XSTAT® 12 PACKAGE INSERT

### STUDY DESCRIPTION
GLP animal study to demonstrate the performance of the XSTAT dressing compared to a Standard-of-care wound dressing, using the United States Army Institute of Surgical Research ("USAISR") standard femoral animal injury.

### NUMBER OF SUBJECTS
Ten (10) animals were treated with the XSTAT dressing
Ten (10) animals were treated with the Standard-of-care wound dressing

### INCLUSION / EXCLUSION
**Inclusion**
- Animal breed: Landrace cross swine
- Weight at procedure: 55-65 kg
- Age at procedure: appropriate to weight
- Exclusion criteria included inappropriate vessel anatomy, persistently low MAP (< 55 mmHg) prior to femoral artery injury, and 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 (3.5 cm long) through the skin and subcutaneous tissues in the groin area directly over the right 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 2% 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, injury start time was recorded and the vessel was allowed to bleed freely for 45 seconds before the Test (XSTAT) or Control Article (Standard-of-care wound dressing) was applied.
- The vessel loops were allowed to remain in the wound to facilitate hemorrhage control during test material removal.
- Surgeon and dressing applicator were blinded to the identity of test material prior to application.
- Randomization was accomplished by picking a sealed envelope that contained the name of the test material. The contents of the envelope were revealed in the surgery suite during the 45 seconds free bleed period.

**WOUNDS RANDOMIZED TO XSTAT**
- XSTAT applied as per product label immediately following the 45-second free bleed.
- XSTAT applied as quickly as possible and as many as necessary until the bleeding has stopped, or until the 5-minute limit, whichever was sooner.
- If room within the wound allowed, plain gauze (i.e., 5-Rolled Gauze) was placed on top of the XSTAT-filled wound.
- Cloth bandage used to secure XSTAT/Plain Gauze dressing within the wound.
- Manual compression was permitted if bleeding persisted following application of the dressing.

**WOUNDS RANDOMIZED TO STANDARD-OF-CARE DRESSING**
- Immediately following the 45-second free bleed up to 5 minutes was allowed to apply Standard-of-care wound dressing(s) by packing dressing completely into wound track using enough Standard-of-care wound dressing to fill the wound and contact all bleeding surfaces.
- More than one dressing may be required.
- If room within the wound allowed, plain gauze (i.e., 5-Rolled Gauze) was packed on top of the Standard-of-care wound dressing.
- Cloth bandage used to secure Standard-of-care dressing within the wound.
- Manual pressure applied for 5 minutes.

**POST-RANDOMIZATION CARE**
- Resuscitation began 5 minutes post-injury (i.e., free bleed start time) by infusing approximately 500 mL of Hextend® fluid at a target rate of 3 mL/min through the jugular vein.
- Resuscitation was continued, if necessary, with pre-warmed lactated Ringer's solution (LRS) infused at a target rate of 100 mL/minute, to maintain the mean arterial pressure (MAP) to at least 65 mmHg.
- Following the 6-hour observation period, the Test or Control Article was removed from the wound site and the animal euthanized.
- XSTAT mini-sponges were removed from the wound site manually as well as with a surgical forceps. Standard-of-care wound dressing were pulled out of the wound manually.
- Following sponge removal and euthanasia, the wound site was imaged using a portable fluoroscopy unit. No mini-sponges were identified in the fluoroscopic images or at necropsy.

