STATISTICAL ANALYSIS PLAN
(24-Months)

Title: A Post-Market, Prospective, Multi-Center, Single-Arm Clinical Investigation of Phasix™ Mesh for VHWG Grade 3 Midline Hernia Repair

Protocol No.: DVL-HE-016

Study Device: Phasix™ Mesh

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Protocol Abbreviations/ Acronyms

Abbreviation/Acronym	Definition
ADE	Adverse Device Effect
AE	Adverse event
Bard	C. R. Bard, Inc.
BMI	Body Mass Index
CAD	Coronary Artery Disease
CBGB	Coronary artery bypass graft with both chest and donor site incisions
CCS	Carolina Comfort Scale
CDC	US Centers for Disease Control and Prevention
CE	Conformité Européenne
CIP	Clinical Investigational Plan
cm	Centimeter
COPD	Chronic Obstructive Pulmonary Disease
CRO	Clinical Research Organization
CST	Component Separation Technique
CT	Computed Tomography Scan
CV	Curriculum vitae
DIP	Deep Incisional Primary
DIS	Deep Incisional Secondary
DM	Diabetes Mellitus
DMP	Data Management Plan
e.g.	For Example
early term. /ET	Early Termination Visit
eCRF	Electronic Case Report Form
EEA	European Economic Area
EEC	European Economic Community
EQ-5D	EuroQol 5 Dimensions
etc.	Et Cetera.
FDA	Food and Drug Administration
GCP	Good Clinical Practice
GI	gastrointestinal
HIV	Human Immunodeficiency Virus
Hrs	Hours
i.e.	That Is
ICF	Informed Consent Form
IFU	Instructions For Use
Inc.	Incorporated
ISO	International Organization for Standardization
ITT	Intention-to-treat
LOS	Length of stay
LTF	Lost to Follow-Up
mITT	Modified Intention-to-treat
mm	Millimeter
MRI	Magnetic Resonance Imaging
N	Sample Size

NL	Netherlands
OTC	Over the Counter
P4HB	poly-4-hydroxybutyrate
PE	Physical Examination
PP	Per Protocol
QoL	Quality of Life
RCT	Randomized Controlled Trial
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SIP	Superficial Incisional Secondary
SIS	Superficial Incisional Primary
SOC	Standard of Care
SSI	Surgical Site Infection
SSO	Surgical Site Occurrence
™	Trademark
unsched.	unscheduled
US	United States
VAC	Vacuum Assisted Closure system
VAS	Visual Analogue Scale
VHWG	Ventral Hernia Working Group

1 Change from previous version

-Identification of the SSO events was updated to use the information on AE page only, as the dates on the visit page were not matching with the actual start dates of the events.

- Regarding the summary of Safety monitoring committee adjudicated AE data added.

-Subgroup analyses added.

- Cost of care as secondary endpoint is removed.

-Subjects with active fistula in their medical history will be excluded from the Per Protocol population

-Identification of the hernia recurrence events was updated to use the information on AE page only.

2 Introduction

This document provides details of the statistical analysis plan (SAP) for the C.R. Bard, Inc. protocol DVL-HE-016. The study will be reported at final database lock and at interim analysis. An interim analysis will be performed as soon as all subjects have documented the 3 month visit or have withdrawn from the study earlier. The statistical methods described here are based on the analyses proposed in the Final Protocol issued on **August 24, 2015, Version 1.0**, and its amendment, issued on **October 12, 2018, Version 2.**

All data processing, summarization, and analyses will be performed using Statistical Analysis System (SAS), Version 9.3 software package.

3 Study Objective and Endpoints

3.1 Study Objective

The objective of this study is to collect additional data on safety and performance of Phasix™ Mesh in subjects requiring VHWG Grade 3 midline hernia repair.

3.2 Study Endpoints

3.2.1 Primary Endpoint

Primary endpoint is Surgical Site Occurrence (SSO) rate up to (including) the 3-month (± 14 days) Follow-Up Assessment.
Occurrences at the surgical site will be assessed by physical examination at each study visit through 3 months (± 14 days). Surgical site occurrence will be defined as hematoma, seroma, surgical site infection, wound dehiscence, skin necrosis and fistula requiring intervention.

