HEALTHCARE PURCHASING NEWS

A systematic approach to surgical hemostat use supports standardization and cost efficiencies

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Summary

- A systematic approach to bleeding management, the Hemostasis Optimization Program (HOP), was implemented at a large U.S. teaching hospital
- Implementation of the HOP framework resulted in an annual cost savings of $168,688
- This evaluation demonstrated that cost savings, as well as operating room and supply chain efficiencies, were achieved without sacrificing patient outcomes

Surgical bleeding and variability in hemostat utilization

Disruptive bleeding remains a critical challenge in surgery, as it can lead to suboptimal patient outcomes, introduce procedure complexities for surgeons and surgical staff, and result in higher healthcare costs.[1,2] For example, uncontrolled bleeding is associated with significantly higher total hospital costs (25-40% higher) versus bleeding controlled with adjunctive hemostats ($24,203 to $61,323 uncontrolled versus $14,420 to $45,593 controlled).[1] Primary methods of hemostasis, such as electrocautery, sutures, and staples, do not always allow achievement of complete hemostasis, or may be impractical. As such, use of adjunctive topical hemostats may be required to help achieve rapid and effective hemostasis.

Adjunctive hemostats manage bleeding by acting as mechanical barriers, providing a matrix for clotting, triggering coagulation, and/or sealing adjacent surfaces. Compared to primary methods alone, adjunctive hemostats have been shown to reduce utilization of hospital resources: up to 40% fewer patients require blood transfusions, up to 4 days shorter length of stay, up to 25 minutes reduced operating time, and significantly decreased likelihood of hospital readmission.[3-6]

A wide array of various types of adjunctive hemostats are available (e.g., absorbable matrices, gelatins, fibrin sealants, and patches) to accommodate various needs.[7] However, selecting the most appropriate hemostat is challenging given ambiguous bleeding classifications, inconsistent clinical guidance on optimal utilization, and limited indications for use appropriate to specific bleeding situations. These ambiguities can create substantial confusion and potentially unnecessary variability for the management of surgical bleeding, as well as significant clinical and economic hospital burden.

A systematic approach to bleeding management

Because there is no existing universal and practical algorithm that provides guidance for surgical bleeding classification or optimal hemostat utilization, Ethicon, Inc. embarked on a large-scale quantitative research study that characterized hemostat usage. This research involved 450 surgeons from 11 surgical specialties, comprising over 7,800 bleeding occasions. Findings of this endeavor revealed that surgeons' decisions for hemostat selection rely predominantly on the surgical bleeding site (anatomy and critical surrounding anatomic structures) and situation (access, tissue surface, bleeding intensity, and bleeding risk). Specifically, the real-world data categorized five universal bleeding situations and the optimal adjunctive hemostat selection for each situation. For example, continuous oozing bleeding would most optimally be addressed with oxidized regenerated cellulose (ORC) (see table). This guidance on the use of adjunctive hemostats in each bleeding situation is based on their physical and biochemical properties, mode of action, and real-world experience use across a broad range of surgical specialties.

Using the data and recommendations from this research, the Hemostasis Optimization Program (HOP) was developed, which focuses on reducing variation in hemostat use and optimizing performance in surgical bleeding management. The program was designed to provide guidance on adjunctive hemostat use through a systematic, step-wise approach that evaluates product use and performance, educates surgical teams, and provides action plans for the healthcare facility:

1. Collect and analyze hospital-specific data on case observations and product utilization
2. Review data and generate action plan regarding hemostat utilization education and evaluation with multidisciplinary team
3. Hold education sessions on topics such as the burden of bleeding, hemostat marketplace clarification, science of hemostasis, and the program's framework and guidance for recommended hemostat use
4. Establish and conduct in-procedure evaluations of the recommended solutions over a set time period
5. Ask surgeons and nursing staff to share experiences and feedback on the program's effectiveness, as well as hurdles encountered and recommended solutions

As part of the program, several key materials are shared to enhance clinical awareness, including educational modules, procedural bleeding guides, and framework algorithms.

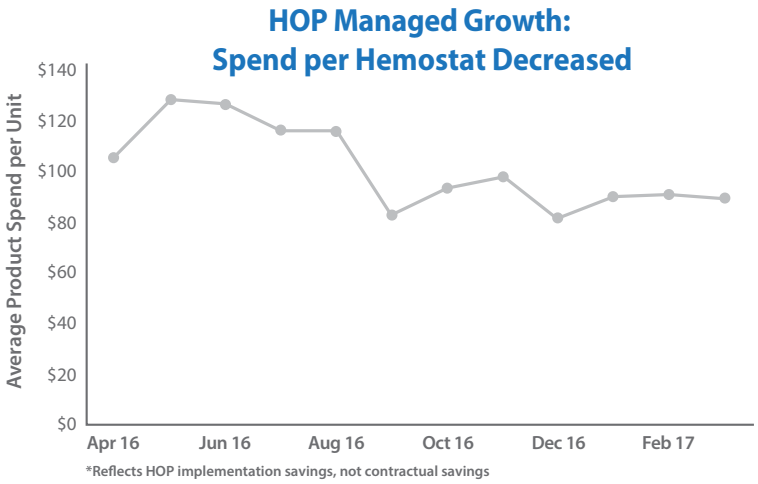
Bleeding Situation	Definition	Product Type
Continuous Oozing	Will not stop with compression/simple packing. The solution for this bleeding is more time consuming than it is difficult.	Oxidized Regenerated Cellulose (ORC)
Problematic	Even though the bleeding is accessible, it could be trouble. It is more than routine, likely to be resistant to conventional means, requires immediate attention, and causes disruption to the normal progression of surgery.	Fibrin Patch
Difficult to Access	Bleeding that occurs in tight and irregular spaces; you cannot see the exact source of the bleed. You are concerned that accessing a tight space will cause more harm.	Flowable Gelatin
Potential Re-Bleeding Risk	Bleeding may be addressed intraoperatively but could later develop into more serious complications, especially in high-risk patients.	Fibrin Sealant
High-Pressure Vessel Bleeding	A leak in high-pressure vessel (aortic peripheral vascular suture line) that has been stopped, but if it leaks post-op, could be catastrophic.	Vascular Sealant

Real-world evidence at a U.S. hospital

The program has been implemented at hospitals across various countries, and the focus of this paper is the program's impact at a large U.S. teaching hospital. At this hospital, as with most healthcare facilities, optimizing patient outcomes is a top priority. Second to this, cost containment has become essential, with the supply chain team increasingly looking for ways to optimize expenditure without sacrificing patient

outcomes. With high volume and variability of hemostat use and product expenditure, implementing the HOP program represented a critical opportunity for the hospital to achieve its goal of continuously improving care based on value and quality.

