

**DE NOVO CLASSIFICATION REQUEST FOR
SAFEBREAK[®] VASCULAR**

REGULATORY INFORMATION

FDA identifies this generic type of device as:

Intravenous catheter force-activated separation device. An intravenous (IV) catheter force-activated separation device is placed in-line with an intravenous catheter and an intravascular administration set, including any administration set accessories. It separates into two parts when a specified force is applied. The device is intended to reduce the risk of IV catheter failure(s) requiring IV catheter replacement.

NEW REGULATION NUMBER: 21 CFR 880.5220

CLASSIFICATION: Class II

PRODUCT CODE: QOI

BACKGROUND

DEVICE NAME: SafeBreak[®] Vascular

SUBMISSION NUMBER: DEN190043

DATE OF DE NOVO: September 18, 2019

SPONSOR INFORMATION:

Site Saver, Inc. d/b/a Lineus Medical
179 N. Church Ave, Suite 202
Fayetteville, AR 72701

INDICATIONS FOR USE

SafeBreak[®] Vascular is intended to separate when excessive tension is exerted across a peripheral IV administration set. When SafeBreak[®] Vascular separates, fluid flow is stopped from the infusion pump and blood flow is stopped from the patient's IV catheter.

SafeBreak[®] Vascular is intended to aid in reduction of peripheral IV mechanical complications requiring IV replacement.

SafeBreak[®] Vascular is intended to be used on peripheral IV catheters in adults and adolescent populations eighteen (18) years of age and older receiving intermittent or continuous infusions with an electronic pump.

LIMITATIONS

Contraindications:

- Not for use in patients less than eighteen (18) years of age.
- Not for intra-arterial use.
- Not for use in-line during the transfusion of blood, blood products or biologics.
- Not for use with power injection systems or high-pressure infusion systems.

Warnings:

- Do not use SafeBreak® Vascular during infusions higher than 999 ml/hour or lower than 1 ml/hour
- SafeBreak® Vascular should not be used for any type of fluid administration other than intravenous (e.g., not for use with feeding tubes, drains, etc.)
- Not for use with Central Venous Catheters, Peripherally Inserted Central Catheter (PICC) lines, or Midline catheters. Note: Use of SafeBreak® Vascular with these device types was not evaluated in the randomized clinical study.
- Not for use with gravity IV infusions.
- Any delays in therapy, including SafeBreak® Vascular exchanges, during infusions of medications with short half-lives, may impact patient safety. Note: SafeBreak® Vascular was not studied in Critical Care Areas.
- Do not attempt to withdraw blood or fluids through the device: SafeBreak® Vascular contains a one-way valve.

Precautions:

- Not all types of peripheral IV securement devices were tested in a clinical study. Please see the clinical study summary for the type of dressing used in the study. The safety and effectiveness of this device when used with other types of peripheral IV dressings or securements has not been evaluated.

The sale, distribution, and use of SafeBreak® Vascular are restricted to prescription use in accordance with 21 CFR 801.109.

PLEASE REFER TO THE LABELING FOR A MORE COMPLETE LIST OF WARNINGS, PRECAUTIONS AND CONTRAINDICATIONS.

DEVICE DESCRIPTION

SafeBreak® Vascular is used with peripheral intravenous (IV) catheters and installed for in-line use with an IV administration set. It connects between the IV administration tubing and the patient’s peripheral IV access device. When excessive force is applied to the IV administration set, SafeBreak® Vascular separates at a force lower than the force required to dislodge the peripheral IV catheter or disrupt the IV securement dressing (4 ± 1 lbf). When SafeBreak® Vascular separates, fluid flow is stopped from the infusion pump, and blood flow is stopped from the patient’s IV catheter. SafeBreak® Vascular may be used for a maximum of seven days.



Figure 1. Assembled SafeBreak Vascular



Figure 2. Separated SafeBreak Vascular

SUMMARY OF NONCLINICAL/BENCH STUDIES

The non-clinical/bench studies conducted on the SafeBreak® Vascular are summarized in the sections below.

BIOCOMPATIBILITY/MATERIALS

SafeBreak® Vascular is an externally communicating device with indirect contact with circulating blood with prolonged contact duration (>24hr to 30 days). The biocompatibility testing summarized below was performed in accordance with FDA’s Guidance Document titled Use of International Standard ISO 10993-1, "*Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process,*" and demonstrated that the device is biocompatible for its intended use.

