SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Polymerizing Sealant

Device Trade Name: PREVELEAK Surgical sealant

Device Procode: NBE

Applicant's Name and Address: Mallinckrodt Pharma IP Trading DAC
Damastown Industrial Estate
Mulhuddart, Dublin 15
Ireland

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P100030/S008

Date of FDA Notice of Approval: December 21, 2017

The original PMA P100030 was approved on March 1, 2013 and indicated ArterX Surgical Sealant (previous name for PREVELEAK Surgical sealant) for use in vascular reconstructions to achieve adjunctive hemostasis by mechanically sealing areas of leakage. The SSED to support the indication is available on the CDRH website (https://www.accessdata.fda.gov/cdrh_docs/pdf10/P100030B.pdf) and is incorporated by reference here. The current supplement was submitted to expand the indication for PREVELEAK Surgical sealant to include use in cardiac reconstructions.

II. INDICATIONS FOR USE

PREVELEAK Surgical sealant is indicated for use in vascular and cardiac reconstructions (excluding application to arterial and venous grafts used in coronary artery bypass graft surgery) to achieve adjunctive hemostasis by mechanically sealing areas of potential leakage.

III. CONTRAINDICATIONS

Not for use in patients with known allergies to materials of bovine or shellfish origin.
Not for intravascular use.
Not for cerebrovascular repair or cerebrospinal leak repair.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the PREVELEAK Surgical sealant labeling.

V. DEVICE DESCRIPTION

PREVELEAK Surgical sealant (PREVELEAK) is a sealant developed to seal suture holes formed during surgical repair of the circulatory system and to reinforce sutured anastomoses. When applied, PREVELEAK creates an elastic biocompatible gel that seals suture holes or gaps formed between synthetic grafts or patches and native vessel anastomosis. PREVELEAK adheres to the native tissues as well as synthetic materials, including Polytetrafluoroethylene (PTFE) and Dacron grafts, and facilitates sealing along anastomotic closure lines. After application, PREVELEAK is a golden color and stays soft and flexible. Animal studies showed significant absorption by 12 months with biodegradation that continues beyond 24 months.

PREVELEAK is provided in a double-barreled syringe assembly (**Figure 1**) containing equal volumes of purified bovine serum albumin (BSA) and polyaldehyde. PREVELEAK is supplied in a double pouch, with two delivery tips and terminally sterilized.

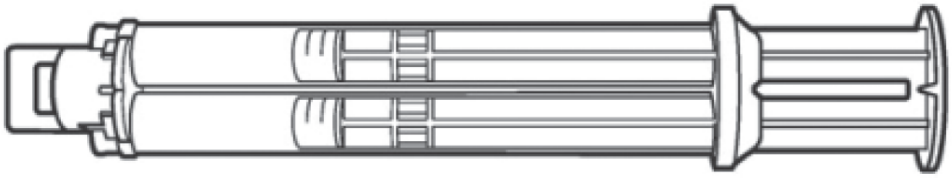


Figure 1. PREVELEAK Surgical Sealant Double Barrel Syringe

PREVELEAK is ready to use once the pouch is opened, the syringe cap removed, the delivery tip is attached and the tip is primed. When the plunger is depressed, the two components are thoroughly mixed as they pass through the delivery tip. After application, the sealant is allowed to remain undisturbed for at least 60 seconds before unclamping and exposing the anastomosis to arterial pressure. PREVELEAK is applied as a viscous liquid that gels within approximately 10-15 seconds. PREVELEAK is terminally sterilized by e-beam irradiation and is provided in a double pouch with two delivery tips. Additional sterile delivery tips are available separately. PREVELEAK is provided for single-use only.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several alternative practices for adjunctive measures to achieve hemostasis. Conventional methods to control bleeding include the use of direct pressure, sutures, electrocautery, and pledgets. Other commercially available devices such as sealants, absorbable hemostatic agents and adhesives are also used to control bleeding, including products composed of gelatin, cellulose, bovine collagen, thrombin, fibrinogen, polyethylene glycol polymers, bovine albumin/glutaraldehyde, and cyanoacrylate. Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

PREVELEAK Surgical Sealant is commercially available in the following countries:

The United States of America and the European Union – BSI CE Marked Recognized Countries (Austria, Albania, Belgium, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Italy, Latvia, Liechtenstein, Lithuania, Luxembourg, Macedonia, Malta, Montenegro, Netherlands, Norway, Poland, Portugal, Serbia, Slovakia, Slovenia, Spain, Sweden, Switzerland, Turkey).

