

# TRIDYNE™

## Vascular Sealant

The TRIDYNE™ Vascular Sealant (TRIDYNE™ VS) package is provided sterile.

**Caution:** Federal law restricts this device to sale by or on the order of a licensed physician or properly licensed practitioner.

Information for the use of TRIDYNE™ VS is provided in this labeling for physicians.

**Before using TRIDYNE™ VS, please read the following information thoroughly.**

### 1.0 DEVICE DESCRIPTION

TRIDYNE™ VS is a single-use medical device that is formed by mixing two components: (1) a solution of human serum albumin (HSA) and (2) a synthetic cross-linking component of polyethylene glycol (PEG). Upon mixing, a clear, flexible hydrogel is formed.

TRIDYNE™ VS is supplied as a sterile, single-use, two-component kit which, when mixed, makes a 4 mL total sealant volume for use in aortic surgery when adjunctive measures to achieve hemostasis are required by mechanically sealing areas of leakage. As TRIDYNE™ VS degrades it is metabolized and cleared primarily through the kidneys.

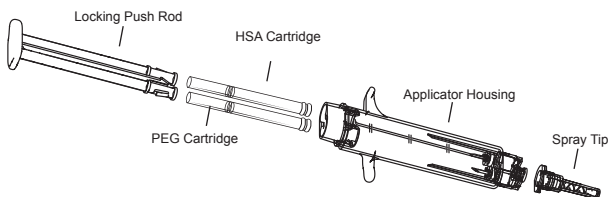
Each TRIDYNE™ VS kit includes:

- One (1) chemistry kit with:
  - One (1) preloaded cartridge containing 2 mL of human serum albumin (HSA).
  - One (1) preloaded cartridge containing the polyethylene glycol (PEG) crosslinker as a dry white powder.
- One (1) applicator kit with:
  - One (1) 3 mL plastic syringe with needle.
  - One (1) 5 mL vial of Sterile Water for Injection, USP (2 mL to be used to reconstitute PEG powder).
  - One (1) applicator assembly with locking push rod.
  - Two (2) spray tips.
- One (1) Instructions for Use pamphlet (complete product labeling).
- One (1) Instructions for Use reference card.
- One (1) Room Temperature Log label located on the unit package.
- Four (4) patient record labels.

Optional replacement spray tips are available as needed for convenience and positioning according to surgeon preference:

- TRIDYNE™ Vascular Sealant Applicator Spray Tips (pack of 2) REF TDST0020, 10 units/box with instructions.
- TRIDYNE™ Vascular Sealant Extended Applicator Spray Tip 6 in. REF TDET0006, 4 units/box with instructions.

**FIGURE 1. TRIDYNE™ Vascular Sealant Delivery System**  
(Sterile water and syringe not shown)



## 2.0 INTENDED USE / INDICATIONS FOR USE

TRIDYNE™ Vascular Sealant is indicated for use in aortic surgery when adjunctive measures to achieve hemostasis are required by mechanically sealing areas of leakage.

## 3.0 DOSAGE, FORMS, AND STRENGTHS

TRIDYNE™ VS is supplied as a 4 mL (total volume) kit.

## 4.0 CONTRAINDICATIONS

- TRIDYNE™ VS is not for intravascular use.
- Do not use TRIDYNE™ VS in patients who have a history of allergic reaction to HSA, PEG or other device components.
- Do not apply TRIDYNE™ VS on oxidized regenerated cellulose, absorbable gelatin sponges or any other surface or material other than the target tissue or graft, as adherence and intended outcome may be compromised.
- Do not use TRIDYNE™ VS in patients who have insufficient renal capacity for clearance of the PEG load.

## 5.0 WARNINGS

- Do not use TRIDYNE™ VS as a substitute for standard closure techniques.
- Excessive pressure against the vessel/graft edges or surrounding tissue during application may result in separation of the vessel/graft edges, allowing sealant into the vessel.
- Do not apply TRIDYNE™ VS when the vessel lumen is under negative pressure to avoid product from being drawn into the vessel (e.g., avoid applying in vessels that are not pressurized).
- Do not use more than 30 mL of TRIDYNE™ VS per patient.
- Do not allow non-polymerized TRIDYNE™ VS to contact circulating blood.

## 6.0 PRECAUTIONS

- The safety and effectiveness of TRIDYNE™ VS has not been established in the following:
  - Patients less than 18 years of age and pregnant or nursing women.
  - The presence of an active infection.
  - The presence of other sealants, hemostatic devices or products other than sutures and grafts. Patients receiving TRIDYNE™ VS in more than one application session (surgery) before and/or after resorption of TRIDYNE™ VS that was applied in any previous surgical session.
  - When mixed with any additive (e.g., antibiotics).
  - Coronary artery bypass graft (CABG) procedures or procedures on cardiac structures.
  - Operations other than aortic surgery with cardiopulmonary bypass.
- The use of ePTFE grafts or any vascular patches was not studied in the clinical trial.
- Do not use if sterile package or seal is damaged or open, as sterility may be compromised. Do not resterilize the contents.
- Do not remove the contents of the TRIDYNE™ VS unit package until they are to be used in a surgical procedure.
- Store TRIDYNE™ VS within the recommended temperature range. Failure to do so may result in poor product performance. TRIDYNE™ VS should be refrigerated between 2°C and 8°C (36°F and 46°F). Do not freeze.
  - Removal from refrigeration to controlled room temperature between 8°C and 25°C (46°F to 77°F) is allowed as long as the duration of non-refrigerated storage does not exceed 35 cumulative days (840 hours). Storage at controlled room temperature may be on *consecutive* days or over multiple shorter periods, as long as the *cumulative* (total) time of non-refrigerated storage does not exceed 35 days.
  - Do not use TRIDYNE™ VS after 35 days of storage at controlled room temperature (8°C to 25°C). If on the 35th consecutive or cumulative day of storage at controlled room temperature TRIDYNE™ VS has not been used, it can be returned to refrigerated storage for the remainder of the shelf life indicated by the expiration date on the unit package. Upon its next removal from refrigeration, this product should be used promptly or discarded.
- Do not use TRIDYNE™ VS after the expiration date, as sterility or performance may be compromised.
  - Product that has reached its expiration date or has exceeded 35 days of storage at controlled room temperature should not be used and should be discarded.