Endpoint	Test Method
Cytotoxicity	MEM Elution using L-929 Mouse Fibroblast Cells (ISO 10993-5:2009)

Sensitization	Guinea Pig Maximization Sensitization Test (ISO 10993-10:2010)
Irritation	Intracutaneous Irritation Test (ISO 10993-10:2010)
Acute Systemic Toxicity	Acute Systemic Injection Test (ISO 10993-11:2006)
Hemocompatibility	Hemolysis Assay- Extract Method (ASTM F756:2017)
Pyrogenicity	ISO Materials Mediated Rabbit Pyrogen (ISO 10993-11:2006)
Subacute/Subchronic Toxicity	14 Day IV/IP Mouse Study (ISO 10993-11:2006)
Particulates	USP <788>

SHELF LIFE/STERILITY

The shelf-life of SafeBreak[®] Vascular has been established at 1 year, based on testing a combination of non-aged devices after simulated shipping (per ASTM D4169, *Standard Practice for Performance Testing of Shipping Containers and Systems* according to distribution cycle 13), 1 year accelerated aged devices (per ASTM F1980-16, *Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices*), and 1 year real-time aged devices. Devices passed dye penetration testing (ASTM F1929, *Standard Test Method for Detecting Seal Leaks in Porous Medical Packaging by Dye Penetration*) and burst strength testing (Burst Package Testing per ASTM F1140-13, *Standard Test Methods for Internal Pressurization Failure Resistance of Unrestrained Packages*), in accordance with FDA recognized consensus standards.

SafeBreak[®] Vascular is labeled as sterile and is sterilized using a validated ethylene oxide sterilization cycle to achieve a sterility assurance level (SAL) of 10⁻⁶. The sterilization validation was conducted in accordance with ISO 11135:2014, *Sterilization of health care Products - Ethylene oxide Requirements for development, validation, and routine control of a sterilization process for medical devices*. Sterilant residuals were assessed per ISO 10993-7:2008 *Biological evaluation of medical devices – Part 7: Ethylene oxide sterilization residuals*. In addition, bacterial endotoxin testing was conducted per ANSI/AAMI ST72:2011, and demonstrated endotoxin levels of < 20 EU/device.

MICROBIAL INGRESS

SafeBreak[®] Vascular is intended to separate once an excessive force is applied to the IV administration line. The interface at which the device separates is an area where microbial ingress may occur. Furthermore, once the device has separated, there is a risk of microbial ingress into either the IV administration line side or the patient side of the device. Microbial ingress testing was performed on the non-separated and separated devices using a worst-case simulated use test methodology and implementing recommendations given in the FDA guidance document, *Intravascular Administration*

Sets Premarket Notification Submissions [510(k)]. A detailed protocol and full test report were provided which demonstrated that, under the specified test conditions, no ingress occurred in non-separated and separated device configurations.

HUMAN FACTORS AND USABILITY TESTING

Human factors (HF) validation testing was executed following the FDA guidance document, *Applying Human Factors and Usability Engineering to Medical Devices*. There were fifteen registered nurses (RNs) as participants. Formal training was provided for up to two RNs simultaneously in a 15-minute session prior to the HF validation test session. The training consisted of watching an instructional video, orienting the participants to the other instructional materials (i.e., Instructions for Use, instructional poster), and a walkthrough on using the product by a Lineus representative.

The following activities (use scenarios (US) and knowledge tasks (KT)) were evaluated to validate mitigations implemented to reduce the risks associated with critical tasks:

- Install SafeBreak® Vascular for new infusion (US)
- Replace separated SafeBreak® Vascular (US)
- Remove SafeBreak® Vascular from IV line (US)
- Select a suitable SafeBreak® Vascular for use (KT)
- Instructions for Use (IFU), contraindications, warnings, precautions (KT)

