### Study Description

GLP animal study to demonstrate the performance of the XSTAT Dressing compared to the XSTAT 30 predicate dressing, using the United States Army Institute of Surgical Research ("USARI") standard femoral animal injury.

<table>
<thead>
<tr>
<th>Inclusion / Exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Inclusion</strong></td>
</tr>
<tr>
<td>- Animal breed: Landrace cross swine</td>
</tr>
<tr>
<td>- Weight at procedure: 55-65 kg</td>
</tr>
<tr>
<td>- Age at procedure: 3-5 months (appropriate to weight)</td>
</tr>
<tr>
<td><strong>Exclusion</strong></td>
</tr>
<tr>
<td>- Exclusion criteria included inappropriate vessel anatomy, persistently low MAP (&lt; 55 mmHg) prior to femoral artery injury, and significant blood loss (&gt;300 mL)</td>
</tr>
</tbody>
</table>

### Exclusion Criteria

- Inappropriate vessel anatomy
- Persistently low MAP (< 55 mmHg) prior to femoral artery injury
- Significant blood loss (>300 mL)

### Study Procedure

**All Wounds Prior to Randomization**

- An incision was created (3.5 cm long) through the skin and subcutaneous tissues in the groin area directly over the left femoral artery and an approximately 3 cm section of femoral artery was exposed.
- The femoral artery was covered with a small piece of gauze and bathed with 25% lidocaine HCl solution to relax the vasospasm and dilate the artery to a 5 mm outer diameter.
- Non-traumatic vessel loops were placed proximally and distally on the femoral artery.
- Using a 6.0 mm vascular punch, an arteriotomy was created.
- The vessel loops were released, the injury start time was recorded and the vessel was allowed to bleed freely for 45 seconds before the Test (XSTAT) or Control Article (XSTAT 30) was applied.
- The vessel loops were allowed to remain in the wound to facilitate hemorrhage control during test material removal.

### Wounds Randomized to XSTAT Dressing (Test Article)

- XSTAT dressing was applied as per product instructions for use (IFU) starting immediately following the 45-second free bleed.
- XSTAT was applied as quickly as possible and as many as necessary until the bleeding has stopped, until the 5-minute limit, whichever was sooner.
- A cloth bandage was wrapped around the limb and firmly secured over the packed wound.
- Manual pressure was permitted if bleeding persisted following application of the dressing as per the IFU.

### Wounds Randomized to XSTAT 30 Predicate (Control Article)

- XSTAT 30 dressing was applied as per product instructions for use (IFU) starting immediately following the 45-second free bleed.
- XSTAT 30 dressing was applied as quickly as possible and as many as necessary until the bleeding stopped, until the 5-minute limit, whichever was sooner.
- A cloth bandage was wrapped around the limb and firmly secured over the packed wound.
- Manual pressure was permitted if bleeding persisted following application of the dressing as per the IFU.

### Post-Randomization Care

- Resuscitation began 5-25 minutes post-injury (i.e., free bleed start time) by infusing colloidal fluid (Hetastarch) at a target volume of 500 mL into the jugular vein.
- Resuscitation was continued, if necessary, with pre-warmed lactated Ringer's solution (LRS). The total volume of LRS infused was based on pre-and post-use weights of the LRS infusion bags, assuming 1 g – 1 mL. The actual rate was then based on the volume of LRS divided by the duration of infusion for each bag. If the MAP dropped to ~ 60 mmHg or less, LRS was infused into the jugular vein and discontinued when the MAP of at least 65 mmHg was reached.
- Following the 6-hour observation period, the Test or Control Article was removed from the wound site and the animal euthanized.
- XSTAT minisponges were removed from the wound site manually as well as with surgical forceps for both animals treated with test articles and control articles.
- Following sponge removal and euthanasia, the wound site was imaged using a portable fluoroscopy unit.