A voluntary class II recall of the Tenaxis Medical ArterX Surgical Sealant (previous manufacturer and name of PREVELEAK Surgical Sealant) was initiated in the United Kingdom on October 17, 2014 due to the product being improperly labeled, which led to improper storage; no U.S. products were impacted. Product removal and a labeling correction was conducted. To date, there have been no other market withdrawals of the PREVELEAK Surgical Sealant for reasons related to safety or effectiveness.

VIII. PROBABLE ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the probable adverse effects (e.g., complications) associated with the use of the device (**Table 1**).

Table 1. Probable Adverse Events Associated with Surgical Sealants

• Application of the sealant to tissue not targeted for the procedure. • Failure of the sealant to adhere to the tissue. • Hypersensitivity reaction such as swelling or edema at the application site. • Possible transmission of infectious agents from materials of animal origin. • Thrombosis and thromboembolism.

Below is a list of the potential adverse effects associated with vascular and cardiac reconstructions (**Table 2**).

Table 2. Probable Adverse Events Associated with Vascular and Cardiac Reconstructions

• Adhesions	• Ischemia
• Anastomotic pseudoaneurysm	• Lymphocele/lymph fistula
• Aortic insufficiency	• Myocardial infarction
• Cardiac tamponade	• Neurological deficits
• Cerebral emboli	• Organ system dysfunction/failure
• Coagulopathy	• Pain
• Death or irreversible morbidity	• Paraplegia
• Dissection	• Pleural effusion
• Edema	• Pulmonary emboli
• Erythema	• Pyrexia
• Hematoma	• Renal dysfunction/failure
• Hemorrhage	• Stroke or cerebral infarction

• Infection • Injury to normal vessels or tissue	• Thrombosis • Vasospasm • Vessel rupture and hemorrhage

For the specific adverse events that occurred in the clinical study, please see Section X below.

IX. SUMMARY OF NONCLINICAL STUDIES

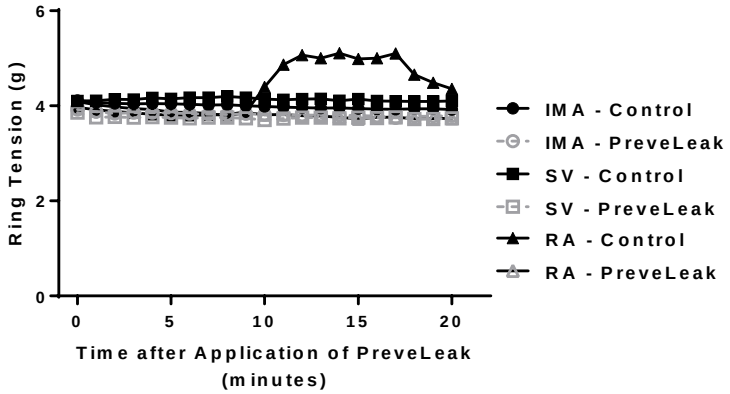
The majority of nonclinical data was leveraged from the original PMA. A summary of the nonclinical data (i.e., bench testing, animal studies, biocompatibility, sterilization, and shelf life evaluation) is available on the CDRH website.

A. Ex-vivo Vasoreactivity Study

An in vitro study was conducted to explore possible spontaneous vasoconstriction and vasoreactivity to constrictors and dilators after the application of PREVELEAK to the abluminal surface of isolated internal mammary artery (IMA), radial artery (RA), and saphenous vein (SV) vascular rings. Harvested vessels discarded from patients undergoing coronary artery bypass grafting (CABG) procedures were sectioned into cylindrical rings approximately 3 mm in length, suspended between two hooks, and treated with PREVELEAK circumfrentially. After equilibration, the rings were exposed to various concentrations of vasoconstrictors (U46619 and phenylephrine) and vasodilators (ADP and SNP).