- Do not use reconstituted PEG solution after 20 minutes, as the performance of TRIDYNE™ VS may be compromised.
- Initial application in a wet field can lead to product dilution and affect product performance.
- Interruption of TRIDYNE™ VS application for approximately 10 seconds can result in clogging of the spray tip. If clogging occurs, remove the spray tip, wipe the end of the applicator to remove any fluid, and attach a new spray tip (provided) onto the end of the applicator.
- TRIDYNE™ VS is intended for single use only. Do not reuse any component.
- HSA in the TRIDYNE™ VS kit is obtained from a U.S. Food and Drug Administration (FDA) licensed supplier and meets all United States Pharmacopeia (USP) standards. The HSA protein is derived from plasma collected from donors who have been screened and tested according to the methods specified by the FDA. These methods minimize the possibility that drawn blood will contain communicable diseases or viruses such as hepatitis and human immunodeficiency virus (HIV).
- Do not apply TRIDYNE™ VS to anastomoses or vascular suture lines when the vessel lumen is under suction or negative pressure to avoid unpolymerized product being drawn into the vessel, as this may result in local thrombus or distant vascular embolism.
- Do not use blood-saving devices when suctioning excess sealant from the surgical field.
- TRIDYNE™ VS resorption time in humans has not been studied. In rats, over 50% of a 14C-labeled device was excreted after 24 hours, and virtually all radioactivity was recovered at 14 days post-implant. Following implantation on porcine tissue, TRIDYNE™ VS was largely absent at 4 days, with only isolated fragments of TRIDYNE™ VS apparent at 7 days post-implant.
- Discard unused material in accordance with standard practice for TRIDYNE™ VS components.
- The sealant may swell up to a maximum of 17.3% in any dimension or 61.5% in volume. Caution should be taken when applying sealant to confined areas where sealant swelling could impinge on adjacent structures.

## 7.0 ORIGINAL PIVOTAL CLINICAL STUDY

Study Title: A Prospective, Randomized Study to Compare TRIDYNE™ Vascular Sealant to GELFOAM® PLUS as an Adjunct for the Control of Bleeding in Subjects Undergoing Thoracic Aortic Surgery.

### 7.1 Study Objectives

The primary study objective was to compare the time to hemostasis at the aortic anastomotic suture lines involving the aortic valve, ascending aorta, or aortic arch while on cardiopulmonary bypass in subjects randomized to TRIDYNE™ VS compared to subjects randomized to Control (GELFOAM® PLUS).

### 7.2 Study Design

This was a prospective, multicenter, randomized, single-blind (subject), superiority trial to evaluate the safety and effectiveness of the TRIDYNE™ VS compared to Control for the control and prevention of intraoperative bleeding after conventional reconstructions during thoracic surgery on the aorta. Subjects were randomized 2:1 to TRIDYNE™ VS or Control respectively. The Control was GELFOAM® PLUS, supplied as a ready-to-use medical device kit containing GELFOAM® Sterile Sponge, Thrombin (Human) lyophilized powder, two 10 mL Prefilled Saline Syringes (0.9% Sodium Chloride Injection, USP), and a Vial Access Device. The GELFOAM® Sterile Sponge component is an absorbable gelatin sponge (USP) measuring 100 cm<sup>2</sup> (8 x 12.5 cm).

Subjects scheduled for non-emergent thoracic surgery involving the aortic valve, ascending aorta, or aortic arch on cardiopulmonary bypass with or without concomitant coronary artery bypass graft (CABG) procedure(s) were assessed for eligibility.

### Key Eligibility Criteria

#### Inclusion Criteria

##### Preoperative Inclusion Criteria:

1. Subject must be ≥ 18 years of age.
2. Subject is scheduled for elective, primary thoracic surgery involving the aortic valve, ascending aorta, or aortic arch on cardiopulmonary bypass.
3. Subject has an expected life expectancy ≥ 6 months.
4. Subject is willing and able to comply with all aspects of the study including follow-up schedule.

5. Subject, or authorized representative, has the ability to provide voluntary written informed consent.

Intraoperative Inclusion Criteria:

6. Subject is able to undergo an antegrade cardioplegia injection for evaluation of a leak at the aortic anastomotic site(s) during the procedure.
7. Following this injection, subject has a leaking site where a topical sealant/hemostatic agent may be used to control bleeding.

**Exclusion Criteria**

1. Subject has Type A or other acute thoracic aortic dissection.
2. Subject has undergone prior thoracic surgery (open thoracotomy not including interventional cardiology procedures).
3. Subject is undergoing a planned concomitant procedure other than coronary artery bypass graft (CABG).
4. Subject has a previous organ transplant.
5. Subject has known or suspected preoperative coagulation disorder.
6. Subject is allergic to human thrombin or has a history of allergic reactions after application of human thrombin.
7. Subject is allergic to protamine.
8. Subject has a Left Ventricular Assist Device (LVAD) or plans to receive an LVAD.
9. Subject is undergoing emergency surgery.
10. Subject is in chronic renal failure.
11. Subject has a hematocrit < 21% preoperatively.
12. Subject has a serum creatinine  $\geq$  2.5 mg/dl at baseline or is currently on dialysis.
13. Subject has a cardiac ejection fraction < 25%.
14. Subject is scheduled for another cardiac surgery within 30 days of enrollment.
15. Subject has an active or latent infection which is systemic or at the intended surgery site.
16. Subject is immunocompromised such as that resulting from chronic oral steroid use, chemotherapeutic agents, or immune deficiency disorders.
17. Subject is pregnant by a positive pregnancy test or has plans to become pregnant during the study period or is currently breastfeeding.
18. Subject is unwilling to receive blood products.
19. Subject has participated in another investigational research study within 30 days of enrollment.
20. In the opinion of the Investigator, the subject has a clinical condition that would preclude the use of the study device, preclude the subject from completing the follow-up requirements, or complicate the evaluation of this study.