PERFORMANCE TESTING – BENCH

Test	Description/Acceptance Criteria
Separation Force characterization study	The defined specification was the result of the characterization testing of peripheral IV securement devices to understand when the catheter would move or dislodge, and when the securement device itself may be disrupted on a clinically relevant model (swine skin). The study was designed to ensure that SafeBreak® Vascular would separate at a force that is not too high or too low
Separation Force Testing	The device separates at the specified force, 4 ±1 lbf.
Tensile Strength of all joints	The welded joints have joint strength > (b) (4)
Validation of Anti-reconnect Feature	After the separation of the two sub-assemblies, the device cannot be reconnected by hand.
Air Leak Testing	Air leakage on aged non-separated and separated device meets the following acceptance criteria:
	Non-separated (intact) (b) (4)
	Patient side (male) (b) (4)
	Administration set side (female) (b) (4)
Valve Testing per ISO	

8536-12: Burst Pressure (check valve leakage)	No signs of air or water leakage when the IV tubing line is under pressure, in accordance with ISO 8536-12
Counterflow (check valve leakage)	The check valve from the IV tubing line withstands a pressure of 200 kPa in the counter flow direction, while it is subjected to a water excess pressure at 40°C for fifteen (15) minutes per ISO 8536-12 A.1
Duckbill Valve testing	The valve on the patient side withstands (b) (4) back pressure.
Luer Connection Testing	Device passes tests for the following (ISO 80369-7, ISO 80369-20): Falling Drop Positive Pressure Liquid Leakage Sub-atmospheric pressure air leakage Stress Cracking Resistance to Separation from Axial load Resistance to Separation from Unscrewing Resistance to Overriding
Pump Occlusion Alarm Testing	The check valve on the IV tubing side (separated) withstands (b) (4) of back pressure at various flow rates and triggers the occlusion alarm
Flow Inhibition Testing	The device does not impact the flowrate accuracy of commonly used infusion pumps
Crush Testing	The snap fit fingers are not broken or dislodged when the device is subjected to force of 200 lbf, which simulates a patient lying on the device.
Feature Verification: Transparency	The air-water interface is visually detectable, when the device is partially filled with distilled water, per ISO 8536-9, A.1.
Priming	No air bubbles are observed, when the device is primed.

SUMMARY OF CLINICAL INFORMATION

A prospective, non-randomized feasibility study was conducted in (b) (4) subjects. No safety concerns were identified. The study was underpowered to assess benefit.

A prospective, randomized, controlled trial was then conducted to assess the safety and effectiveness of the device when used with peripheral intravenous (IV) catheters in subjects ages 18 years and older. It was performed in (b) (4)

The primary objective was to assess whether the use of SafeBreak® Vascular resulted in delays of therapy that were non-inferior to the delays in the Control Group (standard of care). The secondary objective was to compare the number of peripheral IV mechanical complications between the two

groups, including intravenous (IV) catheter dislodgement, infiltration, occlusion, and phlebitis; it also assessed the need for intravenous catheter replacements. The study also documented Adverse Events as part of the Safety Evaluation and included subject and nurse satisfaction surveys.

Results:

^{(b) (4)} subjects ages 21-90 were enrolled in the Intention to Treat (ITT) population ^{(b) (4)} SafeBreak[®], ^{(b) (4)} Control), and 139 were evaluated as the Per Protocol (PP) population (70 SafeBreak[®], 69 Control). Notable reasons that subjects were not included in the Per Protocol population were that four Control Group subjects had a SafeBreak[®] Vascular device placed (which was a protocol violation) and one SafeBreak[®] Group subject had the SafeBreak[®] Vascular used in a contraindicated manner (used with IV immunoglobulin). All of the peripheral IV catheters in the study except for two were secured using a PrevaHex CHX Bordered Dressing and a secondary strip of tape to secure the J-loop (98.9% of catheters in the Per Protocol population).

Primary Endpoint: To evaluate if use of the SafeBreak[®] Vascular device resulted in a delay of therapy that was non-inferior to the delays in the Control Group by comparing the total delay of therapy per 24 hours per subject between the following groups:

- Control Group: Delays from peripheral IV mechanical complications/events
- SafeBreak[®] Group: Delays from peripheral IV mechanical complications/events, SafeBreak[®] Vascular separations, and SafeBreak[®] Vascular failures

In the pre-specified primary endpoint analysis, all subjects were included. If a subject did not experience any events, a zero-delay time (i.e., 0 min) was used.