3.2.2 Secondary Endpoints

1. Surgical Site Occurrence (SSO) rate > 3-month follow-up assessment
2. Hernia Recurrence Rate (via physical exam, if uncertain via ultrasonography, if uncertain, via CT/MRI).
3. Surgical Site Infection rate
4. Pain - Visual Analog Scale (VAS)
5. Device-related adverse event incidence
6. Rate of reoperation due to the index hernia repair
7. Quality of life assessments (Carolinas Comfort Scale® and EQ-5D™)
8. Surgical procedure time as measured from incision to closure (skin to skin)
9. Return to Work
10. Length of stay in hospital (day of index surgery until day of discharge, LOS)

3.3 Overview

This is a Post-market, prospective, single-arm, multicenter, open-label study.

Patient population is Ventral Hernia Working Group (VHWG) Grade 3 midline hernia patients. Grade 3 (potentially contaminated) includes the presence of a nearby stoma, bowel resection, violation of the gastrointestinal tract, or history of wound infection.

Approximately 85 subjects, at approximately 12 sites across Europe will be enrolled and treated to study the use of Phasix™ Mesh. All treated subjects will be followed for 2 years post-implantation.

The plan is to study the use of Phasix™ Mesh in VHWG Grade 3 midline hernia patients.

The objective of this study is to collect additional data on safety and performance of Phasix™ Mesh in subjects requiring VHWG Grade 3 midline hernia repair. Follow-up visits will be conducted at drain removal (per standard of care, SOC), 1, 3, 6, 12, 18, and 24 months following surgery.

3.4 Sample Size Consideration

This is a feasibility study aiming to collect additional data on safety and performance of Phasix™ Mesh in subjects requiring VHWG Grade 3 midline hernia repair. There is no formal hypothesis test in this study and the result of the study is not for claiming purpose.

The study plans to include 85 subjects for follow-up, meaning 84 subjects having been treated with Phasix™ Mesh. Assuming an attrition rate of about 10%, 75 subjects will be evaluable to assess the primary endpoint of Surgical Site Occurrence (SSO) at 3 months. The expected rate of SSO at 3 months is 37% based on historically data. With 75 subjects, the accuracy of the estimated rate of SSO will be +/- 11% (i.e., half of the width of the 95% confidence interval of the estimated rate of SSO is 11%).

3.5 Study Procedure

Subjects with a diagnosis of incisional midline hernia requiring surgical repair to close the defect who are presenting at the study site will be considered potential subjects for inclusion in this clinical study and should be pre-screened for study eligibility. If inclusion criteria are potentially met and no exclusion criteria are anticipated to be present at the time of such pre-screening (except for the informed consent which still needs to be obtained), the Investigator will discuss the study and invite the patient to participate in accordance with the processes as described in protocol section 14.3.3 in order to seek their informed consent to be given. Within 60 days from having obtained the subjects' informed consent, they 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).

Written informed consent must be obtained prior to performance of any protocol specific procedures.

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

Table 1: Table of Study Events

Study Procedure	**Screening and Baseline**	**Index Surgery**	**Drain Removal** [4]	**1 Month Visit**	**3 Month Visit**	**6 Month Visit**	**12 Month Visit**	**18 Month Visit**	**24 Month Visit**	**Unsched Visit / Early Term**
Visit Window (days)	**Within 60 days of ICF signed**	**0**	**Per SOC**	**30 ± 7**	**90 ± 14**	**180 ± 30**	**365 ± 60**	**545 ± 60**	**730 ± 60**	**--**
Describe study to potential subject	**X**									
Obtain informed consent	**X**									

Collect demographics and medical history	**X**									
Verify eligibility criteria	**X**	**X[1]**								
Physical examination	**X**		**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**
Placement of Device		**X**								
Pain Scale (VAS)	**X**		**X[2]**	**X**	**X**	**X**	**X**	**X**	**X**	**X**
Carolinas Comfort Scale®	**X**			**X**	**X**	**X**	**X**	**X**	**X**	**X**
EQ-5D™	**X**			**X**	**X**	**X**	**X**	**X**	**X**	**X**
Collect adverse events		**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**
Collect pain medications[3]	**X**						**X**		**X**	
Schedule follow-up visit	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**		

1 Intraoperative verification of inclusion/ exclusion criteria
2 Assessment BEFORE Drain Removal
3 AE related pain medication should be documented on the pain medication log page
4 In the case no drains were placed, the assessments will be done at day of discharge. In case several drains are placed and pulled at different time points, assessments on any of the days of drain removal is allowed.