Subjects with at least one confirmed leaking site after final antegrade cardioplegia injection were randomized to either TRIDYNE™ VS or Control. Time to hemostasis (TTH) measurement began after either TRIDYNE™ VS or Control was applied to the anastomotic suture line(s) and bypass cross clamp was released. Hemostasis was assessed continuously until hemostasis was achieved at each applied anastomotic site or up to 10 minutes. Immediate hemostasis was defined as zero (0) seconds or no observable bleeding from the time the clamps were released to achieving hemostasis.

Additional standard-of-care surgical hemostatic measures could be performed (e.g., other sealants, stitches, pledgets, administration of protamine, manual pressure) if hemostasis was not achieved at the anastomotic suture line after 10 minutes or if it was deemed by the surgeon to be medically necessary.

Postoperatively, subjects were monitored to assess hemostasis, chest tube output, transfusion volumes and safety. Subjects were followed for 30 days post-index procedure.

Safety data was reviewed by the Clinical Events Committee (CEC).

**7.3 Clinical Endpoints**

The primary effectiveness endpoint of this study was the time to achieve hemostasis at the aortic anastomotic suture line from the time surgical clamps were released to cessation of leakage at the treated anastomotic site with either TRIDYNE™ VS or Control.

Safety endpoints included adverse events and device-related adverse events from the time of randomization through the end of study participation, study completion, or 30 days postoperatively.

This study also assessed the following secondary endpoints:

1. Proportion of subjects who achieved successful hemostasis at all treated aortic anastomotic suture lines following assigned treatment. Success was defined as hemostasis obtained within 5 minutes.
2. Proportion of subjects who achieved immediate hemostasis, defined as 0 seconds, at all treated aortic anastomotic suture lines following assigned treatment.
3. Chest tube drainage volume within 24 hours following surgery.
4. Total transfusion volume within 24 hours following surgery.
5. Time between cross clamp removal and request of surgical wires for sternal closure.
6. Incidence of reoperations for aortic bleeding complications following assigned treatment through 30 days.
7. Number of device-related serious adverse events per patient following assigned treatment through 30 days.

#### 7.4 Subject Accountability

A total of 204 subjects were consented and enrolled into the study of which 158 were randomized. Of the 158 randomized subjects (107 TRIDYNE™ VS and 51 Control), 153 subjects completed the study. Disposition of the five subjects that did not complete the study: two subjects were randomized and not treated, three subjects prematurely discontinued due to death; two (1.9%) from the TRIDYNE™ VS treatment group and one (2.0%) from the Control group.

Table 1 provides a summary of the subject accountability.

**TABLE 1 Subject Accountability**

	TRIDYNE™ VS n (%)	Control n (%)	Total n (%)
Enrolled			204
Not randomized			46
Eligibility criteria not met <sup>1</sup>			38
Sponsor's decision <sup>2</sup>			5
Withdrawal of consent			3
Randomized (intent-to-treat)	107 (100.0)	51 (100.0)	158 (100.0)
Treated (modified intent-to-treat) <sup>3</sup>	106 (99.1)	50 (98.0)	156 (98.7)
Randomized not treated <sup>4</sup>	1 (0.9)	1 (2.0)	2 (1.3)
Discharged after index procedure	107 (100.0)	50 (98.0)	157 (99.4)
Completed one month follow-up	104 (97.2)	49 (96.1)	153 (96.8)
Primary reason for discontinuation			
Death	2 <sup>5</sup> (1.9)	1 <sup>6,7</sup> (2.0)	3 (1.9)

1. Preoperative inclusion not met: One subject was not scheduled for elective, primary thoracic surgery involving the aortic valve, ascending aorta, or aortic arch on cardiopulmonary bypass. Intraoperative inclusion criteria not met: Two subjects were unable to undergo an antegrade cardioplegia injection for evaluation of a leak at the aortic anastomotic site(s) during the procedure. Twenty subjects did not have a leaking site where a topical sealant/hemostatic agent may be used to control bleeding following cardioplegia injection. Exclusion criteria: One subject had thoracic surgery (open thoracotomy not including interventional cardiology procedures). Eight subjects had a planned concomitant procedure other than coronary artery bypass graft (CABG). One subject had a previous organ transplant. Two subjects had a known or suspected preoperative coagulation disorder. One subject had a serum creatinine greater than or equal to 2.5 mg/dl at baseline. Three subjects had an active or latent infection which was systemic or at the intended surgery site. One subject was immunocompromised such as that resulting from chronic oral steroid use, chemotherapeutic agents, or immune deficiency disorders. One subject had participated in another investigational research study within 30 days of enrollment. Three subjects in the opinion of the Investigator had a clinical condition that would preclude use of the study device, preclude the subject from completing follow-up requirements, or complicate evaluation of the study.
2. Subjects met eligibility criteria but were not randomized as enrollment numbers were already met.
3. The subjects that were treated represent the modified intent-to-treat population.
4. Two Control subjects and one TRIDYNE™ VS subject were randomized, however, the cross clamp was removed prior to application of the sealant.
5. Subject deaths due to cardiac arrest and ischemic cardiomyopathy.
6. Subject died during hospitalization and therefore was not discharged.
7. Subject death due to gastrointestinal bleed.