As shown in Figure 2, PREVELEAK had no effect on baseline tension when applied to IMA, SV, or RA rings. The only incidence of spontaneous constriction was in control RA rings. There was no evidence of spontaneous vasoconstriction or vasodilation in rings treated with PREVELEAK compared to control.

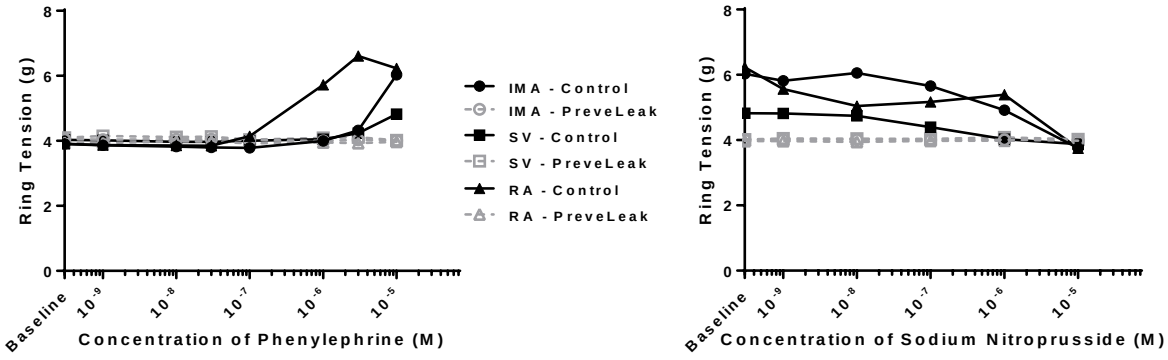
Figure 2. Stability of Baseline Tension of Rings From the IMA, SV, and RA After Treatment With PREVELEAK or Control



Each Value Represents a Single Observation

Control vascular rings exposed to KCl produced an increase in ring tension. In contrast, rings treated with PREVELEAK showed no change. Control rings exposed to increasing concentrations of U46619 produced concentration-related increases in ring tension. After treatment with PREVELEAK, increasing concentrations of U46619 had no effect on ring tension, regardless of baseline tension. After maximal contraction with U46619, control rings showed a concentration-dependent decrease in ring tension when exposed to ADP. Vessel rings treated with PREVELEAK failed to respond to increasing concentrations of ADP after exposure to U46619 preconstriction. Control rings showed increases in ring tension with increasing concentrations of phenylephrine (Figure 3). In contrast, rings treated with PREVELEAK showed no change. After maximal precontraction-induced with phenylephrine, increasing concentrations of SNP produced dilation in control rings. Phenylephrine constricted rings treated with PREVELEAK showed no change in ring tension with increasing concentrations of SNP (Figure 3).

Figure 3. Response to Increasing Concentrations of Phenylephrine Followed by SNP on IMA, SV, and RA Vascular Rings



Each Value Represents a Single Observation

The results from this ex vivo study demonstrated that application of PREVELEAK did not likely cause vasoconstriction when applied to the abluminal surface of vascular rings from the IMA, RA, and SV. However, PREVELEAK blocked the responses to the vasoconstrictors and vasodilators tested.

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical study in the European Union (referred to as the EU Cardiac Study) to establish a reasonable assurance of safety and effectiveness of PREVELEAK Surgical sealant for use in cardiac reconstructions to achieve adjunctive hemostasis by mechanically sealing areas of leakage. Data from this clinical study were the basis for the PMA approval decision. A summary of the clinical study is presented below.

A. Study Design

Patients were treated between June and December of 2013. The database for this Panel Track Supplement reflected data collected on 44 patients. There were 3 investigational sites.