Such goals are aligned with the "Triple Aim,", "Quadruple Aim," and the increasing push for value-based healthcare. At the hospital, the Supply Chain team, which has the combined role of product value analysis for perioperative products and inventory management, led the implementation of the HOP program and the conversion of the adjunctive hemostat portfolio to the new manufacturer (Ethicon).



*Reflects HOP implementation savings, not contractual savings

A critical first step for the decision to implement the HOP program was to conduct a clinical and cost value analysis on the integration of the new manufacturer's hemostats. The results of this analysis showed the potential for substantial cost savings, with similar or superior clinical benefits compared with using hemostats from the previous manufacturer. A trial period, then full conversion, of the adjunctive hemostat category was initiated in 2016. Essentially, the process involved switching 95% of the adjunctive hemostat category from prior manufacturers to a full-line supplier. The suite of value-added solutions offered by the HOP program was a key factor in the conversion decision-making process. Consolidating from two manufacturers to predominately one also facilitated more efficient inventory management. Furthermore, converting to a full-line supplier allowed the hospital to have a broader portfolio of products to address their bleeding management needs.

Lessons were learned from this conversion and program implementation. Obtaining surgeon buy-in was critical to the success of this initiative, and the HOP framework facilitated constructive dialogue. Sharing details on the economic evidence was also critical in validating the process, for example, shifting utilization to more cost-effective products. In addition, education on the rationale for conversion, explanation of product differences and advances over time, and product demonstrations were key factors in obtaining buy-in from clinician and non-clinician stakeholders. Importantly, the support and active engagement of the new manufacturer's representatives, for continual education on the HOP program during procedures and across the surgical community facilitated comprehensive deployment of this initiative.

Once the hospital achieved value analysis and clinician buy-in, the next step was determining how best to customize and integrate the HOP program, which the Supply Chain team felt was the most comprehensive program of its kind seen at their hospital. A hands-on process was required both inside and outside the operating room to bring in training and manage hurdles. The HOP framework was open to all specialties across all operating rooms; the highest level of interest came from cardiothoracic, vascular, spine, and neurosurgery, where multiple hemostats per procedure are sometimes used. Training was provided through various formats to accommodate different needs for the surgeons and staff, including in-services, audiovisual materials, handouts, presentations, and hands-on product training. To help with seamless delivery and minimize interruption, education was offered across shifts and was integrated into the normal workflow; for example, part of the training occurred at weekly staff meetings. Approximately 100 individuals were trained, including surgeons, nurse managers, inventory personnel, and perioperative technicians.

Finally, a system was set up to track hemostat costs as part of the program implementation. The number of hemostat units, by type, was analyzed to determine hemostat expenditure over a one-year observation period. In addition, a team outside of perioperative supply chain services tracked clinical outcomes, which were continuously monitored for changes in the data over time—no differences were detected before versus after conversion and HOP program implementation.

Achieving the goals

The economic analysis of the program's impact revealed an annual cost savings of $168,688, not including contractual savings from switching to the full-line supplier. These findings aligned with the predicted savings calculated as part of the project's initiation. To appropriately compare hemostat costs before and after program implementation, it was necessary to control for several factors, including new products introduced that were not part of the initial analysis, contracted price changes, and the case volume increase that occurred over the one-year observation period. Interestingly, the spend per hemostat unit trended downward 15% over the year (see figure), from a higher average to a lower average spend per unit of product, while case volume trended higher. This hemostat spend optimization was enabled by a shift toward the manufacturer's more cost-effective products appropriate to each bleeding situation, in particular, advanced ORC hemostats (SURGICEL SNoW™ Absorbable Hemostat) and optimal utilization of flowable hemostats (SURGIFLO® Hemostatic Matrix). These findings indicate that the hospital managed the growth of its resource needs well and increasingly optimized its use of adjunctive hemostats over time.

These cost savings and product utilization efficiencies were observed alongside high surgeon and nurse satisfaction. For instance, it was reported that the team of nurses and surgeons were "Very Satisfied" (on a five-point rating scale) with the success of both product conversion and implementation of the HOP program. The hospital also noted improved product education and enhanced communication and support through a solid partnership with the manufacturer, which was integral to the program's success. Furthermore, operating room efficiencies were observed, which can be partially attributed to having a predominantly single supplier. From a supply chain perspective, inventory monitoring became easier, contracting became more efficient, product waste was reduced, and higher-priced items were eliminated. Periodic evaluation and maintenance strategies were also put in place to ensure continued success.

Final Words

The Hemostasis Optimization Program was effectively implemented, and it represents one of the most comprehensive programs of its kind by this large U.S. teaching hospital. This evaluation demonstrated that cost savings, as well as operating room and supply chain efficiencies, were achieved without sacrificing patient outcomes. In addition, the portfolio conversion and program implementation were met with high staff satisfaction. Manufacturer support and provision of staff resources, through a consultative partnership, were integral to the success of this value-added initiative. The favorable outcomes of this evaluation warrant further partnership with the manufacturer and evaluation of the HOP program, to improve efficiencies in other applicable medical device categories. **HPN**

References:

1. Corral M et al. Clinicoecon Outcomes Res 2015; 7: 409-421.
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EVITHROM® Thrombin, Topical (Human) for Topical Use Only
Lyophilized Powder for Solution

EVITHROM® is a topical thrombin indicated as an aid to hemostasis whenever oozing blood and minor bleeding from capillaries and small venules is accessible and control of bleeding by standard surgical techniques (such as suture, ligature or cautery) is ineffective or impractical.
EVITHROM® may be used in conjunction with an Absorbable Gelatin Sponge, USP.