The following visit windows will be conducted and used for analysis.

Table 2: Table of Visit Windows

Visit	Visit Window	Interval (cumulative)		Interval (disjoint)	
		Term	Days	Term	Days
1 month	Day 30 ± 7 days	Until 1 month	0-37 days	Surgery Day; Post Surgery Day-1 month	0 day; 1-37 days
3 month	Day 90 ± 14 days	Until 3 months	0-104 days	>1 month – 3 months	38-104 days
6 month	Day 180 ± 30 days	Until 6 months	0-210 days	>3 months – 6 months	105-210 days
12 month	Day 365 ± 60 days	Until 12 months	0-425 days	>6 months – 12 months	211-425 days
18 month	Day 545 ± 60 days	Until 18 months	0-605 days	>12 months – 18 months	426-605 days
24 month	Day 730 ± 60 days	Until 24 months	0-end of study/790 days (whichever is earlier)	>18 months – 24 months	606 days-end of study/790 days(whichever is earlier)
End of Study (if >24 month upper window)	NA	Until End of Study	0-end of study	>24 months-end of study	791 days-end of study

4 Population Sets

Subjects who sign an informed consent will be considered enrolled in this study. Subjects who provide consent for participation but do not meet all of the study eligibility criteria and do not receive the study device will be considered screen failures.

The Intention-to-treat (ITT) population consists of all enrolled subjects. The mITT population is defined as those subjects in the ITT population in whom Phasix™ Mesh has been implanted.

A Per-Protocol (PP) population may be created if there are subjects who have any major protocol deviations. The PP population will consist of any subjects in the mITT population who do not have any major protocol deviation.

Subject who failed to meet the inclusion exclusion criteria and treated with the study device will be considered as major protocol deviations and will be excluded from the Per-protocol population. Additionally subjects who had active fistula as medical history will be excluded from the Per protocol population.

All analyses will be primarily based on the mITT population. Primary analyses may be performed for PP population as well.

5 Primary Endpoints

The primary endpoint is Surgical Site Occurrence (SSO) rate up to (including) the 3-month (± 14 days) Follow-Up Assessment.

5.1 Definitions

Occurrences at the surgical site will be assessed by physical examination at each study visit through 3 months (± 14 days). Surgical site occurrence will be defined as hematoma, seroma, surgical site infection, wound dehiscence, skin necrosis and fistula requiring intervention.

SSO is defined as based adverse events report with lower level term correspond to one of the above listed events, provided that some clinical action was taken to treat the adverse event. If the mesh was fully explanted prior to the onset of the adverse event then the event is not included in the SSO counts -.

5.2 Statistical Hypothesis

There are no statistical hypotheses to be tested.

5.3 Primary Analysis

The proportions of subjects with SSO up to 3-month upper window, and 95% confidence intervals of the rate from exact binomial test, will also be reported. Primary analysis is based on mITT population and PP population.

Reported SSO date will be used to determine if a SSO occurred within 3 months window from index surgery. Any subjects discontinued before 3 month lower window (<76 days) and did not have SSO are considered as not evaluable and will be excluded from the analysis. If subjects discontinued before 3 month lower window but had SSO, they are already known as failures and will be included in analysis. If subjects stayed in study longer than 76 days and are free of SSO, even if they did not come for 3 month visit, they are included in the analysis as free of SSO, as long as no unscheduled visits indicating they had SSO.

5.4 Sensitivity Analysis and Handling of Missing Data

The proportion of subjects with SSO up to 3-month visit window along with 95% confidence interval will be estimated using the Kaplan-Meier method. Number of subjects with events, number of subjects censored and number of subjects left will also be presented.