### RESULTS

<table>
<thead>
<tr>
<th>ENDPOINTS</th>
<th>XSTAT</th>
<th>STANDARD-OF-CARE DRESSING</th>
</tr>
</thead>
<tbody>
<tr>
<td>1: Bleeding Time, mean (sd): Duration of bleeding (visible blood shed from the wound site) (occuring at any time immediately following test material application until was at exsanguination or end of the 6-hour observation period)</td>
<td>0 minutes</td>
<td>6 minutes</td>
</tr>
<tr>
<td>2: Post-Treatment Blood Loss, mean (sd): Amount of blood shed from the wound cavity during the time period following the 45 second free bleed until exsanguination or end of the 6-hour observation period.</td>
<td>21.7 (9.5) mL</td>
<td>28.3 (8.3) mL</td>
</tr>
<tr>
<td>3: Final Mean Arterial Pressure (MAP), mean (sd): Mean arterial pressure recorded just prior to exsanguination or end of the 6-hour observation period.</td>
<td>62.0 (3.0) mmHg</td>
<td>64.0 (3.0) mmHg</td>
</tr>
<tr>
<td>4: Survival Time, mean (sd): Time period immediately following the 45 second free bleed during which vital signs are: MAP &gt;30mmHg and PCO2 &gt;55 mmHg to exsanguination or end of the 6-hour observation period.</td>
<td>6.0 (0.0) hours</td>
<td>6.0 (0.0) 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;20 mmHg and PCO2 &gt;35 mmHg.</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>6: Wound Packing Time, mean (sd):</td>
<td>1.1 (0.3) minutes</td>
<td>4.6 (0.5) minutes</td>
</tr>
<tr>
<td>7: Wound Compression Time</td>
<td>0 minutes</td>
<td>0 minutes</td>
</tr>
</tbody>
</table>

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.

### DRESSING REMOVAL
Mean XSTAT removal time of 10.5 ± 3.4 minutes. Mean Standard-of-care dressing removal time 1 ± 0.8 minutes. Neither test nor Standard-of-care material adhered to the wound or were found to be retained in the wound at necropsy.
STUDY PROCEDURE:

- Animal anesthetized and 4.5-cm incision was created to access the subclavian artery and vein.
- Subclavian artery and vein transected.
- After 30-second free bleeding, the wound cavity was filled with the XSTAT dressing with no external pressure.
- Resuscitative fluids were administered to the animal as needed to support a mean arterial blood pressure of 60 mmHg.
- No additional wound care was provided during the 1-hour observation period.
- Following the 1-hour observation period, the XSTAT dressing was removed from the wound site and the animal euthanized.

RESULTS:

- **1. Animals with hemostasis at 4 min after dressing application.**
  - Mean XSTAT removal time 10.5 minutes.
- **2. Animals with hemostasis at 60 min after dressing application.**
  - 11/12 (91.7%)
- **3. Animal Survival at 60 min where survival was defined as the MAP > 20 mmHg and PCO2 > 15 mmHg**
  - 7/8 (87.5%)
- **4. Bleeding Time, mean (StdDev) Duration of bleeding occurring at any time following the material application until study termination.**
  - 7.9 (1.1) seconds
- **5. Post-TBL, mean (StdDev) Amount of blood shed from the wound cavity during the time following the 45 second free bleed until study termination.**
  - 331.5 (818.9) mL

The failure to achieve hemostasis in one of the animals was due to an applicator tip breaking off and falling into the wound. The location of the tip in the wound created a small gap (1 cm) that prevented minisponges from accessing the point of bleeding. As a result, applicator tips are now secured with glue.

DRESSING REMOVAL:

Mean XSTAT removal time 10.5 ± 3.4 minutes. Mean standard of care dressing removal time 3 ± 0.8 minutes. Neither test nor standard of care material adhered to the wound or were found to be retained in the wound at necropsy.

NAME OF STUDY/CITED PUBLICATION

**EVALUATION OF XSTAT DRESSING IN A SWINE SUBCLAVIAN MODEL**

STUDY DESCRIPTION

Animal study to demonstrate the performance of the XSTAT dressing in a swine subclavian injury.

NUMBER OF SUBJECTS

8

INCLUSION / EXCLUSION

- Inclusion
  - Animal Breed: Landrace cross swine
  - Weight at procedure: 55-65 kg
  - Age at procedure: appropriate to weight
- Exclusion criteria included inappropriate vessel anatomy, persistently low MAP (<65 mmHg) prior to femoral artery injury

STUDY PROCEDURE

- Animal anesthetized and 4.5-cm incision was created to access the subclavian artery and vein.
- Subclavian artery and vein transected.
- After 30-second free bleeding, the wound cavity was filled with the XSTAT dressing with no external pressure.
- Resuscitative fluids were administered to the animal as needed to support a mean arterial blood pressure of 60 mmHg.
- No additional wound care was provided during the 1-hour observation period.
- Following the 1-hour observation period, the XSTAT dressing was removed from the wound site and the animal euthanized.