Important Safety Information
- For topical use only.
- Do not inject.
- Apply EVITHROM® on the surface of bleeding tissue only.
- The amount of EVITHROM® required depends upon the area of tissue to be treated and the method of application. In clinical studies, volumes up to 10 ml were used in conjunction with Absorbable Gelatin Sponge.
- Do not use for the treatment of severe or brisk arterial bleeding.
- Do not use in individuals known to have anaphylactic or severe systemic reaction to human blood products. Hypersensitivity reactions, including anaphylaxis, may occur.
- There is a potential risk of thrombosis if absorbed systemically.
- May carry a risk of transmitting infectious agents such as viruses and theoretically, the Creutzfeldt-Jakob disease (CJD) agent, despite manufacturing steps designed to reduce the risk of viral transmission.
- The most common adverse reactions during clinical trial (reported in at least 2% of subjects treated with EVITHROM®) were prolonged activated partial thromboplastin time, increased INR, decreased lymphocyte count, prolonged prothrombin time and increased neutrophil count.
- None of the patients treated with EVITHROM developed antibodies to human thrombin or to human Factor V/Va. The clinical significance of these findings is unknown.

For complete indications, contraindications, warnings, precautions, and adverse reactions, please reference full package insert.

SURGIFLO® Hemostatic Matrix Kit Essential Product Information
(Made from Absorbable Gelatin Sponge, USP) with Thrombin

DESCRIPTION
SURGIFLO® with Thrombin (SURGIFLO® Hemostatic Matrix Kit) is intended for hemostatic use by applying to a bleeding surface.

ACTIONS
When used in appropriate amounts SURGIFLO® is absorbed completely within 4 to 6 weeks.

INTENDED USE/INDICATIONS
SURGIFLO®, mixed with thrombin solution, is indicated in surgical procedures (other than ophthalmic) as an adjunct to hemostasis when control of bleeding by ligature or other conventional methods is ineffective or impractical.

CONTRAINDICATIONS
- Do not use SURGIFLO® in intravascular compartments because of the risk of embolization.
- Do not use SURGIFLO® in patients with known allergies to porcine gelatin.
- Do not use SURGIFLO® in closure of skin incisions because it may interfere with the healing of skin edges. This interference is due to mechanical interposition of gelatin and is not secondary to intrinsic interference with wound healing.

WARNINGS
- SURGIFLO® should not be used in the presence of infection and should be used with caution in contaminated areas of the body
- SURGIFLO® should not be used in instances of pumping arterial hemorrhage. SURGIFLO® will not act as a tampon or plug in a bleeding site.
- SURGIFLO® should be removed from the site of application when used in, around, or in proximity to foramina in bone, areas of bony confine, the spinal cord, and/or the optic nerve and chiasm because it may swell resulting in nerve damage.
- Excess SURGIFLO® should be removed once hemostasis has been achieved.
- The safety and effectiveness of SURGIFLO® for use in ophthalmic procedures has not been established.
- SURGIFLO® should not be used for controlling post-partum intrauterine bleeding or menorrhagia.
- The safety and effectiveness of SURGIFLO® has not been established in children and pregnant women.
- The blue flexible applicator tip should not be trimmed to avoid exposing internal guidewire.
- The white straight applicator tip should be trimmed away from the surgical area. Cut a square angle to avoid creating a sharp tip.

PRECAUTIONS
- Safe and effective use of SURGIFOAM® Sponge has been reported in a published neurologic retrospective study involving 1700 cases in Europe. Safe and effective use in neurosurgery has not been proven through randomized, controlled clinical studies in the United States.
- SURGIFLO® is supplied as a sterile product and cannot be resterilized.
- SURGIFLO® should not be used for packing unless excess product that is not needed to maintain hemostasis is removed. SURGIFLO® may swell up to 20% upon contact with additional fluid.
- SURGIFLO® should not be used in conjunction with autologous blood salvage circuits.
- SURGIFLO® should not be used in conjunction with methylmethacrylate adhesives.
- In urological procedures, SURGIFLO® should not be left in the renal pelvis or ureters to eliminate the potential foci for calculus formation.

ADVERSE EVENTS

A total of 142 patients received SURGIFOAM® Sponge during a clinical trial comparing SURGIFOAM® Sponge to another absorbable gelatin sponge. In general, the following adverse events have been reported with the use of absorbable porcine gelatin-based hemostatic agents:

- Gelatin-based hemostatic agents may serve as a nidus for infection and abscess formation and have been reported to potentiate bacterial growth.
- Giant cell granulomas have been observed at implant sites when used in the brain.
- Compression of the brain and spinal cord resulting from the accumulation of sterile fluid have been observed.
- Multiple neurologic events were reported when absorbable gelatin-based hemostatic agents were used in laminectomy operations, including cauda equina syndrome, spinal stenosis, meningitis, arachnoiditis, headaches, paresthesias, pain, bladder and bowel dysfunction, and impotence.
- The use of absorbable gelatin-based hemostatic agents during the repair of dural defects associated with laminectomy and craniotomy operations, has been associated with fever, infection, leg paresthesias, neck and back pain, bladder and bowel incontinence, cauda equina syndrome, neurogenic bladder, impotence, and paresis.
- The use of absorbable gelatin-based hemostatic agents has been associated with paralysis, due to device migration into foramina in the bone around the spinal cord, and blindness, due to device migration in the orbit of the eye, during lobectomy, laminectomy, and repair of a frontal skull fracture and lacerated lobe.
- Foreign body reactions, "encapsulation" of fluid, and hematoma have been observed at implant sites.
- Excessive fibrosis and prolonged fixation of a tendon have been reported when absorbable gelatin-based sponges were used in severed tendon repair.
- Toxic shock syndrome was reported in association with the use of absorbable gelatin-based hemostats in nasal surgery.
- Fever, failure of absorption, and hearing loss have been observed when absorbable hemostatic agents were used during tympanoplasty.