All subsequent data presented is utilizing the modified intent-to-treat population unless otherwise indicated.

## 7.5 Demographics

A total of 156 subjects were treated (two subjects were randomized and not treated, one TRIDYNE™ VS and one Control) across 19 investigational sites.

Table 2 provides a summary of subject demographic characteristics.

**TABLE 2 Subject Demographic Characteristics**

		TRIDYNE™ VS	Control	Total
<b>Number of subjects treated</b>		<b>106</b>	<b>50</b>	<b>156</b>
Age (years)	Mean (SD)	61.5 (14.42)	62.4 (14.30)	61.8 (14.34)
	Median	63.5	64.0	64.0
	Min-Max	23.0 - 87.0	20.0 - 89.0	20.0 - 89.0
<b>Age categories (years)</b>				
	< 65	54 (50.9%)	28 (56.0%)	82 (52.6%)
	≥ 65	52 (49.1%)	22 (44.0%)	74 (47.4%)
Gender	Male	74 (69.8%)	35 (70.0%)	109 (69.9%)
	Female	32 (30.2%)	15 (30.0%)	47 (30.1%)
BMI (kg/m <sup>2</sup> )	Mean (SD)	31.2 (7.52)	28.3 (5.50)	30.2 (7.05)
	Median	30.1	27.5	29.2
	Min-Max	19.9 - 60.1	17.4 - 41.9	17.4 - 60.1
Ethnicity	Hispanic or Latino	2 (1.9%)	3 (6.0%)	5 (3.2%)
	Not Hispanic or Latino	100 (94.3%)	44 (88.0%)	144 (92.3%)
	Unknown	4 (3.8%)	3 (6.0%)	7 (4.5%)
<b>Race</b>				
	American Indian	2 (1.9%)	0 (0.0%)	2 (1.3%)
	Asian	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Black or African American	3 (2.8%)	3 (6.0%)	6 (3.8%)
	Native Hawaiian or other Pacific Islander	0 (0.0%)	1 (2.0%)	1 (0.6%)
	White Caucasian	94 (88.7%)	43 (86.0%)	137 (87.8%)
	Other	1 (0.9%)	0 (0.0%)	1 (0.6%)
	Unknown	6 (5.7%)	3 (6.0%)	9 (5.8%)

## 7.6 Types of Surgical Procedures

There were 156 subjects treated overall with 172 treated suture lines; 119 suture lines in the TRIDYNE™ VS group, and 53 treated suture lines in the Control group.

Table 3 provides the number of suture lines treated in the different types of surgeries.

**TABLE 3 Number of Suture Lines Treated in Various Surgery Types**

	TRIDYNE™ VS n = 119	Control n = 53	Total n = 172
<b>Surgery type</b>			
Aortic aneurysm repair	18 (15.1%)	7 (13.2%)	25 (14.5%)
Aortic root replacement	16 (13.4%)	8 (15.1%)	24 (14.0%)
Aortic valve procedure	50 (42.0%)	30 (56.6%)	80 (46.5%)
Ascending aorta replacement	28 (23.5%)	5 (9.4%)	33 (19.2%)
Other	7 <sup>1</sup> (5.9%)	3 <sup>2</sup> (5.7%)	10 (5.8%)

- One subject had hemiarch. One subject had aortic root replacement and aortic aneurysm repair. Two subjects had aortic valve procedure and aortic aneurysm repair. Two subjects had aortic valve replacement, ascending aorta replacement and aortic root replacement. One subject had aortic root replacement and ascending aorta replacement.
- One subject had aortic valve replacement and hemiarch procedure. One subject had aortic valve replacement. One subject had the David procedure, aorta root replacement and ascending aorta replacement.

## 7.7 Number of Treatment Sites and Amount of Product Used per Subject

Some subjects had more than one suture line treated. The number of suture lines treated and the amount of product used per subject is presented below.

Table 4 provides the number of subjects that had more than one suture line treated.

**TABLE 4 Number of Treated Suture Lines by Treatment Group**

Treated Suture Lines	Treatment Group		Total n = 156
	TRIDYNE™ VS n = 106	Control n = 50	
1	93 (87.7%)	47 (94.0%)	140 (89.7%)
2	13 (12.3%)	3 (6.0%)	16 (10.3%)

Table 5 provides the amount of product that each subject received.

**TABLE 5 Amount of Product Used per Subject**

	TRIDYNE™ VS (mL) n = 106	Control (cm x cm) n = 49 <sup>1</sup>
Mean (SD)	3.3 (2.25)	117.9 (206.9)
Min-Max	0.5 - 12.0	2.0 - 864.0

1. Amount of product used was not recorded for one subject, therefore, the denominator is 49.

## 7.8 Safety and Effectiveness Results

### 7.8.1 Safety Results

Overall, there were no major differences in the incidence of adverse events between treatment groups.

#### Serious Adverse Events

Approximately half of the subjects in each treatment group experienced a serious adverse event (SAE) while in the study (51 subjects [48.1%] treated with TRIDYNE™ VS; 29 subjects [58.0%] treated with Control). Seven SAEs, described below, were considered by the Clinical Events Committee (CEC) to be possibly device related (three patients [2.8%] treated with TRIDYNE™ VS; four patients [8.0%] treated with Control).

Nearly all CEC-adjudicated SAEs were considered to be related to the procedure (87 of 88 SAEs in patients treated with TRIDYNE™ VS; 48 of 48 SAEs in patients treated with Control). Most SAEs occurred in only one or two patients in either treatment group, with the exception of atrial fibrillation that occurred in 27 patients (25.5%) treated with TRIDYNE™ VS and 17 patients (34.0%) treated with Control. Some of these were considered not to be serious by the Investigator and were upgraded by the CEC as a result of treatment by cardioversion or prophylactic use of antiarrhythmics.