Delay of Therapy (minutes) per 24h per subject, All ITT or PP Subjects

(b) (4)	(b) (4)
Intention to Treat (ITT)	(b) (4)
Per Protocol (PP)	(b) (4)

*Of note, since at least 70% of the subjects in each group had no events, this lowered the mean in each group and resulted in a median total delay of therapy time per 24 hours of 0 minutes in each group.

As shown in the table above, since the upper confidence limit (UCL) of the two-sided ^{(b) (4)} confidence interval (CI) of the treatment difference (SafeBreak[®] minus Control) was within the non-inferiority margin ^{(b) (4)} minutes), the total delay of therapy for the subjects in the SafeBreak[®] Group was non-inferior to the total delay in the Control Group (standard of care) in both the ITT and PP populations.

As supportive evidence, additional analyses were performed for only those subjects who had mechanical IV complications and/or SafeBreak[®] Vascular separations (i.e., subjects without any delays were not included).

Delay of Therapy (minutes) per 24h per subject, Including Only Subjects with Events

	(b) (4)
Intention to Treat (ITT)	
Per Protocol (PP)	

As shown in the table above, when only subjects who experienced at least one mechanical complication and/or SafeBreak® Vascular separation were analyzed, the median total delay of therapy time per 24 hours was (b) (4) minutes for the SafeBreak® Group ((b) (4)) and (b) (4) minutes for the Control Group ((b) (4)), in favor of the SafeBreak® Group. Of note, given the small number of subjects, these sub-analyses were underpowered to test the hypothesis of non-inferiority.

Secondary Endpoints: To compare the number of peripheral IV mechanical complications between the Control and SafeBreak® groups. These included events such as intravenous (IV) catheter dislodgement, infiltration, occlusion, and phlebitis, and also assessed the need for intravenous catheter replacement.

Peripheral IV Mechanical Complications (MCs) Requiring an IV Replacement (PP Population)

Type of Mechanical Complication (MC)	SafeBreak® Group			Control Group		
	#MCs	% Subjects with MCs (n=70)	% Catheters with MCs (n=81)	#MCs	% Subjects with MCs (n=69)	% Catheters with MCs (n=93)
Dislodgement	2	2.9%	2.5%	4	5.8%	4.3%
Infiltration	8*	11.4%	9.9%	10	14.5%	10.8%
Occlusion	2**	2.9%	2.5%	1	1.5%	1.1%
Phlebitis (VIP*** Score ≥2)	1	1.4%	1.2%	10	14.5%	10.8%
Total	13	18.6%	16.0%	25	36.2%	26.9%

*Not included in this table: In the ITT population, one subject in the Control Group had two infiltrations after a SafeBreak® Vascular device was placed on their IV catheter which was a protocol violation. Therefore, there were a total of 10 infiltrations in the study associated with a SafeBreak® Vascular device: 8 infiltrations in subjects in the SafeBreak® Group and 2 infiltrations in one subject in the Control Group who inadvertently received the SafeBreak® Vascular device.

**There were two additional “occlusions” reported in the SafeBreak® Group: one resolved with replacement of the SafeBreak® Vascular device and the other resolved with replacement of the SafeBreak® Vascular device and the administration set.

***The study evaluated phlebitis using the Visual Infusion Phlebitis (VIP) score. A VIP score of ≥2 required an IV catheter replacement

As described in the table above:

- SafeBreak® Group: 13 peripheral IV mechanical complications required an IV catheter replacement (in 70 subjects)

- Control Group: 25 peripheral IV mechanical complications required an IV catheter replacement (in 69 subjects)

There were fewer peripheral IV mechanical complications in the SafeBreak[®] Group as compared to the Control Group. Reducing the number of mechanical complications that require replacement of an intravenous catheter is a clinically significant benefit to the SafeBreak[®] Vascular device.

SafeBreak[®] Vascular Separations: In the 70-subject Per Protocol population, there were 10 SafeBreak[®] Vascular separations in 9 subjects. The surrounding events included descriptions such as “tubing caught in bed/bed rail,” “tubing pulled while reaching from bed,” and “tubing caught during toileting/hygiene in bathroom.” There were no fluid spills or blood loss events related to SafeBreak[®] Vascular separations.