The study was a prospective, open-label, multi-center, single-arm clinical study to evaluate the safety and effectiveness of PREVELEAK sealing suture lines at proximal and distal coronary anastomoses, aortic anastomoses, cannulation sites, and access incision sites on the aorta, atrium, and ventricle. All patients were followed for 3 months after treatment. Descriptive statistics were provided.

There was no core lab or Data Safety Monitoring Board (DSMB) for the study; however, the study utilized independent medical monitors for review of adverse events along with local Ethics Committee reviews.

1. Clinical Inclusion and Exclusion Criteria

   Enrollment in the European Union (EU) Cardiac Study (CLN-015) was limited to patients who met the following inclusion criteria:

   - The subject was ≥ 18 years old.
   - The subject had a known indication that required cardiac surgery and determined to be at risk for poor hemostasis.
   - The subject had no child bearing potential or negative serum or urine pregnancy test within 7 days of the index procedure.
   - The subject was willing and able to be contacted for the follow up visits at 6 weeks (± 7 days) and 3 months (± 7 days).
   - The subject or guardian must have provided written informed consent using a form that was reviewed and approved by the Institutional Review Board.

   Patients were not permitted to enroll in the EU Cardiac Study (CLN-015) if they met any of the following exclusion criteria:

   - The subject had a known hypersensitivity or contraindication to heparin, bovine or seafood products.
   - The subject had a history of bleeding diathesis or coagulopathy, or might refuse blood transfusions.
   - The subject was currently enrolled in this, or another investigational device or drug trial that had not completed the required follow-up period.

2. Follow-up Schedule

   All patients were examined during their hospital stay, and were scheduled to return for follow-up examinations at 6 weeks (±7 days) and at 3 months (±7 days) post-operatively. Adverse events and complications were recorded at all visits.

   The key timepoints are shown below in the tables summarizing safety and effectiveness.

3. Clinical Endpoints

With regards to safety, the primary endpoint was the cumulative incidence of significant bleeding, infection, neurological deficit or immune/inflammatory allergic response observed within 6 weeks post-treatment. Additional safety endpoints included adverse event assessment at the following time points: in hospital, 6 weeks and 3 months post-surgery.

With regards to effectiveness, the primary endpoint was immediate sealing of the suture/staple line at the point of use upon release of the clamps or taking the patient off-pump as evidenced by an absence of clinically significant bleeding (minor oozing was not considered clinically significant) which was determined by the investigator using the PREVELEAK device.

Additional endpoints included sealing at intervals of 1, 3, 5 and 10 minutes after clamp release or taking the patient off-pump. Re-operation, intra-operative complications, mortality rates, and device usage parameters were also assessed, inclusive of exposure to blood replacement products, and peri-/post- operative medications.

With regard to success/failure criteria, the analysis was based upon the primary effectiveness endpoint. The hypothesis was that immediate sealing of the suture/staple line would occur in ≥ 55% of the surgical procedures.

B. Accountability of PMA Cohort

Forty-six subjects were enrolled in the study. Two subjects withdrew informed consent prior to undergoing a qualifying surgical procedure. The remaining 44 subjects all underwent a surgical procedure, had PREVELEAK applied to at least one site, and were included in both safety and effectiveness analyses. One subject died during the study and two were lost to follow-up. The subject accountability is provided in **Table 3**.

Table 3. Subject Accountability

	PREVELEAK (N = 46)
Treated	44 (95.7%)
Completed 6-Week Follow-Up	42 (91.3%)
Completed 3-Month Follow-Up	41 (89.1%)

C. Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for a surgical sealant study. Subject demographics and medical history are provided in **Table 4**.

Of the 44 subjects treated with PREVELEAK, 70.5% were male. The mean age was 64.6 years and average BMI was 28.4 kg/m^2. Hypertension (35/44, 79.5%) was the most prevalent concomitant condition. Thirty-two of 44 subjects (72.7%) received anticoagulants (low molecular weight heparin or vitamin K antagonists) and/or antiplatelet medications (cyclooxygenase or P2Y12 inhibitors) intra-operatively or ≤ 5 days prior to surgery.