The CEC adjudicated the SAEs of seven patients to be possibly device related following completed surgery through the follow-up evaluation; three (2.9%) in the TRIDYNE™ VS treatment group and four (8.2%) in the Control treatment group. None of the SAEs were unexpected given the procedures performed. The events are described below:

#### TRIDYNE™ VS SAEs

- Patient had a cerebrovascular accident on Study Day 1, which was severe in intensity.
- Patient had a cerebrovascular accident on Study Day 15, which was severe in intensity.
- Patient had pericardial effusion on Study Day 4, which was considered moderate in intensity. The subject underwent mediastinal re-exploration which found serosanguineous pericardial effusion with no active bleeding. Surgery was completed without complication, and the event was considered resolved on Study Day 9.

#### Control SAEs

- Patient had a cerebrovascular accident on Study Day 1, which was moderate in intensity.
- Patient had a cerebrovascular accident on Study Day 0, which was moderate in intensity.
- Patient had a hematoma on Study Day 0, which was moderate in intensity. The patient was taken back to the operating room on the same day for mediastinal re-exploration, where a large amount of hematoma in the mediastinum was noted and evacuated.
- Patient reported hypotension on Study Day 0, which was moderate in intensity.

#### Non-Serious Adverse Events

At least one non-serious adverse event (AE) was reported in almost all of the patients in this study (92.5% of patients treated with TRIDYNE™ VS and 100.0% of patients treated with Control).

Table 6 lists AEs occurring in 5% or more of either treated or Control patients. None of these were CEC adjudicated to be device related.

**TABLE 6 Number of Patients with Frequently Reported (Greater than 5% in Either Treatment Group) Adverse Events**

<b>Adverse Event</b>	<b>TRIDYNE™ VS n = 106</b>	<b>Control n = 50</b>
Pleural effusion	43 (40.6%)	18 (36.0%)
Anemia	39 (36.8%)	13 (26.0%)
Atelectasis	37 (34.9%)	15 (30.0%)
Atrial fibrillation	27 (25.5%)	17 (34.0%)
Leukocytosis	25 (23.6%)	13 (26.0%)
Thrombocytopenia	19 (17.9%)	8 (16.0%)
Peripheral edema	18 (17.0%)	4 (8.0%)
Nausea	16 (15.1%)	7 (14.0%)
Fluid overload	14 (13.2%)	9 (18.0%)
Hypotension	13 (12.3%)	5 (10.0%)
Pulmonary edema	11 (10.4%)	2 (4.0%)
Pneumothorax	10 (9.4%)	5 (10.0%)
Hyperglycemia	9 (8.5%)	6 (12.0%)
Hypoxia	8 (7.5%)	3 (6.0%)
Hypokalemia	7 (6.6%)	2 (4.0%)
Back pain	7 (6.6%)	2 (4.0%)
Tachycardia	6 (5.7%)	2 (4.0%)
Dizziness	6 (5.7%)	3 (6.0%)
Renal injury	5 (4.7%)	3 (6.0%)
Dyspnea	4 (3.8%)	3 (6.0%)
Fatigue	3 (2.8%)	5 (10.0%)
Hyponatremia	3 (2.8%)	3 (6.0%)
Respiratory failure	3 (2.8%)	3 (6.0%)
Atrial flutter	2 (1.9%)	3 (6.0%)
Pyrexia	2 (1.9%)	3 (6.0%)
Musculoskeletal pain	2 (1.9%)	4 (8.0%)
Vomiting	1 (0.9%)	4 (8.0%)
Musculoskeletal chest pain	0 (0.0%)	3 (6.0%)

There were two patients, one in each treatment group, with reported AEs considered device related by the Investigator. The subject treated with TRIDYNE™ VS reported azotemia on Study Day 10, which the Investigator considered to be related to both the device and the procedure. The event was mild in severity and was adjudicated by the CEC to not be device related. The subject treated with the Control reported nausea on Study Day 5, which the Investigator considered possibly related to the device and definitely related to the procedure. The event was mild in severity and was adjudicated by the CEC to not be device related.

#### Unanticipated Adverse Device-Related Events

No adverse events were considered to be Unanticipated Adverse Device-Related Events.

#### Patient Deaths

There were three patient deaths during the study; two deaths (cardiac arrest, ischemic cardiomyopathy) in the TRIDYNE™ VS group; and one death (gastrointestinal bleed) in the Control group. None of the deaths were considered by the Investigators or adjudicated by the CEC to be device related.

### **7.8.2 Effectiveness Results**

#### Primary Effectiveness Endpoint

The primary endpoint was evaluated by the following hypotheses:

H<sub>0</sub>: The mean time to hemostasis for subjects receiving TRIDYNE™ VS at leaking sites involving the aortic valve, ascending aorta, or aortic arch is the same as for subjects receiving Control.

H<sub>1</sub>: The mean time to hemostasis for subjects receiving TRIDYNE™ VS at leaking sites involving the aortic valve, ascending aorta, or aortic arch is different for subjects receiving Control.



The distribution of time to hemostasis was significantly different between the TRIDYNE™ VS treatment group and the Control treatment group (Wilcoxon rank-sum test p-value < 0.0001). The adjusted mean time to hemostasis was lower in subjects in the TRIDYNE™ VS treatment group compared to subjects in the GELFOAM® PLUS treatment group (124.3 seconds compared to 377.8 seconds). The term “adjusted” is used because an imputation to a value of 600 seconds was used in subjects that did not achieve hemostasis in 10 minutes. This imputation technique underestimated the time to hemostasis for the subjects who did not achieve hemostasis by 600 seconds. Since more subjects in the Control group did not achieve hemostasis by 600 seconds, this likely provided a conservative assessment of the TTH comparison.