Adverse Events: There were no Serious Adverse Events related to the device. There were no subject harms documented as a result of interruptions/delays of therapy. There were no catheter-related infections, episodes of sepsis, or air emboli. There were two events where the SafeBreak[®] Vascular device appeared to be leaking and was replaced, and two events where the device appeared to be occluded and was replaced. No harm was documented from these events. There were no unanticipated adverse device effects (UADEs).

Clinical Study Summary:

- **Safety:** The delays of therapy for the Control Group and SafeBreak[®] Groups were similar. No harms were documented related to delays of therapy in either study group.
- **Effectiveness:** Overall, there were 13 peripheral IV mechanical complications that required an IV catheter replacement in the SafeBreak[®] Group (70 subjects) as compared to 25 peripheral IV mechanical complications that required an IV catheter replacement in the Control Group (69 subjects). Given the importance of maintaining peripheral intravenous access for inpatient populations, this is a clinically significant benefit.

Forces applied across IV administration sets and peripheral IV catheters can contribute to catheter failures. These forces may cause inadvertent removal of the catheter (e.g., IV dislodgement) or may cause traumatic movement of the catheter relative to the vessel wall, which may cause phlebitis, infiltration, or occlusion (e.g., if a catheter migrates to a position against the vessel wall).¹ In this clinical study, although the force exerted across the SafeBreak[®] Vascular device at the time of separation is unknown, given the totality of the study data, it is reasonable to consider that the force may have caused one of the mechanical complications described above if the SafeBreak[®] device were not in place. Therefore, for subjects in the SafeBreak[®] Group, the addition of the SafeBreak[®] device to the standard of care probably prevented mechanical complications which would have required IV catheter replacement.

Pediatric Extrapolation

¹ Helm RE, Klausner JD, Klemperer JD, Flint LM, Huang E. Accepted but unacceptable: peripheral IV catheter failure. J Infus Nurs. 2015 May-Jun;38(3):189-203. doi: 10.1097/NAN.000000000000100. PMID: 25871866.

SafeBreak® Vascular is indicated for patients age 18 and older. For medical devices, the FD&C Act defines patients before their 22nd birthday as pediatric patients. In this De Novo request, data from subjects over 21 were used to support the use of the device in patients over the age of 18. It was appropriate to indicate the device for individuals 18 and older, because patients aged 18 to 20 do not carry additional risks relative to the population studied.

LABELING

SafeBreak® Vascular labeling is sufficient and meets the labeling requirements of 21 CFR 801. The Instructions for Use include the Indications for Use, description of the device, contraindications, warnings, precautions, summary of the clinical trial, shelf life, and steps in installation and removal of separated and intact SafeBreak® Vascular.

RISKS TO HEALTH

The table below identifies the risks to health that may be associated with use of an intravenous catheter force-activated separation device and the measures necessary to mitigate these risks.

Identified Risks to Health	Mitigation Measures
Delays of therapy due to failure of device to function as expected (e.g., if separation force too low)	Performance data, Non-clinical performance testing, and Labeling
Mechanical complications (e.g., IV dislodgement, IV infiltration, occlusion, and phlebitis events requiring IV replacement) due to failure of device to function as expected (e.g., if separation force too high)	Performance data, Non-clinical performance testing, and Labeling
Infection	Sterilization validation, Shelf life testing, Non-clinical performance testing, and Labeling
Air embolism	Non-clinical performance testing, and Labeling
Adverse tissue reaction	Biocompatibility evaluation, Pyrogenicity testing, and Non-clinical performance testing

SPECIAL CONTROLS

In combination with the general controls of the FD&C Act, intravenous catheter force-activated separation device is subject to the following special controls:

1. Performance data must be provided to demonstrate clinically acceptable performance for the intended use of the device.
2. Non-clinical performance testing must demonstrate that the device performs as intended under anticipated conditions of use. The following performance characteristics must be tested:
 - i. Separation force testing;
 - ii. Validation of anti-reconnect features;
 - iii. Air and liquid leakage testing, both before and after separation;
 - iv. Luer connection testing;
 - v. Flow rate testing;
 - vi. Particulate testing; and
 - vii. Microbial ingress testing.
3. The device must be demonstrated to be biocompatible.
4. Performance testing must demonstrate that the device is sterile and non-pyrogenic.
5. Performance testing must support the shelf life of the device by demonstrating continued sterility and device functionality over the identified shelf life.
6. Device labeling must include:
 - i. Instructions for use; and
 - ii. A discussion of catheter dressings intended to be used with the device.

