Arsenal Trauma Foam System

Overview for FDA workshop

arsenal medical

September 3, 2014

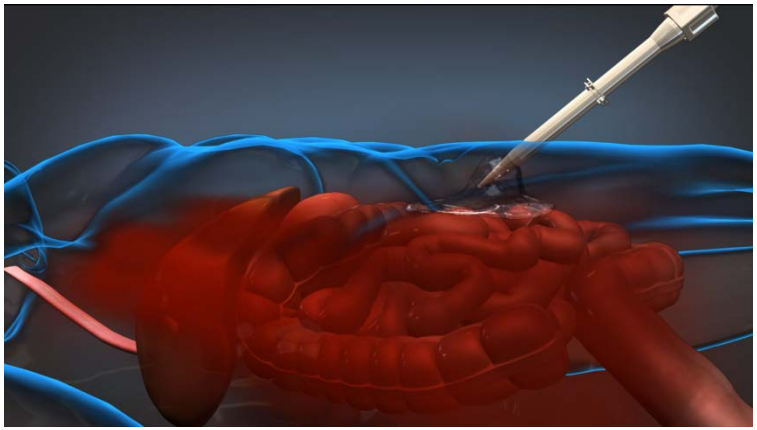
Arsenal Medical

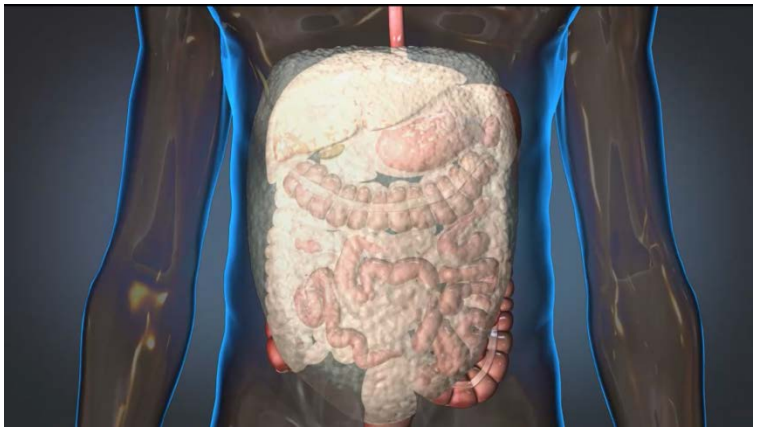
- Medical device start-up company located in Boston metro area
- Focused on coupling conventional biomaterials with innovative engineering
- R&D Team
  - 22 scientists and engineers; 7 PhD's
    - Chemistry, biology, materials science
    - Mechanical, chemical, and biomedical engineering
    - In house quality assurance and histology capabilities

Product Requirements

- Achieve hemostasis quickly
- Maintain hemostasis for 3 hours
- Administered by an advanced medic
- Simple to use, without requiring identification or direct access to wounds
- Easy removal at time of surgery
- Compatible with field use (compact, extreme temperatures)