SURGICEL Essential Product Information

INDICATIONS

SURGICEL® Absorbable Hemostat (oxidized regenerated cellulose) is used adjunctively in surgical procedures to assist in the control of capillary, venous, and small arterial hemorrhage when ligation or other conventional methods of control are impractical or ineffective. SURGICEL® ORIGINAL, SURGICEL® FIBRILLAR™ and SURGICEL® NU-KNIT® Hemostats can be cut to size for use in endoscopic procedures.

PRECAUTIONS

- Use only as much SURGICEL® Absorbable Hemostat as is necessary for hemostasis, holding it firmly in place until bleeding stops. Remove any excess before surgical closure in order to facilitate absorption and minimize the possibility of foreign body reaction.
- In urological procedures, minimal amounts of SURGICEL® Absorbable Hemostat should be used and care must be exercised to prevent plugging of the urethra, ureter, or a catheter by dislodged portions of the product.
- Since absorption of SURGICEL® Absorbable Hemostat could be prevented in chemically cauterized areas, its use should not be preceded by application of silver nitrate or any other escharotic chemicals.
- If SURGICEL® Absorbable Hemostat is used temporarily to line the cavity of large open wounds, it should be placed so as not to overlap the skin edges. It should also be removed from open wounds by forceps or by irrigation with sterile water or saline solution after bleeding has stopped.
- Precautions should be taken in otorhinolaryngologic surgery to assure that none of the material is aspirated by the patient. (Examples: controlling hemorrhage after tonsillectomy and controlling epistaxis.)
- Care should be taken not to apply SURGICEL® Absorbable Hemostat too tightly when it is used as a wrap during vascular surgery (see Adverse Reactions).

ADVERSE EVENTS

- "Encapsulation" of fluid and foreign body reactions have been reported.
- There have been reports of stenotic effect when SURGICEL® Absorbable Hemostat has been applied as a wrap during vascular surgery.
- Paralysis and nerve damage have been reported when SURGICEL® Absorbable Hemostat was used around, in, or in proximity to foramina in bone, areas of bony confine, the spinal cord, and/or the optic nerve and chiasm.
- Blindness has been reported in connection with surgical repair of a lacerated left frontal lobe when SURGICEL® Absorbable Hemostat was placed in the anterior cranial fossa.
- Possible prolongation of drainage in cholecystectomies and difficulty passing urine per urethra after prostatectomy have been reported.

For more information, please consult your doctor or for product quality and technical questions, call 1-800-795-0012.

SURGIFLO® Hemostatic Matrix Kit
***(Made from Absorbable Gelatin Sponge, USP)* with Thrombin**

Caution: Federal (U.S.A.) law restricts this device to sale by or on the order of a physician (or properly licensed practitioner).

Do not inject into blood vessels.

DESCRIPTION

SURGIFLO® Hemostatic Matrix Kit with Thrombin (SURGIFLO® Hemostatic Matrix Kit) is intended for hemostatic use by applying to a bleeding surface.

The Kit contains:

1. A sterile tray with *all* sterile components to prepare the Flowable Gelatin Matrix,
2. A sterile tray with *all* surface sterilized Thrombin kit components to prepare the Thrombin Solution.
    1. The Flowable Gelatin Matrix comes in a tray with *all* sterile components:
        - A sterile pre-filled blue plunger syringe containing the porcine Gelatin Matrix that is off-white in appearance,
        - A sterile empty syringe,
        - A sterile liquid transfer cup,
        - A sterile blue flexible applicator tip that is bendable in all directions, and
        - A sterile white applicator tip that can be trimmed to desired length
    2. The surface sterilized components to prepare the Thrombin Solution include:
        - A Thrombin vial, EVITHROM® Thrombin, Topical (Human), containing 2000 International Units (IU) of sterile lyophilized human thrombin powder for reconstitution,
        - A needle-free syringe containing 2 mL of Sterile Water for Injection (Sterile WFI),
        - A sterile vial adapter.

For prescribing information on the Thrombin component, please refer to the EVITHROM® Thrombin, Topical (Human) Prescribing Information on page 9.

Thrombin should be reconstituted using the vial adapter and the needle-free syringe with Sterile WFI.

The Thrombin Solution must be added to the Flowable Gelatin Matrix prior to use.

Once the hemostatic matrix is mixed with the Thrombin Solution, the appropriate applicator tip should be attached to the syringe for product delivery onto the bleeding site.

ACTIONS

SURGIFLO® Hemostatic Matrix Kit has hemostatic properties. When used in appropriate amounts SURGIFLO® Hemostatic Matrix is absorbed completely within 4 to 6 weeks. In an animal implantation study, tissue reactions were classified as minimal.

INTENDED USE/INDICATIONS

SURGIFLO® Hemostatic Matrix, mixed with thrombin solution, is indicated in surgical procedures (other than ophthalmic) as an adjunct to hemostasis when control of bleeding by ligature or other conventional methods is ineffective or impractical.

CONTRAINDICATIONS

- Do not use SURGIFLO® Hemostatic Matrix in intravascular compartments because of the risk of embolization.
- Do not use SURGIFLO® Hemostatic Matrix in patients with known allergies to porcine gelatin.
- Do not use SURGIFLO® Hemostatic Matrix in closure of skin incisions because it may interfere with the healing of skin edges. This interference is due to mechanical interposition of gelatin and is not secondary to intrinsic interference with wound healing.