### Results

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>XSTAT 30 (Control Article)</th>
<th>XSTAT (Test Article)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1: Bleeding Time, mean: Duration of bleeding (visible blood shed from the wound site) occurring at any time immediately following test material application until was at exsanguination or end of the 6-hour observation period.</td>
<td>1.6 (3.7) minutes</td>
<td>1.8 (5.7) minutes</td>
</tr>
<tr>
<td>2: Post-Treatment Blood Loss, mean (stdev): Amount of blood shed from the wound cavity during the time period following the dressing application until exsanguination or end of the 6-hour observation period.</td>
<td>1.0 (3.0) mLkg</td>
<td>0.1 (0.2) mLkg</td>
</tr>
<tr>
<td>3: Final Mean Arterial Pressure (MAP), mean (stdev): Mean arterial pressure recorded just prior to exsanguination or end of the 6-hour observation period.</td>
<td>65 (3) mmHg</td>
<td>66 (4) mmHg</td>
</tr>
<tr>
<td>4: Survival Time, mean (stdev): Time period immediately following the 45 second free bleed during which vital signs are: MAP &gt; 200 mmHg and PCO2 &gt; 35 mmHg to exsanguination or end of the 6-hour observation period.</td>
<td>5:46 (0:01) hours</td>
<td>5:45 (0:00) hours</td>
</tr>
<tr>
<td>5: Percentage Survival: Percentage of animals surviving to the end of the study observation period (6 hours) for a given treatment, where survival was defined as the MAP &gt; 200 mmHg and PCO2 &gt; 35 mmHg.</td>
<td>100%</td>
<td>100%</td>
</tr>
</tbody>
</table>

Observations from Animal Study:

Pre-clinical studies of device performance of deployment and surgical removal of XSTAT sponges demonstrated that not all minisponges expanded during successful tamponade of the bleeding site and that some sponges may fall from the wound outside the body or may be retained in the applicator. Comprehensive accounting for minisponges deployed and retrieved from wounds may be inexact. In a pre-clinical animal study, a minisponge retained in the wound was not initially recognized by the veterinary surgical team but was identified on subsequent review.

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# GLP EVALUATION OF XSTAT DRESSING IN A SWINE SUBCLAVIAN MODEL

## STUDY DESCRIPTION
GLP animal study to demonstrate the performance of the XSTAT Dressing compared to the XSTAT 30 Predicate dressing, using the United States Army Institute of Surgical Research ("USAISR") standard subclavian animal injury.

## NUMBER OF SUBJECTS
Ten (10) animals treated with XSTAT dressing (Test Article) and Ten (10) animals treated with XSTAT 30 predicate device (Control Article)

## INCLUSION / EXCLUSION
- **Inclusion**
  - Animal Breed: Landrace cross swine
  - Weight at procedure: 41-62 kg
  - Age at procedure: 3-5 months (appropriate to weight)
- **Exclusion**
  - Inappropriate vessel anatomy
  - Persistently low MAP (< 55 mmHg) prior to femoral artery injury
  - Significant blood loss (> 300 mL) because of surgical complication or error before femoral artery injury

## STUDY PROCEDURE
### ALL WOUNDS PRIOR TO RANDOMIZATION
- An incision was created (5.0 cm long) through the skin and subcutaneous tissues over the left superficial pectoralis directly over the left subclavian artery and an approximately 4.0 cm section of subclavian artery was exposed.
- The femoral artery was covered with a small piece of gauze and bathed with 2% lidocaine HCl solution to relax the vasospasm and dilate the artery to ≥ 5 mm outer diameter.
- The subclavian artery and vein were transected and allowed to bleed freely for 30 seconds.

### WOUNDS RANDOMIZED TO XSTAT Dressing (Test Article)
- XSTAT dressing was applied as per product instructions for use (IFU) starting immediately following the 30-second free bleed.
- XSTAT was applied as quickly as possible and as many as necessary until the bleeding has stopped, or until the 5-minute limit, whichever was sooner.
- At the discretion of the surgeon, a cloth bandage was wrapped around the limb and firmly secured over the packed wound.
- Manual pressure was permitted if bleeding persisted following application of the dressing as per the IFU.

### WOUNDS RANDOMIZED TO XSTAT 30 Predicate (Control Article)
- XSTAT 30 dressing was applied as per product instructions for use (IFU) starting immediately following the 30-second free bleed.
- XSTAT 30 dressing was applied as quickly as possible and as many as necessary until the bleeding stopped, until the 5 minute limit, whichever was sooner.
- At the discretion of the surgeon, a cloth bandage was wrapped around the limb and firmly secured over the packed wound.
- Manual pressure was permitted if bleeding persisted following application of the dressing as per the IFU.

