XSTAT®12

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XSTAT 12 PACKAGE INSERT

NAME OF STUDY	**GLP EVALUATION OF XSTAT DRESSING IN A SWINE FEMORAL MODEL**
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 / EXLUSION	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 ≥ 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., S-Rolled Gauze) was packed 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., S-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 3 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 33 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 minisponges 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 minisponges were identified in the fluoroscopic images or at necropsy.

RESULTS	ENDPOINTS	XSTAT	STANDARD-OF-CARE DRESSING
	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.	0 minutes	0 minutes
	2: Post-Treatment Blood Loss, mean (stdev): 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.	21.7 (17.5) mL	28.3 (18.1) mL
	3: Final Mean Arterial Pressure (MAP), mean (stdev): Mean arterial pressure recorded just prior to exsanguination or end of the 6-hour observation period.	62.0 (5.0) mmHg	64.0 (3.0) mmHg
	4: Survival Time, mean (stdev): Time period immediately following the 45 second free bleed during which vital signs are; MAP >20mmHg and PCO_2 >15 mmHg to exsanguination or end of the 6-hour observation period.	6.0 (0.0) hours	6.0 (0.0) 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 PCO_2 >15 mmHg.	100%	100%
	6: Wound Packing Time, mean (stdev)	1.1 (0.3) minutes	4.6 (0.5) minutes
	7: Wound Compression Time	0 minutes	3 minutes
	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 2 ± 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 o Animal Breed: Landrace cross swine o Weight at procedure: 55-65 kg o 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. — 7/8 (87.5%)
	2: Animals with hemostasis at 60 min after dressing application — 7/8 (87.5%)
	3: Animal Survival at 60 min where survival was defined as the MAP > 20 mmHg and PCO_2 > 15 mmHg — 8/8 (100%)
	4: Bleeding Time, mean (StDev) Duration of bleeding occurring at any time following the material application until study termination — 7.9 (21.1)
	5: Post-TBL, mean (stdev) Amount of blood shed from the wound cavity during the time following the 45 second free bleed until study termination. — 331.5 (818.9)
	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 (1cm) 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 2 ± 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	**USER EVALUATION OF XSTAT 12 APPLICATION**			
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 12 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		
	2	41	Add detail on resistance when using device; improve outer packaging	Statement regarding resistance included in IFU and training video; final package labeled with easy open tear notches.
	3	39	Show areas where device is not indicated	Final training video comprises images highlighting areas that are contraindicated.
	4	34		
	5	30	Include real and animation in video if possible; improve outer packaging	Final training video comprises mostly animation; final package labeled with easy open tear notches
	6	33		
	7	38	Improve outer packaging	Final package labeled with easy open tear notches
	8	53		
	9	46	IFU and packaging should hold up to rain and wind conditions.	Final IFU printed on water resistant material and tested for water exposure and legibility.
	10	39	Ensure proper pronunciation in video; improve outer packaging; make plunger brighter	Pronunciation of key medical terms confirmed; final package labeled with easy open tear notches; final plunger is white.
	11	53	Improve outer packaging	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 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 2 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)	31
	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	ACTION TAKEN
	Add reminder that all sponges must be removed before wound closure.	Package label and casualty card contain explicit instructions for surgical sponge removal.
	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 12 TRAINING INFORMATION

XSTAT 12 is a hemostatic dressing for the control of bleeding from junctional wounds in the groin or axilla. In narrow, deep wounds, XSTAT 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.

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 XSTAT dressing, hemorrhage from the groin was created in a swine using a 6.0 mm 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 wound, XSTAT is not the preferred dressing to achieve hemorrhage control and alternative methods 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 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 one (1) 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 has a 30 mm outer diameter. If the entrance of the junctional 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.
- The XSTAT dressing exhibited a moderate pyrogenic response in a materials mediated rabbit pyrogen test. If a rise in patient temperature is observed, continue to monitor the patient's temperature during transport.

- After completion of treatment, fill out the casualty card completely. A line has been added above the notes depicting the amount of XSTAT applicators used to treat the wound. Circle the appropriate number.
- 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 band are included with the casualty card to facilitate attachment.
- 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.