Table 7 provides the adjusted mean and the minimum-maximum time to hemostasis. The time to hemostasis is missing for one subject; therefore, the denominator is 105 subjects.

**TABLE 7 Time to Hemostasis (Seconds) for Individual Subjects**

Treatment	n	Adjusted Mean	Adjusted Min-Max
TRIDYNE™ VS	105	124.3	0.0 - 600.0
Control	50	377.8	0.0 - 600.0

If immediate hemostasis was achieved, 0 minutes was used as time to hemostasis (TTH). If hemostasis was not achieved within 10 minutes (600 seconds), 10 minutes (600 seconds) was used as the TTH. Imputation was performed for subjects who did not achieve hemostasis in 10 minutes (600 seconds). 10 minutes (600 seconds) was used as the TTH in this group. This imputation technique results in an underestimation of the TTH when hemostasis was not achieved in 10 minutes (600 seconds). For subjects with more than one aortic anastomotic suture line treated, the site with the longest TTH was used for analysis.

### Secondary Effectiveness Endpoint

Immediate hemostasis defined as hemostasis at 0 seconds was achieved in 60.0% of subjects treated with TRIDYNE™ VS compared to 16.0% of subjects treated with Control. The percentage of subjects that achieved hemostasis within 10 minutes for TRIDYNE™ VS was 87.6% compared to 52.0% for the Control. By the 10-minute cut-off, only 12.4% of subjects in the TRIDYNE™ VS treatment group failed to achieve hemostasis, compared to 48.0% of the subjects in the Control treatment group.

Table 8 provides the information regarding whether hemostasis was immediate, successful (within 5 minutes), or within 10 minutes. The time to hemostasis is missing for one subject; therefore, the denominator is 105 subjects.

**TABLE 8 Summary of Time to Hemostasis for Individual Subjects**

	TRIDYNE™ VS n = 105	Control n = 50
Immediate (0 second)	63 (60.0%)	8 (16.0%)
0 < TTH < 5 minutes	90 (85.7%)	20 (40.0%)
0 < TTH ≤ 10 minutes	92 (87.6%)	26 (52.0%)

If the immediate hemostasis was achieved, 0 minutes was used as time to hemostasis (TTH). For subjects with more than one aortic anastomotic suture line treated, the site with the longest TTH was used for analysis.

### Use of Additional Adjunctive Agents to Achieve Hemostasis

As described above, additional standard-of-care surgical hemostatic measures could be performed if hemostasis was not achieved at the anastomotic suture line after 10 minutes or if it was deemed by the surgeon to be medically necessary.

Table 9 describes the adjunctive treatments of the anastomotic suture lines. The denominator is the total number of suture lines treated.

**TABLE 9 Summary of Adjunctive Treatment of Aortic Anastomotic Suture Lines<sup>1</sup>**

	TRIDYNE™ VS n = 119	Control n = 53	Total n = 172
None	86 (72.3%)	17 (32.1%)	103 (59.9%)
Additional application(s) of assigned treatment	16 (13.4%)	13 (24.5%)	29 (16.9%)
Sutures	18 (15.1%)	14 (26.4%)	32 (18.6%)
Pledgets	2 (1.7%)	2 (3.8%)	4 (2.3%)
Protamine	3 (2.5%)	8 (15.1%)	11 (6.4%)
Manual Pressure	0 (0.0%)	3 (5.7%)	3 (1.7%)
Other <sup>2</sup>	4 (3.4%)	6 (11.3%)	10 (5.8%)

1. Data was analyzed by suture line, not per subject.

2. Other includes: BioGlue®, GELFOAM®, and Thrombin.

### 7.8.3 Other Secondary Endpoints Results

- The amount of chest tube drainage within 24 hours of surgery was not significantly different between treatment groups.
- There was no significant difference of total transfusion volume between the treatment groups.
- There was no appreciable difference in surgical time between subjects treated with TRIDYNE™ VS compared to subjects treated with Control.
- There was no appreciable difference in the time between cross clamp removal and request of surgical wires for sternal closure.
- One subject (Control treatment group) required a reoperation for aortic bleeding complications following completed surgery through 30 days.

## 8.0 POTENTIAL ADVERSE EVENTS

Table 10 lists the potential adverse events that have been associated with this class of surgical sealants.

**TABLE 10 Potential Adverse Events Associated with Surgical Sealants**

A hypersensitivity reaction such as swelling or edema at the application site
Thrombosis and thromboembolism
An exacerbation of renal dysfunction in patients with pre-existing or unknown renal disease
Failure of the sealant to adhere to target tissue
Failure of the sealant to stop diffuse persistent bleeding
Possible transmission of infectious agents from materials of human origin.
Application of the sealant to tissue not targeted for the procedure.

Table 11 lists the potential adverse events that have been associated with aortic procedures.

**TABLE 11 Potential Adverse Events Associated with Aortic Procedures**

Adhesions	Graft occlusion	Paraplegia
Aneurysm and anastomotic pseudoaneurysm	Hematoma	Pleural effusion
Aortic insufficiency	Hemorrhage	Pulmonary Emboli
Cardiac tamponade	Infection	Pyrexia
Cerebral emboli	Injury to normal vessels or tissue	Renal dysfunction / failure
Coagulopathy	Ischemia	Stroke or cerebral infarction
Death or irreversible morbidity	Lymphocele / lymph fistula	Thrombosis
Dissection	Myocardial infarction	Vasospasm
Edema	Neurological deficits	Vessel dissection
Emboli	Organ system dysfunction / failure	Vessel occlusion
Erythema	Pain	Vessel rupture and hemorrhage

## 9.0 PATIENT COUNSELING INFORMATION

The physician should discuss the following with patients potentially receiving TRIDYNE™ VS:

- The indication for TRIDYNE™ VS use.
- The risks and benefits associated with TRIDYNE™ VS use.