## POST-RANDOMIZATION CARE
- Resuscitation began 5-25 minutes post-injury (i.e., free bleed start time) by infusing colloidal fluid (Hetastarch) at a target volume of 500mL into the jugular vein.
- Resuscitation was continued, if necessary, with pre-warmed lactated Ringer’s solution (LRS). The total volume of LRS infused was based on pre- and post-use weights of the LRS infusion bags, assuming 1 g – 1 mL. The actual rate was then based on the volume of LRS divided by the duration of infusion for each bag. If the MAP dropped to ~ 60 mmHg or less, LRS was infused into the jugular vein and discontinued when the MAP of at least 65 mmHg was reached.
- Following the 1-hour observation period, the Test or Control Article was removed from the wound site and the animal euthanized.
- XSTAT minisponges were removed from the wound site manually as well as with surgical forceps for both animals treated with test articles and control articles.
- Following sponge removal and euthanasia, the wound site was imaged using a portable fluoroscopy unit.

## RESULTS
### ENDPOINTS
- **1: Bleeding Time**: Mean: Duration of bleeding (visible blood shed from the wound site) occurring at any time immediately following test material application until was at exsanguination or end of the 6-hour observation period.
  - XSTAT (Test Article): 0.7 (±0.3) minutes
  - XSTAT 30 (Control Article): 0.9 (±0.4) minutes
- **2: Post-Treatment Blood Loss, mean (stddev)**: Amount of blood shed from the wound cavity during the time period following the dressing application until exsanguination or end of the 6-hour observation period.
  - XSTAT (Test Article): 0.01 (±0.03) mL/kg
  - XSTAT 30 (Control Article): 0.2 (±0.6) mL/kg
- **3: Final Mean Arterial Pressure (MAP)**, mean (stddev): Mean arterial pressure recorded just prior to exsanguination or end of the 6-hour observation period.
  - XSTAT (Test Article): 65 (5) mmHg
  - XSTAT 30 (Control Article): 68 (4) mmHg
- **4: Survival Time, mean (stddev)**: Time period immediately following the 45-second free bleed during which vital signs are; MAP >20 mmHg and PCO2 >15 mmHg to exsanguination or end of the 6-hour observation period.
  - XSTAT (Test Article): 100 (±0.00) hours
  - XSTAT 30 (Control Article): 101 (±0.03) hours
- **5: Percentage Survival**: Percentage of animals surviving to the end of the study observation period (6 hours) for a given treatment, where survival was defined as the MAP >20 mmHg and PCO2 >15 mmHg.
  - XSTAT (Test Article): 100%
  - XSTAT 30 (Control Article): 100%

The presence or absence of distal limb ischemia was not assessed in this study. There was no postmortem evidence of blood tracking beneath the skin.

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XSTAT 30 GENERATION 2 TRAINING INFORMATION

XSTAT 30 is a hemostatic dressing for the control of severe, life-threatening bleeding from junctional wounds in the groin or axilla not amenable to tourniquet application in adults and adolescents.

XSTAT 30 is a hemostatic dressing for the control of severe, life-threatening bleeding from narrow entrance extremity wounds in the arms or legs in adults and adolescents.

XSTAT 30 is a temporary dressing for use up to four (4) hours until surgical care is acquired. XSTAT should only be used for patients at high risk for immediate life-threatening bleeding from, hemodynamically significant (Advanced Trauma Life Support class 3 or 4 hemorrhagic shock), non-compressible junctional wounds or narrow entrance extremity wounds, and when definitive care at an emergency care facility cannot be achieved within minutes.

XSTAT 30 is NOT indicated for use in: the thorax, the pleural cavity, the mediastinum, the abdomen, the retroperitoneal space, the sacral space; tissues above the inguinal ligament, or tissues above the clavicle.

XSTAT 30 contains rapidly expanding cellulose sponges and individually marked with an X-shaped radiopaque marker.

XSTAT 30 works by applying the small sponges into a wound cavity using a lightweight applicator. In the wound, the XSTAT 30 sponges expand and create a barrier to blood flow, present a large surface area for clotting, and provide gentle pressure.

The XSTAT 30 applicator is comprised of two primary parts:
- The main applicator which holds approximately 108 XSTAT minisponges
- A plunger

XSTAT 30 works by expansion of cellulose sponges against the walls of the cavity to apply pressure inside the wound.

Prior to using XSTAT, fully examine the injured patient and assess for signs of bleeding. Arterial bleeding is caused by the laceration of an artery and is the most difficult type of blood loss to control. Arterial hemorrhage is characterized by spurting blood that is bright red in color. Even a small, deep, arterial puncture wound can produce significant blood loss.

