. An abscess or other evidence of infection involving the deep incision is found on direct examination, during reoperation, or by histopathologic or radiologic examination.
4. Diagnosis of a deep SSI by a surgeon or attending physician.

Notes:

1. Report infection that involves both superficial and deep incision as deep incisional SSI.
2. Report an organ / space SSI that drains through the incision as deep incisional SSI.

Appendix 4: Surgical Wound Classification[27]

- Class I/Clean: An uninfected operative wound in which no inflammation is encountered and the respiratory, alimentary, genital, or uninfected urinary tract is not entered. In addition, clean wounds are primarily closed and, if necessary, drained with closed drainage. Operative incisional wounds that follow non-penetrating (blunt) trauma should be included in this category if they meet the criteria.

- Class II/Clean-Contaminated: An operative wound 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.

- Class III/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, non-purulent inflammation is encountered including necrotic tissue without evidence of purulent drainage (e.g., dry gangrene) are included in this category.

- Class IV/Dirty-Infected: 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.