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XSTAT-30 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 / EXCLUSION	<ul style="list-style-type: none"> Inclusion: <ul style="list-style-type: none"> 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	<p>ALL WOUNDS PRIOR TO RANDOMIZATION</p> <ul style="list-style-type: none"> 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 \geq 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 second free bleed period. <p>WOUNDS RANDOMIZED TO XSTAT</p> <ul style="list-style-type: none"> 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 at if bleeding persisted following application of the dressing. <p>WOUNDS RANDOMIZED TO STANDARD OF CARE DRESSING</p> <ul style="list-style-type: none"> 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. <p>POST-RANDOMIZATION CARE</p> <ul style="list-style-type: none"> 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 PCO2 >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 PCO2 >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 10.5 \pm 3.4 minutes. Mean standard-of-care dressing removal time 2 \pm 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.		

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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	<ul style="list-style-type: none"> Inclusion: <ul style="list-style-type: none"> 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	<ul style="list-style-type: none"> 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 PCO2 > 15 mmHg.	8 / 8 (100%)
	4: Bleeding Time, mean (StDev) Duration of bleeding occurring at any time immediately following 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 (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 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 APPLICATION			
STUDY DESCRIPTION	A user evaluation (human factors) was completed to determine the ability of medics and civilian EMS to understand and execute instructions for using XSTAT and applying XSTAT on a simulated casualty.			
NUMBER OF SUBJECTS	10			
INCLUSION / EXCLUSION	Military medic or civilian EMS with no prior knowledge or experience XSTAT dressing prior to the study.			
STUDY PROCEDURE	<ul style="list-style-type: none"> 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 3 cm and a length of 8 cm and was pre-filled with 150-200 mL of saline. Participants were tested in a low-light environment. Participants were evaluated on the time needed to ready the device for use, as well as the time necessary to deploy the appropriate amount of material to stop bleeding. 			
RESULTS	PARTICIPANT	TIME	USER COMMENTS	ACTIONS TAKEN
	1	45		
	2	31	Add detail on pulling/locking applicator.	Revised instruction on pulling/cocking application handle.
	3	47	Add detail on preclinical data.	Added detailed information on preclinical testing to product insert.
	4	70		
	5	43	Explain importance of direct pressure.	Added detailed instructions regarding application of direct pressure and bandage.
	6	71		
	7	53		
	8	47		
	9	54	Add detail on pulling/locking applicator.	Revised instruction on pulling/cocking application handle.
10	40			

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	<ul style="list-style-type: none"> 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. 	
ENDPOINTS / 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 TRAINING INFORMATION

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

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

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

The XSTAT applicator is composed of three primary parts:

- The main body which holds approximately 92 XSTAT Minisponge
- A telescoping handle
- A bifurcated silicone tip that allows the XSTAT to exit

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 reBleeding events, defined as visible blood shed from the wound site, in either the XSTAT or the Standard-of-care dressing treatment groups. 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 \pm 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 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 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 wound, XSTAT is not the preferred dressing to achieve hemorrhage control and alternative treatments should be used such as other hemostatic dressings or tourniquets.

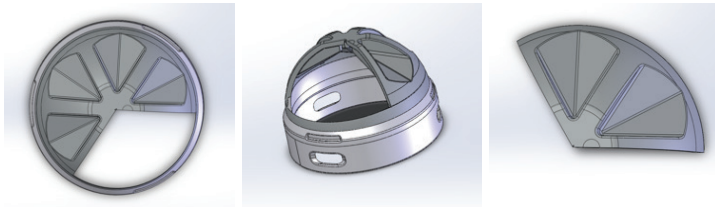
XSTAT is NOT indicated for use in: the thorax, the abdomen, the retroperitoneal space, the sacral space above the inguinal ligament, or tissues above the clavicle.

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.

XSTAT TRAINING INFORMATION

- Open package and remove applicator.
- Pull the black handle out and away from barrel until it stops and locks.
- Place the tip of the applicator into the wound track as close to the bleeding source as possible.
- Firmly depress black handle to deploy dressing into the wound. Material should flow freely into the 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.

- 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.
- 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.
- Assess patient for peripheral circulation and document presence of distal pulse on included casualty card. Vascular compression greater than four hours is not recommended due to concerns related to limb ischemia.
- 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.



Triangular segments of the applicator tip may break away from applicator during treatment. If this occurs, do not attempt to retrieve it from the wound.

Record number of separated applicator tips on casualty card.

After completion of treatment, remove the TCCC casualty card from the package and fill it out completely. A line has been added above the notes depicting the amount of XSTAT applicators used to treat the wound. Circle the appropriate number. If any applicator tips were released from the applicator record that in the notes section.

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.

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

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