In survival analyses, unobserved endpoints are a standard part of the analysis. They are known as censored observations. The time to first event will be the time from index-procedure to the first occurrence of the first event. Subjects who do not have SSO before 3 month upper window and do not discontinue the study before day 104 will be censored at day 104; subject who discontinue before day 104 will be censored at discontinuation day. If subjects discontinue at surgery day then day 0.5 will be used as discontinuation day.

A Kaplan-Meier graph will also be provided showing the survival curves and displayed by gender.

6 Evaluation of Secondary Endpoints

6.1 Surgical Site Occurrence (SSO) rate > 3-month follow-up assessment

The proportion of subjects with SSO after 3 month follow-up upper window (>104 day) and confidence intervals of the rate from exact binomial test will be reported.

If a subject discontinued within (≤) 104 days after index surgery, that subject is considered not evaluable and will be excluded from calculation of SSO rate after 3 month follow-up.

Analysis is based on mITT population.

6.2 Hernia Recurrence Rate

The proportion of subjects with Hernia Recurrence and confidence intervals of the rate from exact binomial test will be reported by each visit window, including both cumulative and disjoint intervals.

If a hernia recurrence occurs, a corresponding adverse event has to be documented. Hernia recurrence recorded in the AE data set will be used for the endpoint. The start date of the corresponding AE is compared with surgery date to determine the interval of hernia recurrence.

Only evaluable subjects will be included in the denominator and evaluable subjects are defined as following: 1) For cumulative intervals, any subjects with Phasix™ Mesh implanted will be included in this analysis. 2) For disjoint intervals, if a subject discontinues before the intervals begins then that subject is considered as not evaluable for that particular interval analysis.

The proportion of subjects with hernia recurrence up to each visit upper window and up to end of study (if any subjects' last visits fall outside of 24 month visit upper window) along with 95% confidence interval will be estimated using the Kaplan-Meier method. Number of subjects with events, number of subjects censored and number of subjects left will also be presented. A Kaplan-Meier graph will also be provided showing the survival curves. The time to first event will be the time from index-procedure to the first occurrence of the event.

Subjects who do not have events are censored at discontinuation/completion day. For interim analysis, subjects without events before upper window of that interim analysis (104 day for 3 month interim, etc.), are censored at earlier of discontinuation day or upper window of that interim analysis. If subjects discontinue at surgery day then day 0.5 will be used as discontinuation day.

Hernia Recurrence in the same location as index procedure is identified by physical exam or any other means from post-operative CRF pages at scheduled or unscheduled visits. Analysis is based on mITT population.

6.3 Surgical Site Infection rate

The proportion of subjects with Surgical Site Infection (SSI) and confidence intervals of the rate from exact binomial test will be reported by each visit window, including both cumulative and disjoint intervals.

SSI date will be compared to surgery date to determine the interval of SSI.

Only evaluable subjects will be included in the denominator and evaluable subjects are defined as following: 1) For cumulative intervals, any subjects with Phasix™ Mesh implanted will be included in this analysis. 2) For disjoint intervals, if a subject discontinues before the intervals begins then that subject is considered as not evaluable for that particular interval analysis.

The proportion of subjects with SSI up to each visit upper window and up to end of study (if any subjects' last visits fall outside of 24 month visit upper window) along with 95% confidence interval will be estimated using the Kaplan-Meier method. Number of subjects with events, number of subjects censored and number of subjects left will also be presented. A Kaplan-Meier graph will also be provided showing the survival curves. The time to first event will be the time from index-procedure to the first occurrence of the event.

Subjects who do not have events are censored at discontinuation/completion day. For interim analysis, subjects without events before upper window of that interim analysis (104 day for 3 month interim, etc.), are censored at earlier of discontinuation day or upper window of that interim analysis. If subjects discontinue at surgery day then day 0.5 will be used as discontinuation day.

The occurrence of an SSI will be determined from the SSI log page. Analysis is based on mITT population.

6.4 Pain - Visual Analog Scale (VAS)

Subjects complete the pain VAS with 0 cm = no pain to 10 cm = severe pain at baseline and at all post procedure visits.

The pain VAS length (cm) and its absolute change from baseline will be described with summary statistics by visit. In case of subjects with chronic pain as documented in medical history, summary statistics by visit and its absolute change from baseline will be presented additionally without these subjects.

Analysis is based on mITT population.