Table 4. Subject Demographics and Medical History

	PREVELEAK (N= 44)
Age (years)	
Mean ± SD	64.6 ± 10.5
Range (min, max)	(42, 84)
Gender	
Female	29.5%
Male	70.5%
Body Mass Index (kg/m^2)	
Mean ± SD	28.4 ± 4.1
Range (min, max)	(18.3, 35.3)
Medical History	
Hypertension	79.5%
Diabetes	31.8%
History of Thrombosis	2.3%

D. Procedural Information

A total of 63 cardiac surgical procedures were performed on the 44 subjects. PREVELEAK was applied to 127 sites and approximately two-thirds of subjects (29/44, 65.9%) had multiple (2 to 7) sites treated (**Table 5**). Distal anastomoses in CABG procedures were the most common application site (60/127, 47.2%).

Grafts were used at 94 of 127 treatment sites (74.0%; **Table 5**). Most grafts (85/94, 90.4%) were harvested from the subjects, with 54.2% (51/94) obtained from a vein and 36.1% (34/94) from an artery. All harvested grafts were used in CABG procedures. The five Dacron grafts were used for aortic aneurysm repair and the four prosthetic grafts were used for aortic root reconstruction (n = 2) and aortic aneurysm repair (n = 2).

Table 5. Surgical Procedures Studied

	PREVELEAK (N=44 Subjects, 127 Sites)
Coronary Artery Bypass Graft	67.7% (86/127)
Aortic Valve Replacement	14.2% (18/127)
Mitral Valve Reconstruction	6.3% (8/127)
Aortic Aneurysm Repair	5.5% (7/127)
Tricuspid Valve Reconstruction	2.4% (3/127)
Aortic Root Reconstruction	1.6% (2/127)
Cannulation Site	1.6% (2/127)
Aortic Valvuloplasty	0.8% (1/127)
Type of Graft	
Vein	40.2% (51/127)
Artery	26.8% (34/127)
Dacron	3.9% (5/127)
Prosthetic	3.1% (4/127)
No Graft Used	26.0% (33/127)

E. Safety and Effectiveness Results

1. Safety Results

The analysis of safety was based on the adverse events reported during the 3 month evaluation of the 44 subjects treated in with PREVELEAK in the EU Cardiac Study (CLN-015). The key safety outcomes for this study are presented below in **Tables 6**. Other adverse effects are reported in **Tables 7 and 8**.

Adverse effects that occurred in the PMA clinical study:

Overall, 71 adverse events (AEs) were reported for 36 subjects. Most events were mild (46/71, 64.8%) or moderate (18/71, 25.4%) in severity and had resolved by the time of study termination (78.9%). The majority of the adverse events (AEs) occurred within the first 6 weeks following surgery (63/71; 88.7%), as anticipated for subjects undergoing cardiac surgery.

The primary safety measure was any instance of significant bleeding, infection, neurological deficit, or immune/inflammatory allergic response observed within 6

weeks post-treatment. The cumulative incidence of such events was nine events in eight subjects (8/44, 18.2%); 1 subject experienced two events (**Table 6**). These events were considered by the investigators as not related to treatment with PREVELEAK and included eight infections (sternal wound: 4, urinary: 2, respiratory: 1, and epidermal: 1) and one neurological deficit (transient confusion that began two days post-operatively and resolved after one day). All of the sternal wound infections were considered to be superficial.

Table 6. Primary Safety Endpoint Events Through 6 Weeks

Safety Measure Within 6 Weeks Post-Treatment	**PREVELEAK (N=44)**
Significant Bleeding	0% (0/44)
Infection	18.2% (8/44)
Neurological Deficit	2.3% (1/44)
Immune/Inflammatory Allergic Response	0% (0/44)
Cummulative Incidence of Safety Measures	18.2% (8/44)

Serious Adverse Events

Eighteen serious adverse events (SAEs) were reported in 12 subjects. The most common serious adverse events were cardiac tamponade and heart block (Types II and III); they occurred in three subjects each.