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If the wound is not amenable to tourniquet use and is located on the groin or axilla, it is a junctional wound. In the testing of the XSTAT dressing, hemorrhage from the groin was created in a swine using a 6.0mm vascular punch on the femoral artery. The injury bled for 45 seconds prior to device application. The XSTAT dressing would be appropriate for use under comparable conditions.

If the hemorrhage cannot be identified or the anatomical location is not a junctional or extremity wound, XSTAT is not the preferred dressing to achieve hemorrhage control and alternative treatments should be used such as other hemostatic dressings or tourniquets.

XSTAT is NOT indicated for use in: the thorax, the abdomen, the retroperitoneal space, the sacral space; tissues above the inguinal ligament, or tissues above the clavicle.

XSTAT has not been tested for use in extremity wounds that are amenable to tourniquet application. XSTAT use in conjunction with tourniquet application has not been assessed for use in extremity wounds that are amenable to tourniquet application.

- Read Indications for use and warnings and cautions on front label and back label.
- Open outer pouch and remove inner package. Open inner package and remove applicator and plunger.
- Insert applicator into wound track as close to bleeding source as possible.
- Insert plunger into applicator and push plunger firmly to deploy sponges into wound. Material should flow freely into the wound. Deploy XSTAT within 30 seconds of insertion into wound.
- DO NOT attempt to forcefully eject the material from the applicator. If resistance is met pull back slightly on the applicator body to create additional packing space, then continue to depress handle.
- Use additional applicators as necessary to completely pack the wound with dressing. Injuries with significant cavitation, such as those from a high-velocity gunshot wound, may require more than three (3) applicators to appropriately pack the wound.

**NOTE:** XSTAT hemostatic devices are available in two sizes: XSTAT 12 and XSTAT 30. The XSTAT 12 applicator has a 12 mm outer diameter and the XSTAT 30 GENERATION 2 applicator has a 25 mm outer diameter. If the entrance of the wound is too narrow to access with an XSTAT 30, then XSTAT 12 is the preferred device to achieve hemorrhage control.

- Cover the wound with an occlusive or pressure dressing. If available, use an elastic bandage.
- If bleeding persists, apply manual pressure until bleeding is controlled.
- Remove the included casualty card from the outer pouch. Assess patient for peripheral circulation and document presence of distal pulse on included casualty card.

**WARNING:** Vascular compression greater than four hours is not recommended due to concerns related to limb ischemia.

- DO NOT attempt to remove dressing from wound. Sponges must be removed intraoperatively by surgeon with the capability and equipment for achieving proximal and distal vascular control.
- After completion of treatment, fill out the casualty card completely. A line has been added above the notes depicting the am
- Document clinical assessments, treatments rendered, and changes in the casualty’s status on the included casualty card. The casualty card also contains instructions for removing XSTAT sponges from the wound. Forward this information with the casualty to the next level of care.
- In addition to directly communicating patient information to the next provider in the chain of care, attach the casualty card to the patient in a visible location. A safety pin and rubber
- Preferably, attach the casualty card near the wound. For example, using the safety pin, the card may be attached to the occlusive or pressure dressing used to cover the wound, or if possible to a nearby portion of clothing.
- If attachment near the wound is not possible, alternative locations may include the wrist, ankle, clothing of the upper/lower torso, patient record holders on the litter or hypothermia prevention kit. It is important that – regardless of the means utilized to attach the card – the information on the card reaches the surgeon with the patient.

**XSTAT DRESSING REMOVAL:**

- Survey the wound site and assess potential vascular bleeding sites and develop plan to achieve surgical control of injured vessel(s).
- Remove sponges from the wound site manually and/or with surgical forceps to the site(s) of bleeding.
- Thoroughly explore wound and removal all sponges.
- Prior to wound closure, obtain plane X-ray optimally in more than one projection. The presence of retained sponge may be easily missed on radiographic images. Thoroughly examine X-ray for radiopaque x-pattern of sponges.
- If sponges are identified via X-ray, carefully re-examine wound cavity and remove sponges. Perform and review second X-ray to confirm complete sponge removal.

**WARNING:**

1. Relying upon sponge count alone post removal is not an accurate means of determining complete minisponge removal from the wound.
2. Careful surgical exploration of the wound site is required to ensure complete sponge removal from the wound.
3. Confirmation of complete removal from the wound by XRay is required to search for possible retained minisponges.
4. Review of XRays to identify potential retained XSTAT minisponges should be performed by physicians trained to review surgical XRay.
5. While the minisponges are designed with a radiopaque marker, it may be confused with other radiopaque material in the wound, such as bone chips and wound clips.

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