WARNINGS

- Do not inject or compress SURGIFLO® Hemostatic Matrix into blood vessels.
- SURGIFLO® Hemostatic Matrix is not intended as a substitute for meticulous surgical technique and the proper application of ligatures or other conventional procedures for hemostasis.
- SURGIFLO® Hemostatic Matrix should not be used in the presence of infection. SURGIFLO® Hemostatic Matrix should be used with caution in contaminated areas of the body. If signs of infection or abscess develop where SURGIFLO® Hemostatic Matrix has been positioned, reoperation may be necessary in order to remove the infected material and allow drainage.
- SURGIFLO® Hemostatic Matrix should not be used in instances of pumping arterial hemorrhage. It should not be used where blood or other fluids have pooled or in cases where the point of hemorrhage is submerged. SURGIFLO® Hemostatic Matrix will not act as a tampon or plug in a bleeding site.
- SURGIFLO® Hemostatic Matrix should be removed from the site of application when used in, around, or in proximity to foramina in bone, areas of bony confine, the spinal cord, and/or the optic nerve and chiasm. Care should be exercised to avoid overpacking. SURGIFLO® Hemostatic Matrix may swell, creating the potential for nerve damage.
- Excess SURGIFLO® Hemostatic Matrix should be removed once hemostasis has been achieved, because of the possibility of dislodgment of the device or compression of other nearby anatomic structures.
- The safety and effectiveness of SURGIFLO® Hemostatic Matrix for use in ophthalmic procedures has not been established.
- SURGIFLO® Hemostatic Matrix should not be used for controlling post-partum intrauterine bleeding or menorrhagia.
- The safety and effectiveness of SURGIFLO® Hemostatic Matrix has not been established in children and pregnant women.
- The blue flexible applicator tip should not be trimmed to avoid exposing internal guidewire.
- The white straight applicator tip should be trimmed away from the surgical area. Cut a square angle to avoid creating a sharp tip. The tray can be used to contain the excess piece for discarding.

PRECAUTIONS

- Safe and effective use of SURGIFOAM® Sponge has been reported in a published neurologic retrospective study involving 1700 cases in Europe. Safe and effective use in neurosurgery has not been proven through randomized, controlled clinical studies in the United States.
- SURGIFLO® Hemostatic Matrix is supplied as a sterile product and cannot be resterilized. Unused open pouches of SURGIFLO® Hemostatic Matrix should be discarded.
- While packing a cavity for hemostasis is sometimes surgically indicated, SURGIFLO® Hemostatic Matrix should not be used in this manner unless excess product that is not needed to maintain hemostasis is removed. When incorporated into a fibrin clot, SURGIFLO® Hemostatic Matrix may swell up to 20% upon contact with additional fluid.
- Only the minimum amount of SURGIFLO® Hemostatic Matrix needed to achieve hemostasis should be used. Once hemostasis is achieved, any excess SURGIFLO® Hemostatic Matrix should be carefully removed.
- SURGIFLO® Hemostatic Matrix should not be used in conjunction with autologous blood salvage circuits. It has been demonstrated that fragments of collagen-based hemostatic agents may pass through 40 µm transfusion filters of blood scavenging systems.
- SURGIFLO® Hemostatic Matrix should not be used in conjunction with methylmethacrylate adhesives. Microfibrillar collagen has been reported to reduce the strength of methylmethacrylate adhesives used to attach prosthetic devices to bone surfaces.
- SURGIFLO® Hemostatic Matrix should not be used for the primary treatment of coagulation disorders.
- Although the safety and effectiveness of the combined use of SURGIFLO® Hemostatic Matrix with other agents such as topical thrombin, antibiotic solution, or antibiotic powder has not been evaluated in controlled clinical trials, if, in the physician's judgment, concurrent use of topical thrombin or other agents is medically advisable, the product literature for that agent should be consulted for complete prescribing information.
- The safety and effectiveness for use in urological procedures has not been established through a randomized clinical study.
- In urological procedures, SURGIFLO® Hemostatic Matrix should not be left in the renal pelvis or ureters to eliminate the potential foci for calculus formation.

ADVERSE EVENTS

A total of 142 patients received SURGIFOAM® Sponge during a clinical trial comparing SURGIFOAM® Sponge to another absorbable gelatin sponge. The most common adverse events recorded during and after the application of the device were fever, tachycardia, and asthenia (a general feeling of weakness). Table 1 lists those adverse events that occurred in greater than 5% of the SURGIFOAM® Sponge patients. The control patients are included for comparison. Other adverse events observed in less than 5% of the SURGIFOAM® Sponge patients were chest pain, somnolence, anorexia, anxiety, dizziness, ecchymosis, oliguria, abdominal pain, thrombocytopenia, agitation, bradycardia, confusion, depression, dyspnea, back pain, urine retention, abdominal enlargement, dry mouth, GI discomfort, dehydration, lung edema, flatulence, abnormal healing, hematuria, hiccups, hyperventilation, ileus, infection of the urinary tract, leukocytosis, vertigo, amblyopia, arrhythmia, cardiomegaly, cellulitis, chills, dysphagia, hyperglycemia, urinary incontinence, melena, mucous membrane discharge, eye pain, and pneumonia.

In general, the following adverse events have been reported with the use of absorbable porcine gelatin-based hemostatic agents:

- Gelatin-based hemostatic agents may serve as a nidus for infection and abscess formation and have been reported to potentiate bacterial growth.
- Giant cell granulomas have been observed at implant sites when used in the brain.
- Compression of the brain and spinal cord resulting from the accumulation of sterile fluid have been observed.
- Multiple neurologic events were reported when absorbable gelatin-based hemostatic agents were used in laminectomy operations, including cauda equina syndrome, spinal stenosis, meningitis, arachnoiditis, headaches, paresthesias, pain, bladder and bowel dysfunction, and impotence.
- The use of absorbable gelatin-based hemostatic agents during the repair of dural defects associated with laminectomy and craniotomy operations, has been associated with fever, infection, leg paresthesias, neck and back pain, bladder and bowel incontinence, cauda equina syndrome, neurogenic bladder, impotence, and paresis.
- The use of absorbable gelatin-based hemostatic agents has been associated with paralysis, due to device migration into foramina in the bone around the spinal cord, and blindness, due to device migration in the orbit of the eye, during lobectomy, laminectomy, and repair of a frontal skull fracture and lacerated lobe.
- Foreign body reactions, "encapsulation" of fluid, and hematoma have been observed at implant sites.
- Excessive fibrosis and prolonged fixation of a tendon have been reported when absorbable gelatin-based sponges were used in severed tendon repair.
- Toxic shock syndrome was reported in association with the use of absorbable gelatin-based hemostats in nasal surgery.
- Fever, failure of absorption, and hearing loss have been observed when absorbable hemostatic agents were used during tympanoplasty.