RESULTS

- **ENDPOINTS**
  - XSTAT
  - 1: Animals with hemostasis at 4 min after dressing application.
  - 2: Animals with hemostasis at 60 min after dressing application.
  - 3: Animal Survival at 60 min where survival was defined as the MAP > 20 mmHg and PCO2 > 15 mmHg
  - 4: Bleeding Time, mean (StdDev) Duration of bleeding occurring at any time following the material application until study termination.
  - 5: Post-TBL, mean (StdDev) Amount of blood shed from the wound cavity during the time following the 45 second free bleed until study termination.

The failure to achieve hemostasis in one of the animals was due to an applicator tip breaking off and falling into the wound. The location of the tip in the wound created a small gap (1 cm) that prevented minisponges from accessing the point of bleeding. As a result, applicator tips are now secured with glue.

DRESSING REMOVAL:

Mean XSTAT removal time 10.5 ± 3.4 minutes. Mean standard of care dressing removal time 3 ± 0.8 minutes. Neither test nor standard of care material adhered to the wound or were found to be retained in the wound at necropsy.

NAME OF STUDY/CITED PUBLICATION

**USER EVALUATION OF XSTAT DRESSING REMOVAL**

STUDY DESCRIPTION

A user evaluation (human factors) was completed to determine the ability of medics and civilian EMS and medical professionals to understand and execute instructions for using XSTAT 12 and applying XSTAT on a simulated casualty.

NUMBER OF SUBJECTS

11

INCLUSION / EXCLUSION

Military or civilian EMS/Medical Professionals with no prior knowledge or experience with XSTAT dressing prior to the study.

STUDY PROCEDURE:

- A medical mannequin torso served as a wound model.
- The wound track – located in the upper thigh region approximately 5 cm distal to the iliac artery – had a diameter of 11 mm.
- Participants were evaluated on the ability to open the package, apply the applicator into the wound and deploy three (3) XSTAT 12 devices. In addition, participants were evaluated on the time needed to ready the device for use and deploy the device. Participants provided their evaluation on the use of the device, the packaging and Instructions for Use of the device, and the Training Video for the device.

RESULTS

- **PARTICIPANT**
  - **TIME**
  - **USER COMMENTS**
  - **ACTIONS TAKEN**
    - 1: 36: Add detail on resistance when using device; improve outer packaging.
    - 2: 41: Add detail on resistance when using device; improve outer packaging.
    - 3: 39: Show areas where device is not indicated.
    - 4: 34: Final training video comprises mostly animation; final package labeled with easy open tear notches.
    - 5: 30: Include real animation in video if possible; improve outer packaging.
    - 6: 33: Final training video comprises mostly animation; final package labeled with easy open tear notches.
    - 7: 38: Improve outer packaging.
    - 8: 53: Final package labeled with easy open tear notches.
    - 9: 46: IFU and packaging should hold up to rain and wind conditions.
    - 10: 39: Ensure proper pronunciation in video; improve outer packaging; make plunger brighter.
    - 11: 53: Final package labeled with easy open tear notches.

NAME OF STUDY/CITED PUBLICATION

**USER EVALUATION OF XSTAT DRESSING REMOVAL**

STUDY DESCRIPTION

A user evaluation was completed to assess the ability of surgeons to understand and execute instructions for removing XSTAT sponges from human cadaver wounds.

NUMBER OF SUBJECTS

4 surgeons; 1 cadaver; 2 wounds; 2 tests/wound

INCLUSION / EXCLUSION

Inclusion: civilian or military surgeon with no prior experience with XSTAT dressing prior to the study.

STUDY PROCEDURE

- Junctional wounds were made in each shoulder the cadaver.
- Saline solution was circulated through cadaver’s vasculature to simulate blood flow.
- Following application of 3 XSTAT devices into the shoulder wounds, each surgeon was handed draft instructions for use and instructed to treat the wound.