## 10.0 DIRECTIONS FOR USE

TRIDYNE™ Vascular Sealant is indicated for use in aortic surgery when adjunctive measures to achieve hemostasis are required by mechanically sealing areas of leakage.

### 10.1 Assess for Bleeding

After standard closure of aortic incisions, assess for bleeding. If bleeding is observed, consider applying TRIDYNE™ VS.

If a patient is a candidate for TRIDYNE™ VS use, perform the following:

### 10.2 Inspect Packaging

Each TRIDYNE™ VS kit includes:

- One (1) chemistry kit, irradiation sterilized.
- One (1) applicator kit, ethylene oxide sterilized.
- One (1) Instructions for Use pamphlet (complete product labeling).
- One (1) Instructions for Use reference card.
- One (1) Room Temperature Log label located on the unit package.
- Four (4) patient record labels.

If package and/or product integrity have been compromised, (i.e., damaged package seal or broken components), do not use or resterilize the contents. Refer to Warnings and Precautions as listed in the beginning of this labeling.

A *Room Temperature Log* label is included on the outer TRIDYNE™ Vascular Sealant unit package. This label is intended to help monitor and record removals from refrigerated storage and the cumulative hours each unit of TRIDYNE™ VS is exposed to controlled room temperature conditions.

**Caution:** TRIDYNE™ VS product that has been stored for greater than 35 days (840 hours) at controlled room temperature (8°C to 25°C) should not be used and should be discarded.

### 10.3 Prepare TRIDYNE™ VS

In a controlled, ambient temperature environment and using aseptic technique, open the sterile package and pass the following contents into the sterile field:

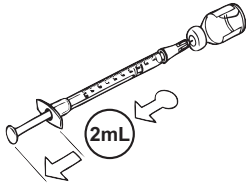
- One (1) preloaded cartridge containing 2 mL of HSA.  
NOTE: The HSA can be identified by examining the differences between the two cartridges. The HSA is in liquid form and has a slight yellow tint to the solution.
- One (1) preloaded cartridge containing PEG crosslinker.  
NOTE: The PEG can be identified by examining the differences between the two cartridges. The PEG is in the form of a dry white powder.
- One (1) 3 mL plastic syringe with needle.
- One (1) 5 mL vial of Sterile Water for Injection, USP (2 mL to be used to reconstitute PEG).
- One (1) applicator assembly with locking push rod.

## 10.4 Follow These Steps:

### Step 1

Using the 3 mL syringe, draw 2 mL of sterile water. Express any air in the syringe.

NOTE: The entire contents of the sterile water vial will not be used.

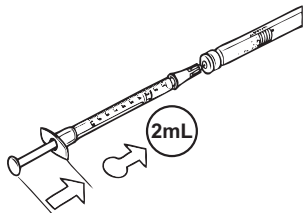


Draw 2 mL sterile water

### Step 2

Inject 2 mL of sterile water into the cartridge containing the PEG crosslinker.

NOTE: The HSA cartridge contains a yellow liquid. Do not inject sterile water into the HSA cartridge.

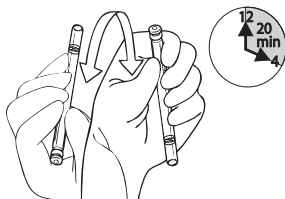


Inject 2 mL sterile water into the white powder crosslinker cartridge

### Step 3

Mix the sterile water and PEG crosslinker by gently rocking the cartridge from end to end until the solution contains no undissolved powder (generally 1-2 minutes). When all powder is dissolved, the solution is ready for use.

NOTE: TRIDYNE™ VS should be used within 20 minutes of dissolving the PEG.

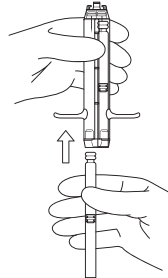


Mix

### Step 4

Before the spray tip is attached, point the applicator tip up and load each cartridge into the twin-chambered applicator housing. Gently press the cartridges to seat them into place. Cartridges may be loaded into either chamber of the applicator housing.

NOTE: When properly loaded the chemistry cartridges should sit flush with the end of the applicator housing.

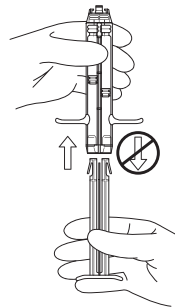


Load cartridges into applicator housing

### Step 5

Without the spray tip attached, point the applicator tip upward to allow any air in the chemistry cartridges to rise to the top of the cartridges. Insert the locking push rod into the openings in the rear of the cartridges until it snaps into place.

NOTE: During applicator assembly, the push rod is designed to lock into the applicator housing. Forced removal of the locking push rod from the applicator housing may result in potential damage to the applicator components or the chemistry cartridges.

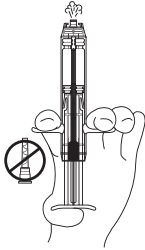


Insert the locking push rod

### Step 6

With the tip of the applicator pointed upward, briskly flick the applicator to free any air bubbles. Express the air by pushing up on the push rod until the stoppers in each cartridge are aligned with one another.

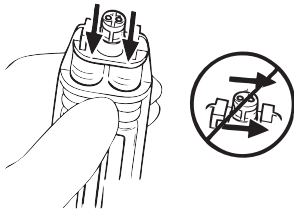
Take care to express as little fluid as possible during this process.