Table 1: Incidence of treatment emergent adverse events by treatment group

TERM	SURGIFOAM® (n=142)	Control Sponge (n=139)	Total (n=281)
Fever	28 (19.7%)	34 (24.5%)	62 (22.1%)
Tachycardia	27 (19.0%)	28 (20.1%)	55 (19.6%)
Asthenia	25 (17.6%)	17 (12.2%)	42 (14.9%)
Peripheral Edema	20 (14.1%)	20 (14.4%)	40 (14.2%)
Hypertonia	20 (14.1%)	12 (8.6%)	32 (11.4%)
Anemia	19 (13.4%)	11 (7.9%)	30 (10.7%)
Nausea	18 (12.7%)	22 (15.8%)	40 (14.2%)
Constipation	17 (12.0%)	17 (12.2%)	34 (12.1%)
Hypertension	16 (11.3%)	12 (8.6%)	28 (10.0%)
Insomnia	16 (11.3%)	13 (9.4%)	29 (10.3%)
Pain	13 (9.2%)	17 (12.2%)	30 (10.7%)
Pharyngitis	13 (9.2%)	11 (7.9%)	24 (8.5%)
Vomiting	13 (9.2%)	8 (5.8%)	21 (7.5%)
Edema	12 (8.5%)	10 (7.2%)	22 (7.8%)
Pruritus	12 (8.5%)	10 (7.2%)	22 (7.8%)
Rash	12 (8.5%)	19 (13.7%)	31 (11.0%)
Headache	11 (7.7%)	9 (6.5%)	20 (7.1%)
Hypokalemia	11 (7.7%)	10 (7.2%)	21 (7.5%)
Hypomagnesemia	11 (7.7%)	11 (7.9%)	22 (7.8%)
Infection	11 (7.7%)	6 (4.3%)	17 (6.0%)
Paresthesia	11 (7.7%)	7 (5.0%)	18 (6.4%)
Dyspepsia	10 (7.0%)	4 (2.9%)	14 (5.0%)
Hypotension	10 (7.0%)	10 (7.2%)	20 (7.1%)
Diarrhea	9 (6.3%)	8 (5.8%)	17 (6.0%)
Hypocalcemia	9 (6.3%)	9 (6.5%)	18 (6.4%)
Cough Increased	8 (5.6%)	9 (6.5%)	17 (6.0%)
Edema General	8 (5.6%)	5 (3.6%)	13 (4.6%)
Hematoma	8 (5.6%)	9 (6.5%)	17 (6.0%)

CLINICAL STUDIES

Study Design: An open-label, randomized, controlled, multi-center, unmasked study was conducted to evaluate the safety and effectiveness of 2 hemostatic agents. The study compared the SURGIFOAM® Sponge to an absorbable gelatin sponge currently legally marketed in the U.S.A. The primary objective of the study was to examine the equivalence of the SURGIFOAM® Sponge to the control device as measured by hemostasis within 10 minutes of application. Cardiovascular, general surgical, and orthopedic patients were eligible for the study. The sponges were used either soaked with saline or dry. Patients were followed for 2 months after surgery to assess the safety of the sponge.

Study Results: Two hundred eighty-one patients were enrolled into the study and received study treatment. The hemostasis data were collected immediately during surgery and the patients were examined at two to four weeks, and again at six to eight weeks, in order to obtain safety data. The study effectiveness results are summarized in Table 2 below.

Table 2: Summary of effectiveness results comparing SURGIFOAM® Sponge to another absorbable gelatin sponge (percent achieving hemostasis)

Minutes	Device	General Surgical	Cardiovascular	Orthopedic	Total
		% (Ratio)	% (Ratio)	% (Ratio)	% (Ratio)
3	SURGIFOAM® Sponge	65.6 (42/64)	57.4 (39/68)	100.0 (10/10)	64.0 (91/142)
	Control Sponge	66.2 (43/65)	62.9 (39/62)	91.7 (11/12)	66.9 (93/139)
6	SURGIFOAM® Sponge	98.4 (63/64)	80.9 (55/68)	100.0 (10/10)	90.1 (128/142)
	Control Sponge	95.4 (62/65)	91.9 (57/62)	100.0 (12/12)	94.2 (131/139)
10	SURGIFOAM® Sponge	100.0 (64/64)	89.7 (61/68)	100.0 (10/10)	95.1 (125/142)
	Control Sponge	95.4 (62/65)	96.8 (60/62)	100.0 (12/12)	96.4 (134/139)

A statistical analysis showed that SURGIFOAM® Sponge and the control sponge were equivalent in the ability to achieve hemostasis within 10 minutes. The study also collected hemostasis data at 3 and 6 minutes. These results are also summarized in Table 2.

Immune Response: Patient sera were tested for the presence of anti-porcine collagen immunoglobulins. Sera were collected prior to surgery, at 2 to 4 weeks post-surgery, and at 6 to 8 weeks following surgery. Two hundred six patients were tested at baseline, 2 to 4 weeks, and at 6 to 8 weeks. Only one of the 206 patients had antibodies at baseline, and 6 of the 206 patients had antibodies at the 6- to 8-week time point. Three of the patients were in the SURGIFOAM® Sponge group and 3 patients were in the control group. The analysis of the immunology data indicated that there was no difference in theability of the SURGIFOAM® Sponge to induce anti-porcine collagen immunoglobulins when compared to the control sponge.