BENEFIT/RISK DETERMINATION

The benefits and risks of the device are based on data collected in the clinical study described above. The probable risks of the device include the risk of patient harm due to an interruption and delay of therapy related to a device separation where the force causing the separation may not have otherwise dislodged or affected the intravenous catheter (i.e., if the separation force is set too low). Risks also include mechanical complications due to the failure of the device to function as expected (e.g., if separation force is set too high). Delay of therapy and mechanical complications are risks associated with intravenous infusion devices and, therefore, constitute probable risks for this device. Of note, during the randomized clinical trial, no patient harms (e.g., adverse patient outcomes due to a delay in drug delivery, etc.) were documented due to interruptions or delays of therapy at the separation force set for the device. Despite these separations, there was not a significant increase in the time of delay of therapy compared with Controls. The clinical study also documented several events where the device appeared to be leaking or occluded and needed to be replaced; no patient harm was documented from these events. In addition, similar to other devices that connect to IV catheters and IV administration sets, there is the risk of infection if connections are not disinfected as per standard practice. There is also the risk of air embolism if the device is not primed.

An assessment of the trial for benefit revealed that there were 13 peripheral IV mechanical complications that required an IV catheter replacement in the SafeBreak[®] Group (70 subjects) as compared to 25 peripheral IV mechanical complications that required an IV catheter replacement in the Control Group (69 subjects). This reduction in mechanical complications is a clinically significant benefit given the importance of maintaining vascular access in the inpatient population. The reduction in peripheral IV mechanical complications is presumed to be related to the ten (10) SafeBreak[®] Vascular separations that occurred in nine (9) subjects during the study.

Additional factors to be considered in determining probable risks and benefits for the SafeBreak® Vascular include uncertainties regarding the benefits, such as the use of descriptive statistics for the outcome measures and that event-specific analyses for the primary endpoint were underpowered to demonstrate non-inferiority. There are additional uncertainties for both the benefits and risks of the device, since these assessments were based on one limited study at one hospital, and because other confounding variables or patient-specific factors may have contributed to the safety and effectiveness outcomes (e.g., the peripheral IV dressing/securement used). Also, the device was not studied with infusions of all types of medications, and it was not studied in Critical Care Areas. Therefore, as risk mitigations, the labeling informs users regarding these limitations of the clinical data.

Overall, despite these uncertainties, given the clinically significant benefit of maintaining vascular access in the inpatient population, and since the device appears to be low-risk when used with peripheral IV catheters and in the defined population, and when considering the labeling mitigations, including contraindications, warnings, and precautions, the probable benefits of the device appear to outweigh the probable risks.

Patient Perspectives

Patient perspectives were considered for the SafeBreak® Vascular device including surveys of study subjects during the randomized controlled trial. Of the subjects in the SafeBreak® Group who responded to survey, 92.4% (49 of 53) agreed or strongly agreed with the statement: “I am glad the hospital used the study device on my IV line.” To the question: “Having the study device in my IV line was a nuisance,” 7.5% (4 of 53) of responding SafeBreak® subjects strongly agreed and 13.2% agreed (7 of 53).

Benefit/Risk Conclusion

In conclusion, given the available information above, for the following indication statement:

SafeBreak® Vascular is intended to separate when excessive tension is exerted across a peripheral IV administration set. When SafeBreak® Vascular separates, fluid flow is stopped from the infusion pump and blood flow is stopped from the patient’s IV catheter.

SafeBreak® Vascular is intended to aid in reduction of peripheral IV mechanical complications requiring IV replacement.

SafeBreak® Vascular is intended to be used on peripheral IV catheters in adults and adolescent populations eighteen (18) years of age and older receiving intermittent or continuous infusions with an electronic pump.

The probable benefits outweigh the probable risks for the SafeBreak® Vascular device. The device provides benefits and the risks can be mitigated by the use of general controls and the identified special controls.

CONCLUSION

The De Novo request for the SafeBreak® Vascular is granted and the device is classified under the following:

Product Code: QOI

Device Type: Intravenous catheter force-activated separation device

Class: II

Regulation: 21 CFR 880.5220