Express air

### Step 7

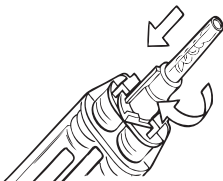
Wipe the applicator tip as often as needed with clean, sterile gauze to remove any liquid that may have been expressed with the air. Avoid mixing of components: Do not wipe from one opening across to the other; wipe each opening separately.



Wipe applicator tip clean

### Step 8

Place a spray tip on the end of the applicator and rotate the spray tip clockwise  $\frac{1}{4}$  turn until locked.



Attach spray tip

### Step 9

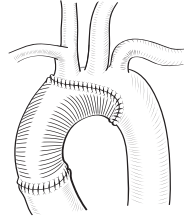
The TRIDYNE™ VS is ready for application.

### Step 10

After standard closure of the suture lines during aortic surgery, assess for bleeding. If bleeding is observed, consider applying TRIDYNE™ VS.

Select the target site to be sealed.

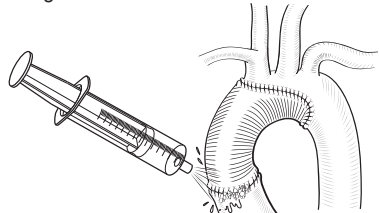
NOTE: Each 4 mL TRIDYNE™ VS kit is intended to cover an area approximately 40 cm<sup>2</sup> (6 in<sup>2</sup>) and 1 mm thick.



Assess for bleeding

### Step 11

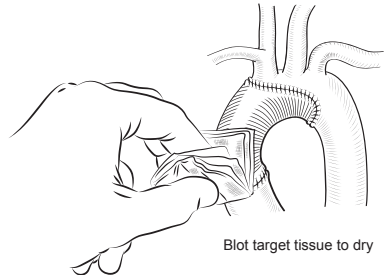
Rinse the surface intended to be treated with sterile saline to remove any pooled blood or blood clots with irrigation and/or suction.



Rinse target tissue

### Step 12

Blot the intended treatment area with a sponge or gauze to remove excess moisture.

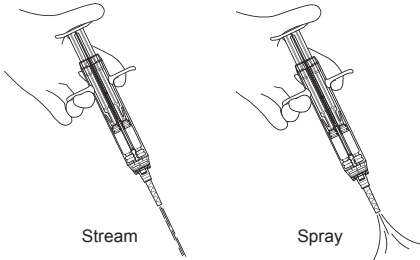


Blot target tissue to dry

## 10.5 Apply TRIDYNE™ VS:

### Step 13

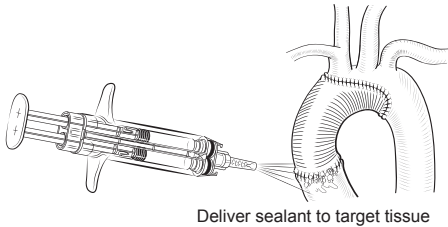
Position the applicator tip over the target area and apply pressure to the push rod to dispense the sealant. Gentle pressure on the push rod will yield a slow, targeted stream; while firm, steady pressure will transition the stream to a spray.



### Step 14

Maintain pressure on the push rod to deliver desired spray or stream onto the target site.

NOTE: Do not apply TRIDYNE™ VS to anastomoses or suture lines when the vessel lumen is under negative pressure or suction (e.g. vessels that are not pressurized) to avoid unpolymerized product being drawn into the vessel, as this may result in local thrombus or distant vascular embolism.



### Step 15

TRIDYNE™ VS will form a flexible hydrogel two minutes after application. Assess the site for hemostasis after two minutes. Application of TRIDYNE™ VS over a site that has continued bleeding may be repeated.

### Step 16

If the applicator's contents are not entirely used, immediately remove the spray tip and wipe residual TRIDYNE™ VS from the applicator tip with sterile dry gauze to prevent clogging.

### Step 17

If additional kits are required follow the product preparation instructions provided above.

NOTE: Do not use more than 30 mL (7.5 kits) of TRIDYNE™ VS per patient.

### Step 18



After use, TRIDYNE™ VS may be a potential biohazard. Handle and dispose of in accordance with any local and federal laws regarding medical waste. Discard unused material in accordance with standard practice for TRIDYNE™ VS components.

## 11.0 HOW SUPPLIED

**STERILE:** TRIDYNE™ VS is supplied sterile, with total reconstituted component volume of 4 mL per unit. It is intended for single use only, and is non-pyrogenic. Do not use if package is opened or damaged.








## 12.0 STORAGE








TRIDYNE™ VS should be refrigerated between 2°C and 8°C (36°F and 46°F). Do not freeze.

Removal from refrigeration to controlled room temperature between 8°C and 25°C (46° F and 77° F) is allowed as long as the cumulative duration of non-refrigerated storage does not exceed 35 days (840 hours). Non-refrigerated storage at 8°C to 25° C should be monitored and recorded using the Room Temperature Log label located on the TRIDYNE™ VS unit package.

NOTE: Store TRIDYNE™ VS within the recommended temperature range and according to these guidelines. Failure to do so may result in poor product performance. TRIDYNE™ VS that has reached the expiration date located on the unit package should not be used and should be discarded. TRIDYNE™ VS that has been stored for greater than 35 days (840 hours) at controlled room temperature (8°C to 25°C) should not be used and should be discarded.

## 13.0 SYMBOL DEFINITIONS

Symbol	Definition
	Catalog number
	Batch code
	Use-by date
	Sterilized using irradiation
	Sterilized using ethylene oxide
	Consult Instructions for Use
	Do not use if package is damaged

Symbol	Definition
	Do not re-use
	Temperature limit
	Refrigerate Do not freeze
	Non-pyrogenic
	Manufacturer
	Federal law (United States) restricts this device to sale by or on the order of a physician or properly licensed practitioner.
	Biohazard

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