One serious adverse event, spasm (or visual narrowing) of the distal left internal mammary artery (LIMA) graft applied to the left anterior descending coronary artery (LAD) during CABG after application of PREVELEAK was determined to be definitely procedure related (due to surgical instrument manipulation during CABG surgery) and possibly device related. There were no EKG changes, no change in cardiac movement, and no change in the color of the myocardium in the distribution of the LAD. Although the investigator could not determine if the vasospasm was due to the procedure alone or at least partly in response to the device, the sealant was removed intra-operatively as a precautionary measure. No bleeding occurred and no damage to the vascular surface was observed and the event resolved during the surgical procedure without sequelae.

SAEs occurring within 6 weeks and between 6 weeks and 3 months post-treatment are shown in **Tables 7** and **8**, respectively.

Table 7. Serious Adverse Events Through 6 Weeks

Serious Adverse Event	**PREVELEAK (N=44)**
Cardiac Tamponade	0.07% (3/44)
Atrioventricular Block (Type III)	0.05% (2/44)
Sternal Instability	0.05% (2/44)
Asystole	0.02% (1/44)
Acute Renal Injury	0.02% (1/44)
Atrioventricular Block (Type 2)	0.02% (1/44)
Cardiac Arrest	0.02% (1/44)
Myocardial Infarction	0.02% (1/44)
Prolonged INR	0.02% (1/44)
Spasm of Coronary Artery Graft	0.02% (1/44)
Wound Healing Disorder	0.02% (1/44)
Wound Healing Infection	0.02% (1/44)

Table 8. Serious Adverse Events – 6 Weeks Through 3 Months

Serious Adverse Event	PREVELEAK (N=44)
Atrial Fibrillation	0.02% (1/44)
Inflammatory Reaction	0.02% (1/44)

Additional safety endpoints included rates of re-operation (due to bleeding or tissue disruption at the site of sealant application), intra-operative complications, and 3-month mortality. There were no re-operations due to bleeding at PREVELEAK-treated sites. There were two intra-operative complications, both of which occurred in one subject who underwent a CABG procedure. One of the events, spasm of the arterial graft after application of the sealant, is described above in the SAE section. The second event (tooth luxation during intubation; mild severity), was not considered related to application of the sealant.

One subject died 22 days after hospital discharge due to cardiac arrest, possibly due to sepsis. The subject had a history of coronary artery disease, chronic obstructive pulmonary disease, and diabetes mellitus. The death was deemed by the investigator as unrelated to PREVELEAK.

2. Effectiveness Results

The analysis of effectiveness was based on the 44 evaluable patients. Key effectiveness outcomes are presented in **Table 9**.

The primary effectiveness endpoint of immediate sealing was achieved at all sites in 42 of 44 subjects (95.5%) and at 125 of 127 treatment sites (98.4%) overall (**Table 9**). One hundred percent of the CABG anastomoses (86/86) and atrium/ventricle incision sites (11/11) and 93.3% of the aortic sites (28/30) met the primary endpoint. There were two primary endpoint failures in two subjects. In one subject, surgical sealant was applied to a total of four haemostasis sites, with three sites at CABG distal anastomoses and one at the ascending aortic access incision site. The failure occurred at the aortic site, where brisk bleeding was observed requiring additional sutures. The other primary endpoint failure was due to a procedural error: PREVELEAK was applied after instead of before clamp release at an aorta-to-graft anastomosis during aortic aneurysm repair.

Table 9. Primary Effectiveness Analysis by Type of Procedure: Immediate Suture Line Sealing

Procedure	Number of Surgical Sealant Application Sites		
	Total Number of Application Sites (N)	**Primary Endpoint Failure (%, n/N)**	**Primary Endpoint Success (%, n/N)**
CABG	86	0% (0/86)	100% (86/86)
Valve procedures	30	3.3% (1/30)	96.7% (29/30)
Other*	11	9.1% (1/11)	90.9% (10/11)
All	127	1.6% (2/127)	98.4% (125/127)

CABG = coronary artery bypass graft

*Other procedures included aortic aneurysm repair, aortic root reconstruction, and cannulation

3. Subgroup Analyses
   Due to the small sample size of the clinical study, no subgroup analyses were performed.

4. Pediatric Extrapolation
   In this premarket application, existing clinical data was not leveraged to support approval of a pediatric patient population.

F. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 3 investigators. None of the clinical investigators had disclosable financial interests/arrangements as defined in sections 54.2(a), (b), (c), and (f). The information provided does not raise any questions about the reliability of the data.

XI. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

In accordance with the provisions of section 515(c)(3) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Cardiovascular Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

Effectiveness of PreveLeak for use in cardiac reconstructions, defined as immediate sealing of the suture/staple line [i.e., absence of clinically significant bleeding (minor oozing was not considered to be clinically significant) as determined by the physician using PREVELEAK] at point of use upon release of the clamps or taking patient off-pump, was achieved in $\geq$ 55% of a diverse spectrum of cardiac surgical surgical procedures completed using PREVELEAK. Primary endpoint success (i.e., immediate sealing as defined above) was achieved at all sites in 42 of 44 subjects (95.5%) and 125 of 127 treatment sites (98.4%). Use of PREVELEAK as a suture line sealant for non-coronary bypass anastomoses during procedures on the heart and great vessels is likely to favorably affect (i.e., reduce or prevent bleeding that occurs as a result of suture induced tissue or graft defects) major anastomotic sites.

B. Safety Conclusions

The risks of the device are based on nonclinical laboratory studies as well as data collected in the clinical study conducted to support PMA approval as described above. In the EU Cardiac Study, there were 9 primary safety events (18.2% of patients) defined as cumulative incidence of significant bleeding, infection, neurological deficit or immune/ inflammatory allergic response observed within 6 weeks post-treatment. Safety events observed within the study included 8 infections and 1 transient neurological deficit. None of the primary safety events were attributed to PREVELEAK use by the study Investigators or the study Medical Monitor. There was a single reported device-related adverse event, a spasm of the coronary arterial graft at the site of PREVELEAK application, which was determined to be definitely procedure-related and possibly device-related. Spasm resolved without clinical sequelae after the sealant was removed intra-operatively as a precautionary measure.

The ex vivo study demonstrated that application of PREVELEAK did not cause vasoconstriction when applied to the abluminal surface of vascular rings from the internal mammary artery (IMA), radial artery (RA) or saphenous vein (SV). However, PREVELEAK was shown to block vasoreactivity to both vasoconstrictors and vasodilators in all three tested vascular rings (IMA, RA, and SV). Given this finding, the indications for use exclude application to coronary grafts used in coronary artery bypass graft surgery.

C. Benefit-Risk Determination

The probable benefits of the device are based on data collected in a clinical study and nonclinical studies conducted to support the initial PMA approval as described above. The primary benefit observed in the EU Cardiac Study is early reduction/cessation of suture line bleeding defects related to minor suture induced tissue and/or graft injury associated with major non-coronary cardiovascular anastomoses.

Additional factors to be considered in determining probable risks and benefits for the PREVELEAK device included: Ex vivo studies that suggest application of PREVELEAK to vascular rings taken from human arteries and veins blocks vasoreactivity to both vasoconstrictors and vasodilators. An appropriate warning has been included in the labeling.

1. Patient Perspectives
   This submission did not include specific information on patient perspectives for this device.

In conclusion, given the available information above, the data support that for use in vascular and cardiac reconstructions (excluding application to coronary grafts used in coronary artery bypass graft surgery) to achieve adjunctive hemostasis by mechanically sealing areas of leakage the probable benefits outweigh the probable risks.

D. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use. Primary endpoint success was achieved in 95.5% of subjects and at 98.4% of treatment sites. The occurrence of primary safety events was low and none were attributed to PREVELEAK. Ex vivo studies suggest application of PREVELEAK blocks vasoreactivity to both vasoconstrictors and vasodilators in harvested grafts and, therefore, the indication for use excludes application to coronary grafts used in coronary artery bypass graft surgery.

XIII. CDRH DECISION

CDRH issued an approval order on December 21, 2017.

The applicant's manufacturing facilities have been inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

XIV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the device labeling.

Post-approval Requirements and Restrictions: See approval order.