Use of SURGIFLO® Hemostatic Matrix as a hemostatic agent for nasal/sinus bleeding: SURGIFLO® Hemostatic Matrix has been successfully used with bovine thrombin intraoperatively as a hemostatic agent for the control of bleeding post-nasal sinus surgery in 30 patients (54 application sites).

Study Design: This was a multi-center, prospective, single-arm study. Thirty (30) subjects from three (3) US centers undergoing elective endoscopic sinus surgery (ESS), who met the eligibility criteria, were treated with SURGIFLO® Hemostatic Matrix and bovine thrombin post ESS. Subjects were followed at 7 days (± 3 days) and at 30 days (± 7 days) post-operatively. This was a single arm study with no control arm. Patients were followed for 30 days following surgery. Post-operative healing and all complications were recorded during this period.

Study Results: Intraoperative bleeding ceased in 29 out of 30 patients. One subject failed to achieve hemostasis within 10 minutes of product application. The median time to hemostasis for 54 operated sites, including manual compression, was 61 seconds. One patient had mild oozing after surgery. This patient was treated with local care with immediate resolution. No intraoperative complications, serious adverse events, or serious complications such as synechiae or infections were reported in this study.

HOW SUPPLIED

SURGIFLO® Hemostatic Matrix Kit consists of:

1. A sterile tray with *all* sterile components to prepare the Flowable Gelatin Matrix
2. A sterile tray with *all* surface sterilized Thrombin kit components to prepare the Thrombin Solution

SURGIFLO® Hemostatic Matrix Kit is provided in the configuration shown in the table below.

SURGIFLO® Hemostatic Matrix Kit with Thrombin	
Flowable Gelatin Matrix Components	**Thrombin Components**
• A sterile pre-filled syringe with blue plunger containing the sterile Gelatin Matrix. The syringe is labeled **SURGIFLO™ Hemostatic Matrix** • A sterile empty syringe • A sterile liquid transfer cup • A sterile blue flexible applicator tip that is bendable in all directions • A sterile white applicator tip that can be trimmed to desired length	• A Thrombin vial, EVITHROM® Thrombin, Topical (Human), containing 2000 International Units (IU) of sterile lyophilized human thrombin powder for reconstitution • A needle-free syringe containing 2 mL of Sterile Water for Injection (Sterile WFI) • A sterile vial adapter

The package also contains the SURGIFLO® Hemostatic Matrix Kit Instructions for Use and tracking labels.

STORAGE AND HANDLING

- SURGIFLO® Hemostatic Matrix Kit should be stored dry at controlled room temperature 36°-77°F (2°-25°C).
- The Flowable Gelatin Matrix may be used up to eight (8) hours after mixing with the Thrombin Solution.
- For prescribing information on the Thrombin component, please refer to the EVITHROM® Thrombin, Topical (Human) Prescribing Information on page 9.
- SURGIFLO® Hemostatic Matrix Kit is for single use only.

DIRECTIONS FOR USE

Before use

Inspect the packages for signs of damage. If the package is damaged or wet, sterility cannot be assured and the contents should not be used.

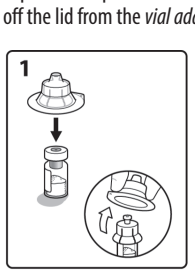
Open packages of SURGIFLO® Hemostatic Matrix Kit should be discarded, since they are not intended for reuse and/or resterilization.

Opening the tray with Flowable Gelatin Matrix and the tray with Thrombin kit components

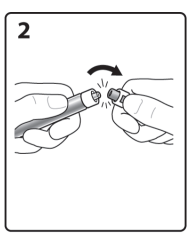
Open the outer packages and deliver the sterile inner trays to the sterile field using aseptic technique. Once placed in the sterile field, the sterile inner tray may be opened.

Preparing the Thrombin Solution inside the sterile field:

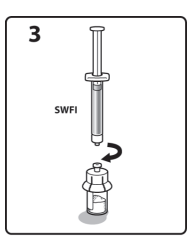
Flip off the cap from the *Thrombin vial,* leaving the aluminum ring and the rubber stopper in place. Peel off the lid from the *vial adapter* package.



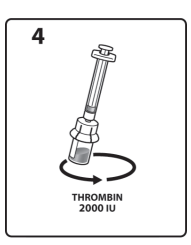
1. Place the *Thrombin vial* on a flat surface, seat the *vial adapter* on the center of the rubber stopper and push down until the spike penetrates the rubber stopper and the *vial adapter* snaps into place. Remove the blister package.



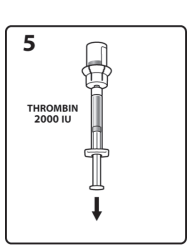
2. **Snap** off the tamper cap on the *needle-free syringe* containing the Sterile Water for Injection (Sterile WFI).



3. Connect and screw on the *needle-free syringe* to the *vial adapter*. Transfer the entire Sterile WFI into the *Thrombin vial*.



4. Gently swirl the *Thrombin vial* until the Thrombin Solution is clear.



5. Draw up the Thrombin Solution into the *needle-free syringe*. Label the *needle-free syringe*: "Thrombin 2000 IU".

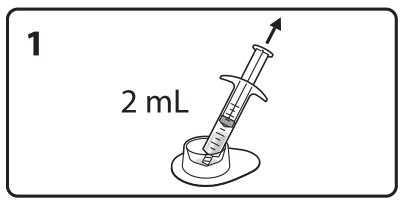
6. Disconnect the *needle-free syringe* from the *vial adapter* and transfer the Thrombin Solution into the sterile liquid transfer cup as shown in the next section (Figure 1).

After reconstitution, discard the components used for the thrombin reconstitution.

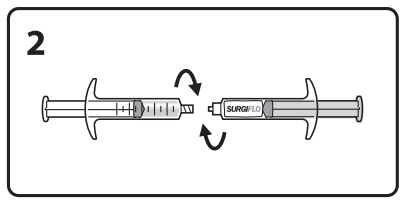
Alternatively, the Thrombin may be reconstituted **outside** the sterile field. Be careful not to touch the rubber stopper of the vial. After reconstitution the Thrombin Solution should be transferred into the sterile liquid transfer cup using aseptic technique.

