XStat – FDA Overview

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De Novo Evaluation

- FDASIA (2012), you can submit a *de novo* directly without first being found NSE.

- Draft Guidance Document:
  - http://www.fda.gov/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm273902.htm

- XSTAT classification order and decision summary, respectively are located here:
  - http://www.accessdata.fda.gov/cdrh_docs/pdf13/K130218.pdf
  - http://www.accessdata.fda.gov/cdrh_docs/reviews/K130218.pdf

De Novo - XStat

- Existing regulations:
  - Absorbable Hemostats
    - 21 CFR 878.4490 – Class III, LMG
    - For example, Avitene Collagen powder with applicator
  - Hemostatic wound dressings for external use
    - Unclassified, FRO – require 510k
    - For example, ChitoGauze XR (K102546) Gauze coated with chitosan
- XStat:
  - XStat is a hemostatic device for control of bleeding from junctional wounds in the groin or axilla not amenable to tourniquet application in adults and adolescent. XStat is a temporary device for use up to four (4) hours until surgical care is acquired. XStat is intended for use in the battlefield.
  - The device can be used in wounds deep enough that they can not be considered external,
  - there are small, individual pieces
  - these pieces expand to generate pressure

- No predicate device exists, however the benefits and risks of the subject device are easily identified, making it possible to develop general and special controls to mitigate the risks. *De novo* is an appropriate pathway.

Xstat De Novo

- The *De Novo* Summary:
  - Summary of the scientific evidence that served as the basis for the decision to grant a *de novo* request. The *de novo* summary also serves as a resource regarding the types of information necessary to support substantial equivalence for device manufacturers that may wish to use the device as a predicate for future 510(k) submissions.
  - Biocompatibility
    - Cytotoxicity, Sensitization, Intracutaneous Reactivity, Acute Systemic toxicity, Hemocompatibility.
  - Stability/Sterility
  - Performance Testing – Bench
    - Absorption capacity, extent of swelling, expansion force/pressure (gel wound simulation and cadaver testing), mechanical properties, and radiopacity.
    - Mechanical testing was also performed for the applicator, e.g. force required to retract or deploy the applicator, and minimum forces required to generate failures. Testing was performed for different environments (high temp, low temp, room temp).

XStat De Novo

- Performance Testing – Animal:
- Three animal studies using XSTAT in swine demonstrated reasonably safe and effective use by verifying that the device controls bleeding, does not promote adverse local or systemic effects, and can be completely removed the wound.
  - Swine Femoral Artery Study
  - Two Swine Subclavian Artery Studies
- Human Factors Testing:
- Human factors testing and analysis validated that the device design and labeling are sufficient for appropriate use by emergency responders deploying the device as well as surgeons retrieving the device from wounds. Human factors assessments were used to modify the labeling to promote reasonably safe and effective use of XSTAT.
  - Device Deployment Human Factors Study
  - Sponge Retrieval Human Factors Study

X-Stat Special Controls

- Risks to Health:

Identified Risk	Mitigation Method
Collateral Tissue Damage (e.g. paralysis, nerve damage, necrosis)	*In Vivo* Performance Data
	Labeling
Reoperation Due to Material Retained in Body	Non-Clinical Performance Data
	In Vivo Performance Data
	Human Factors Testing Labeling

- Special Controls:
- **In vivo performance data** must demonstrate safe and effective use by verifying that the device performs as intended under anticipated conditions of use. Appropriate analysis/testing must demonstrate that the product: controls bleeding, does not promote adverse local or systemic effects, and can be completely removed from the wound. The following performance characteristics must be tested:
- A. Deployment
- B. Control of bleeding
- C. Radiopacity
- D. Retrieval
- E. Assessment of local and systemic effects

X-Stat Special Controls

- Risks to Health:

Identified Risk	Mitigation Method
Adverse Tissue and Allergic Reactions	Materials Characterization
	Biocompatibility
	In Vivo Performance Data
	Labeling
Infection (e.g., cellulitis, Toxic Shock Syndrome, sepsis)	Sterility Testing
	Stability Assessment

- Special Controls:

1. Performance data must demonstrate the biocompatibility of patient-contacting components.
2. 2. Performance data must demonstrate the sterility of patient-contacting components including endotoxin and pyrogenicity assessments.

X-Stat Benefit-Risk Evaluation

- Benefit-Risk profile is considered when evaluating reasonable assurance of safety and efficacy
  - Published Benefit Risk Guidance Document
  - http://www.fda.gov/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm267829.htm#
- Examples of Factors Considered
  - Type of benefit(s), probably of the patient experiencing one or more benefits, duration of effects.
  - Severity, types, number, and rates of harmful events associated with use of the device – Separately and the aggregate effect.
  - Additional Factors
    - Uncertainty (e.g. as the result of poor study design)
    - Availability of alternative treatments or diagnostics
    - Risk mitigation
    - Postmarket data
    - Novel technologies addressing unmet medical needs

X-Stat Benefit-Risk Evaluation

- The risks associated with use of the device include the following:
  - failure to stop bleeding or recurrence of bleeding, obstruction of vital organs, embolization, collateral tissue damage, adverse tissue and allergic reactions, infection, reoperation due to material retained in body, sponge deployment failure, and improper application technique or use error.
- The probable benefits of the XSTAT device are also based on nonclinical laboratory and animal studies.
  - Early control of bleeding is of high value to both patients and providers and can reduce the secondary effects of severe hemorrhage which include hypothermia, coagulopathy and late development of sepsis and multiple-organ system failure.
- Additional factors to be considered in determining probable risks and benefits for the XSTAT device include:
  - the limitations of the animal study designs, clinical expertise required to use the device, and lack of alternative treatments.

XStat Regulation

FDA identifies this generic type of device as:

- **Non-absorbable, expandable, hemostatic sponge for temporary internal use:** A nonabsorbable, expandable, hemostatic sponge for temporary internal use is a prescription device intended to be placed temporarily into junctional, non-compressible wounds, which are not amenable to tourniquet use, to control bleeding until surgical care is acquired. The sponges expand upon contact with blood to fill the wound cavity and provide a physical barrier and pressure that facilitates formation of a clot. The device consists of sterile, non-absorbable, radiopaque, compressed sponges and may include an applicator to facilitate delivery into a wound.
- **NEW REGULATION NUMBER:** 21 CFR 878.4452
- **CLASSIFICATION:** II
- **PRODUCT CODE*:* PGZ**

- You can submit a 510k citing this device as a predicate

- Q & A