RESULTS

- **ENDPOINT**
  - **RESULT**
    - 1. Labeling clear on use of XSTAT device (Yes / No)
      - 45
    - 2. Completed all steps in IFU without assistance (Yes / No)
      - 45
    - 3. IFU conveys necessity of removal of sponges, median*
      - 47
    - 4. IFU conveys steps to assure removal, median*
      - 70
    - 5. Effective order of removal steps, median*
      - 43
    - 6. Ease of removal of sponges, median*
      - 71

*Scale: 1 = Poor, 2 = Fair, 3 = Acceptable, 4 = Good, 5 = Very Good

USER COMMENTS / ACTIONS TAKEN

- **COMMENT**
  - Add reminder that all sponges must be removed before wound closure.
  - Package label and casualty card contain explicit instructions for surgical sponge removal.
- **ACTIONS TAKEN**
  - Note approximate number of sponges per applicator on the package.
  - Package updated to include number of sponges per applicator.
XSTAT 12 TRAINING INFORMATION

XSTAT 12 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 12 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, and when definitive care at an emergency care facility cannot be achieved within minutes.

XSTAT 12 is NOT indicated for use in: the thorax, the pleural cavity, the mediastinum, the abdomen, the retroperitoneal space, the sacral space above the inguinal ligament, or tissues above the clavicle.

XSTAT 12 contains rapidly expanding cellulose sponges coated with Chitosan and individually marked with an X-shaped radiopaque marker.

XSTAT 12 works by applying the small sponges into a wound cavity using a lightweight applicator.

In the wound, the XSTAT 12 sponges expand and create a barrier to blood flow, present a large surface area for clotting, and provide gentle pressure.

The XSTAT 12 applicator is comprised of two primary parts:

- The main applicator which holds approximately 38 XSTAT minisponges
- A plunger

ANIMAL TESTING

In vivo testing evaluated the safety and efficacy of XSTAT versus Standard-of-care dressing in an extreme trauma model of junctional hemorrhage. The model implemented in the study was an application of the United States Army Institute of Surgical Research (“ISR”) standardized model for uncontrolled hemorrhage consisting of a femoral artery vascular injury in swine.

Ten (10) animals were treated with the Test Article, XSTAT dressing, and ten (10) animals were treated with the Control Article, Standard-of-care dressing. The dressings were randomly selected just prior to application to avoid bias. The femoral arterial hemorrhage was created using a 6.0 mm vascular punch after isolating a portion of the femoral artery. The artery was allowed to freely bleed for 45 seconds and the Test or Control Article was applied. The animal was followed and observed while anesthetized for 6 hours during which resuscitative fluids were administered as needed to support blood pressure. No additional wound care was provided during the 6-hour observation period. Following the 6-hour observation period, the Test or Control Article was removed from the wound site and the animal euthanized.

There were no re-bleeding events, defined as visible blood shed from the wound site, in either the XSTAT or the Standard-of-care dressing treatment. Post-treatment blood loss, defined as amount of blood shed from the wound cavity during the time period following the 45 second free bleed until study termination, was 21.7 ± 17.5 mL in the XSTAT group and 28.3 ± 18.1 mL in the Standard-of-care dressing group (mean ± SD). The Final MAP was 62 ± 5 mmHg in the XSTAT group and 64 ± 3 mmHg in the Standard-of-care dressing group. All animals survived the entire 6-hour observation period, thus survival was 100% in both the XSTAT and the Standard-of-care dressing treatment groups.

Histological evaluation of the wound sites treated with either XSTAT dressing or the Standard-of-care dressing in the swine femoral injury model observed at approximately 6 hours’ post-treatment showed no adverse effect of treatment and no qualitative or quantitative differences in tissue response or level of tissue necrosis between the Test and Control Articles.

In conclusion, in vivo testing demonstrates that XSTAT is effective at stopping bleeding in an extreme trauma model of junctional hemorrhage. The pre-clinical investigators administering the study observed no safety concerns or side effects directly associated with application of the XSTAT dressing.
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.