Place the sterile liquid transfer cup near the edge of the sterile field to receive the Thrombin Solution transfer without contaminating the sterile field.

Preparing the Flowable Gelatin Matrix with sterile Thrombin Solution inside the sterile field:

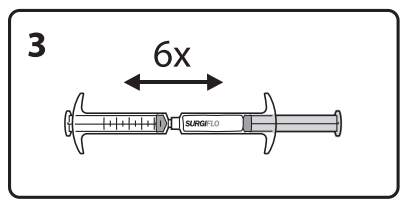


1) Draw up 2 mL sterile Thrombin Solution from the sterile liquid transfer cup into the empty sterile syringe.



2) Connect syringes

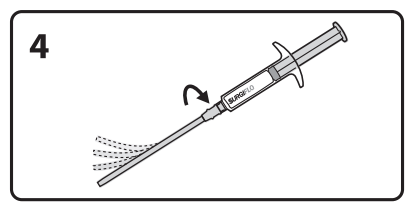
Remove the blue cap from the end of the sterile pre-filled syringe with blue plunger containing the Gelatin Matrix. Attach this syringe to the sterile syringe containing the sterile Thrombin Solution.



3) Mix contents of the two syringes

Begin mixing by transferring the sterile Thrombin Solution into the sterile pre-filled syringe containing the Gelatin Matrix. Push the combined material back and forth 6 times until the consistency is even.

Once mixed, the hemostatic matrix should reside completely in the syringe with the blue plunger that is labeled **SURGIFLO™ Hemostatic Matrix**. Remove the empty syringe and discard.



4) Attach applicator tip

The product is now ready for clinical use.

Do not inject SURGIFLO® Hemostatic Matrix into blood vessels. See the Contraindications, Warnings, and Precautions.

For open procedures:

a. Identify the source of bleeding.
b. Deliver SURGIFLO® Hemostatic Matrix to the source of bleeding. SURGIFLO® Hemostatic Matrix can be used with or without the applicator tip attached to the syringe labeled **SURGIFLO™ Hemostatic Matrix**. Apply sufficient SURGIFLO® Hemostatic Matrix to cover the entire bleeding surface.
c. For tissue defects (cavities, divots, or craters) apply SURGIFLO® Hemostatic Matrix at the deepest part of the lesion, and continue applying material as the syringe (or applicator tip) is withdrawn from the lesion.
d. Apply a sterile saline moistened gauze over the SURGIFLO® Hemostatic Matrix to ensure the material remains in contact with the bleeding tissue.
e. After 1-2 minutes, lift the gauze and inspect the wound site. Once bleeding has ceased, irrigate excess SURGIFLO® Hemostatic Matrix away gently so as not to disturb the new clot.
f. In cases of persistent bleeding indicated by saturation and bleeding through the material, repeat application of SURGIFLO® Hemostatic Matrix.

For endoscopic and/or laparoscopic surgical procedures:

a. Prepare the selected endoscopic applicator according to the product's labeling.
b. Attach the selected endoscopic applicator tip to the **SURGIFLO™ Hemostatic Matrix** syringe. Make sure that the luer connection is secure.
c. Express SURGIFLO® Hemostatic Matrix to the end of the cannula. Introduce the cannula into the trocar port. Insert the cannula using caution not to express SURGIFLO® Hemostatic Matrix.
d. Carefully position the distal end of the endoscopic applicator to the site where SURGIFLO® Hemostatic Matrix is to be delivered. Be careful to avoid damaging tissue with the cannula.
e. While holding the endoscopic applicator in place, express SURGIFLO® Hemostatic Matrix to the bleeding site.
f. If applicable, detach **SURGIFLO™ Hemostatic Matrix** syringe and introduce the stylet to dispense remaining product in the length of the cannula.
g. Observe bleeding and repeat application of SURGIFLO® Hemostatic Matrix if necessary.
h. Carefully remove the endoscopic applicator from the trocar port when sufficient SURGIFLO® Hemostatic Matrix has been delivered to the bleeding site.

For endoscopic sinus surgery and epistaxis:

a. Deliver SURGIFLO® Hemostatic Matrix to the source of bleeding using the selected applicator tip attached to the syringe that is labeled **SURGIFLO™ Hemostatic Matrix**.
b. Apply sufficient SURGIFLO® Hemostatic Matrix to cover the entire bleeding surface. Using forceps or an appropriate instrument, carefully layer a sterile saline moistened gauze over the SURGIFLO® Hemostatic Matrix for 1-2 minutes to ensure the material remains in contact with the bleeding tissue.
c. In cases of persistent bleeding, indicated by saturation and bleeding through the material, insert the applicator tip through the center of the mass of previously placed SURGIFLO® Hemostatic Matrix to deliver fresh material as close as possible to the tissue surface. After reapplication of SURGIFLO® Hemostatic Matrix, use a sterile saline moistened gauze to approximate the material to the tissue for another minute, and then inspect the site. Repeat reapplication if necessary.
d. Once hemostasis has been achieved, remove the gauze. If possible, excess SURGIFLO® Hemostatic Matrix should be removed with gentle irrigation or careful suction. Avoid disrupting the SURGIFLO® Hemostatic Matrix clot complex. The remaining SURGIFLO® Hemostatic Matrix does not have to be removed, as it will be bioresorbed.
e. Use of nasal packing is not necessary when satisfactory hemostasis is achieved.
f. If necessary, gentle irrigation and/or careful suction can be used in the post-operative period to remove the remaining SURGIFLO® Hemostatic Matrix.

Caution: The use of SURGIFLO® Hemostatic Matrix for mechanical support has not been studied.

Caution: Federal (U.S.A.) law restricts this device to sale by or on the order of a physician (or properly licensed practitioner).

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