6.5 Device Related Adverse Event Incidence

Adverse events that are possibly or definitely related to device are considered. In case of a missing classification of the relationship to device a relation to the device is assumed. A frequency table grouped by Medical dictionary for regulatory activities (MedDRA) terms (system organ class (SOC) and preferred term (PT)) will be presented for number of subjects with device related AEs and total number of AEs.

Frequency tables for device related AEs by time intervals (Surgery Day-End of Study/Surgery Day/Post Surgery-1 month/>1 month-3 month/>3 month-6 month/>6 month-12 month/>12

month-18 month/18 month-24 month/>24 month) presenting the number of subjects with events and total number of events will be displayed.

For each time interval, if a subject discontinues before the interval begins then that subject is considered as not evaluable for that particular interval analysis.

Analysis is based on mITT population.

6.6 Rate of Reoperation due to Index Hernia Repair

The proportion of subjects with post procedure reoperation due to the index hernia repair and confidence intervals of the rate from exact binomial test will be reported by each visit window, including both cumulative and disjoint intervals.

Reoperation date will be compared to surgery date to determine the interval of reoperation.

Only evaluable subjects will be included in the denominator and evaluable subjects are defined as following: 1) For cumulative intervals, any subjects with Phasix™ Mesh implanted will be included in this analysis. 2) For disjoint intervals, if a subject discontinues before the intervals begins then that subject is considered as not evaluable for that particular interval analysis.

Other characteristics of reoperation (reason, procedure type, etc.) will also be summarized.

All reoperations documented on the reoperation page are considered as reoperations due to the index hernia repair. Analysis is based on mITT population.

6.7 Quality of life assessments (Carolinas Comfort Scale® and EQ-5D™)

6.7.1 CCS

The CCS is a 23-item questionnaire that measures sensation of mesh, severity of pain and movement limitations in the following eight domains: laying down, bending over, sitting up, performing activities of daily living, coughing or deep breathing, walking, walking up the stairs and exercising. The CCS is completed by the subjects at baseline and at all post procedure visits (except drain removal visit). Each scale (sensation of mesh, pain or movement limitations) score (ranges from 0-5) is the average across the domains, and the total score (ranges from 0-5) is the average of the three scales scores.

CCS will be analyzed in accordance to the CCS user guide. Computational algorithms including the handling of missing values are described in detail in the guideline. In summary, the following rules will be applied:

1. Questions outcomes 0-5 will be used with lower scores indicating a more favorable health status.
2. Not applicable or no response will be handled as missing values.
3. Two or more outcomes ticked per question will be handled as missing value.

Absolute values and changes from baseline will be summarized with mean, standard deviation, minimum, median and maximum for each scale score and total score at each post baseline visit (except drain removal).

For each subject at each visit, if less or equal to two responses are missing within any of the three scales, the missing values will be replaced by the mean of the remaining responses of the scale at that visit. If more than two responses are missing within any scale for a visit, the whole survey at that visit will not be used for that subject.

Due to the fact that only subjects with recurrent hernia and used mesh in situ can answer the questions related to sensation of mesh at baseline, many values concerning sensation of mesh are "not applicable" at baseline. Absolute values at baseline and changes from baseline will be summarized for sensation of mesh and total score by subjects with recurrent hernia and used mesh in situ, if enough values are available.

Analysis is based on mITT population.

6.7.2 EQ-5D

The EQ-5D-3L essentially consists of 2 pages: the EQ-5D descriptive system and the EQ visual analogue scale (EQ VAS). The EQ-5D-3L descriptive system comprises the following 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension has 3 levels: no problems, some problems, extreme problems. The EQ VAS records the respondent's self-rated health and recorded as 'Health Today' in CRF. The EQ-5D is completed by the subjects at baseline and at all post procedure visits (except drain removal visit).

The data of the EQ-5D health states will be converted into a single summary index using European VAS value set rescaling with the mean value for Dead, which is described in following table 3.

Table 3 European VAS Value Set

European VAS value set*		**Example: the value for health state 21232***	
Full health (11111)	1	Full health	= 1
At least one 2 or 3 (N2)	-0.1279	Minus N2	- 0.1279
At least one 3 (N3)	-0.2288	Minus N3	- 0.2288
Mobility = 2	-0.0659	Minus MO level 2	- 0.0659
Mobility = 3	-0.1829		
Self-care = 2	-0.1173	Minus SC level 1	- 0.0000
Self-care = 3	-0.1559		
Usual activities = 2	-0.0264	Minus UA level 2	- 0.0264
Usual activities = 3	-0.0860		
Pain/discomfort = 2	-0.0930		
Pain/discomfort = 3	-0.1637	Minus PD level 3	- 0.1637
Anxiety/depression = 2	-0.0891	Minus AD level 2	- 0.0891
Anxiety/depression = 3	-0.1290		
		State 21232*	= 0.2982

* *The values have been rescaled to a scale with 11111 = 1 and 0 = Dead. This was done using the mean value of Dead.*

The EQ-5D index and its absolute change from baseline will be described with summary statistics by visit. Additionally frequency shift tables for each dimension of the EQ-5D descriptive system will be generated by post baseline visit to present the change from baseline.

The EQ VAS and its absolute change from baseline will be described with summary statistics by each visit.

Analysis is based on mITT population.

6.8 Surgical Procedure Time as Measured from Incision to Closure (Skin to Skin)

The surgical procedure time (mins) of the index procedure is calculated as time of skin closure complete minus time of first incision.

Summary statistics will be presented for surgical procedure time. Analysis is based on mITT population.

6.9 Return to Work

Summary statistics will be presented for the number of days until return to work calculated as date when employed subject was able to fully get back to work minus the date of surgery.

A frequency table will show if the subject is currently employed (outside home) (No/ Yes), the reason if not employed (Unemployed/ Disabled/ Retired/ Student/ Other) and the physical requirements of the subject's job (Minimal physical requirements/ Moderate physical requirements/ Heavy physical requirements).

Analysis is based on mITT population.

6.10 Length of Stay in Hospital (Day of Index Surgery until Day of Discharge, LOS)

The LOS (days) at index procedure is calculated as date of hospital discharge (index procedure, documented at Month 1 visit) minus date of hospital admission (documented at surgery).

The LOS will be descriptively summarized. The days in intensive care unit, days in step down (medium care) unit and the days in the ward will be descriptively summarized as well.

Analysis is based on mITT population.

7 Subgroup Analysis

By sex subgroup analysis will be performed for all primary and secondary parameters, including the PP analysis for primary endpoint, and Kaplan-Meier analysis (tables and curves) for primary and some secondary endpoints. Survival curves will be compared between the male and female subjects using the log-rank test for endpoints performed with Kaplan-Meier analysis.

Where appropriate, further subgroup analysis (based on the mITT set) may be performed for the primary endpoint if enough subjects within the subgroups allow further insight to the data. Following subgroups are subject to further interest:

- Centers: The sites with less than 10 subjects will be sorted by site number within each country and pooled by order to form one or more combined site(s) with at least 10 subjects. The pooling will be restricted within country.
- Pre-operative diagnosis: 'Primary incisional midline hernia' versus 'recurrent incisional midline hernia' (first, second, third and fourth time recurrent midline hernia are combined to one group).

- Surgical procedures: Surgical procedures performed with 'Retro-rectus with CST', 'Retro-rectus without CST', 'Onlay placement with CST', 'Onlay placement without CST' and 'Other'.
- Hernia Size: Above the median vs. below median of Hernia size
- Smoking status (Yes/no)
- BMI (<30 vs. >=30)
- Diabetes (Yes/no)

8 Other Analysis

8.1 Subject Disposition

The summary of the number of subjects enrolled (ITT), implanted with Phasix™ Mesh (mITT), completed the study, and discontinued from the study by reason of discontinuation will be provided. Screen failures will be listed with inclusion/exclusion criteria that were not met. Summary may also be presented by site.

8.2 Protocol Deviation

The number of subjects with protocol deviations will be summarized by nature of the deviation. Protocol deviations will be listed with date of occurrence and the nature of deviation. Additionally the protocol deviations will be summarized by investigational site, and the period they occurred.

8.3 Demography and Background Disease Characteristics

Demographics and background disease characteristics will be summarized with descriptive statistics using the mITT analysis set. Summary statistics for categorical variables will include frequency counts and percentages and for continuous variables will include mean, standard deviation, minimum, median, and maximum.

Demographics and baseline characteristics variables include:

- Age at screening (year)
- Sex (Male, Female)
- Race (Asian, Black or African American, Caucasian and Other)
- Baseline Weight
- Baseline Height
- Baseline Body mass index (BMI) calculated from weight and height.

Background disease characteristics including medical history, pre-operative diagnoses and hernia assessment will be summarized.

8.4 Pain Medication

All current pain medication is captured at baseline. Current hernia associated pain medication is captured at 12 and 24 months.

All documented pain medication will be coded by world health organization drug dictionary (WHO-DD) and will be tabulated by anatomical therapeutic chemical classification (ATC) level 1, level 4 and WHO-DD preferred term, at baseline, 12 month visit, and 24 month visit.

8.5 Physical Examination

Physical examination findings by body system will be summarized by all scheduled post procedure visit and end of study. The categories of the findings (normal/ abnormal) and the specification if abnormal (clinically significant/ not clinically significant) will be summarized.

The frequencies of changes since baseline will be shown for the body systems “abdomen” and “skin” using shift table.

8.6 Follow-up Period

The duration of follow-up period after the surgery during the study is calculated as:

Last day in study – date of the surgery

Last day in study is defined as latest of: discontinuation/completion day, last visit day, last event occurrence day.

Duration of follow-up will be summarized as continuous variable, and frequency in each duration category (Surgery Day-1 month/>1 month-3 month/>3 month-6 month/>6 month-12 month/>12 month-18 month/18 month-24 month/>24 month) will also be presented.

8.7 Intra-Operative Characteristics

Surgical diagnoses and hernia assessment will be summarized by subject. Phasix™ Mesh device implant will be summarized by device.

8.8 Visit Procedures

Visit procedures information will be summarized by each visit.

8.9 Surgical Drain

Surgical drains data will be summarized with number of drains, number of subjects with surgical drains, corresponding surgery, placement, location and duration.

8.10 Wound Vacuum-Assisted Closure (VAC)

Wound VAC data will be summarized with number of VACs, number of subjects with VACs, wound VAC types and duration.

8.11 Device Deficiencies

Device deficiencies will be summarized with number of deficiencies, number of subjects with device deficiencies, deficiency codes and reasons.

8.12 Surgical Site Infection and Phasix™ Mesh Infection

Surgical site infection and Phasix™ Mesh infection will be summarized by disjoint intervals and from post surgery day to end of study.

Surgical site infection will also be summarized by type of infections, and if one subject has multiple infection types, only most severity type will be counted once for each subject. Severity order is: Superficial<Deep<Organ/Space.

8.13 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. Additionally, abnormal laboratory results are to be considered AEs if the results are accompanied by clinical signs or symptoms.

AEs will be tabulated by system organ class (SOC) and preferred term (PT) (MedDRA). The total number of events, as well as the number and percentage of subjects with events will be reported. Subjects will also be summarized by severity groups. SAEs will be tabulated by SOC and PT.

Subjects with AEs related to the procedure (related to procedure is definitely related or possibly related) will be summarized with frequency and percentage. Frequency tables for procedure related AEs by time intervals presenting number of subjects with events and total number of events and will be displayed. Device related AEs are described as secondary endpoint.

Additionally, Serious Adverse Events that occurred within 3-months of the index procedure were adjudicated by an independent Safety Committee for the relatedness of the events with device or/and procedure ,the outcome of the adjudication will be summarized side by side with the site reported assessment.

Signature Page for VV-TMF-155954 v2.0

Reason for signing: Finalize	Name: Dawn Heimer Role: Medical Affairs Date of signature: 09-Sep-2019 19:35:39 GMT+0000

Reason for signing: Finalize	Name: Sandra van Guldener Role: Clinical Project Management Date of signature: 16-Sep-2019 16:27:45 GMT+0000

Reason for signing: Finalize	Name: Indrias Berhane Role: Statistics & Programming Date of signature: 16-Sep-2019 16:42:38 GMT+0000

Signature Page for VV-TMF-155954 v2.0