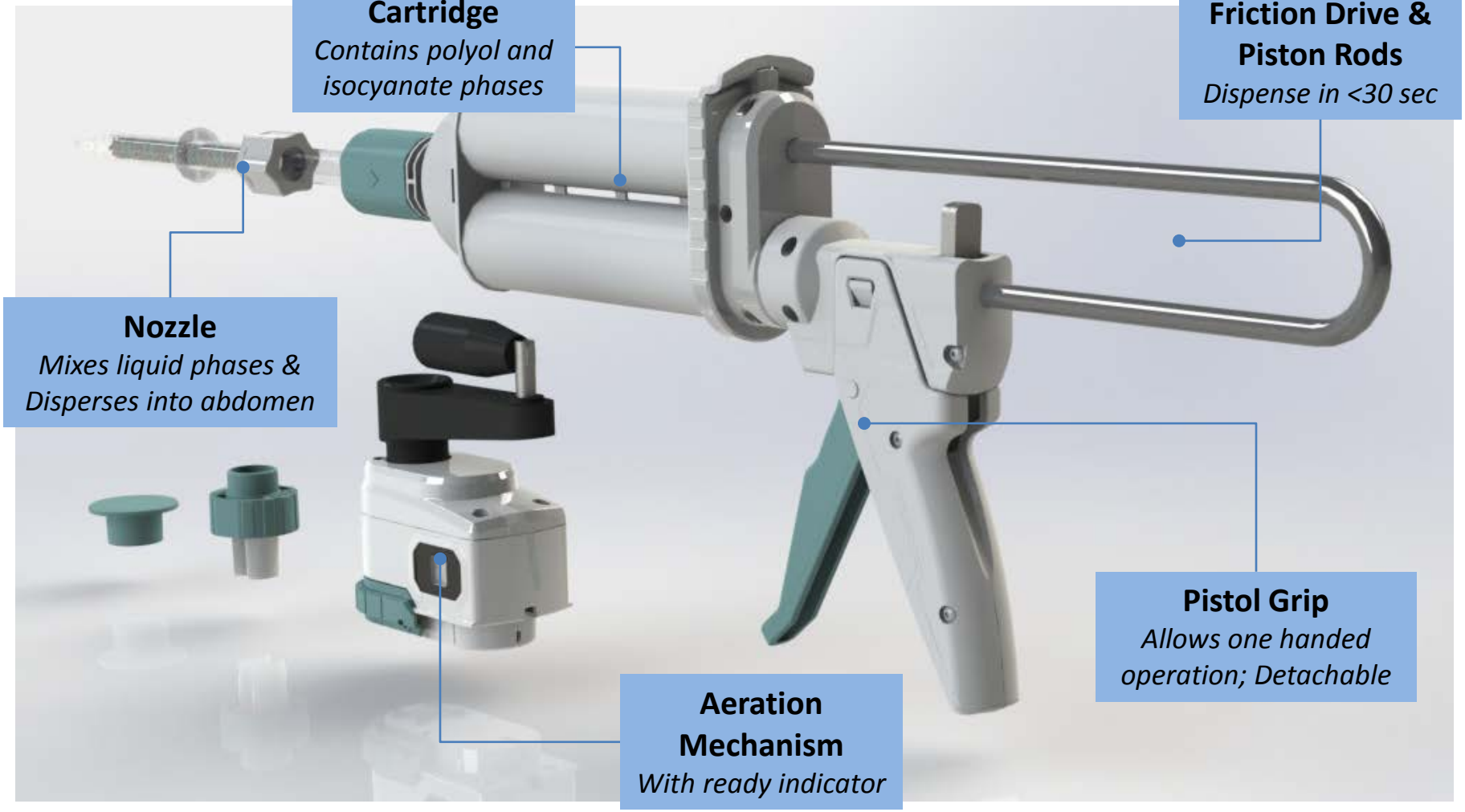
Arsenal's Device: A Treatment for Non-Compressible, Abdominal Hemorrhage





- Two part liquid injected into body; chemical reaction in the body generates a solid, conformal device
- Device delivered using standard, laparoscopic access
- Provides intra-abdominal compression
- Removed at definitive surgery

Delivery System Design



Intended Use

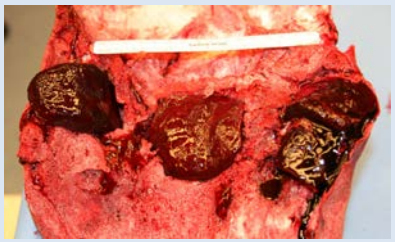
- Emergent control of exsanguinating intraabdominal hemorrhage (Class III or IV hemorrhagic shock)
- Bridge to definitive surgical care – temporary internal use
- Military and civilian use by EMT-P level or higher
  - Personnel must be trained & certified in device use by Arsenal

Summary of Performance Testing

- Bench: Qualified test methods to characterize material and delivery system → over 2300 deployments
- Swine: Established safety and effectiveness based on work in 600+ swine
- Recently deceased study: Evaluation of human dose

Overview of Animal Testing

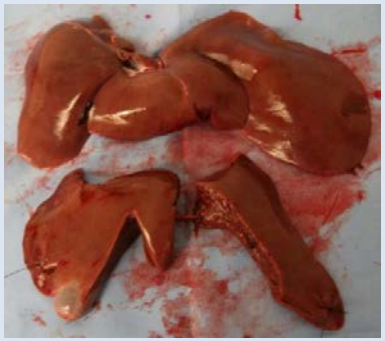
Formulation Selection



Swine
16 formulations evaluated

n = 58

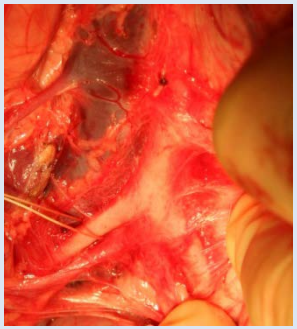
Lethal liver injury



Swine
Venous bleeding
3 Hours

n = 431

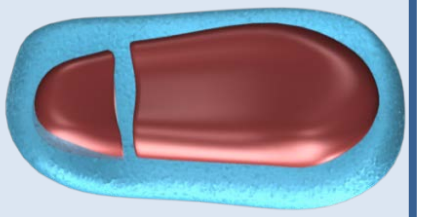
Lethal iliac injury



Swine
Arterial bleeding
3 Hours

n = 39

Non-lethal spleen injury



Swine
Survival study
28 & 90 days

n = 27

ISO-10993 testing used to establish biocompatibility

Summary of Swine Studies

Study	Key Findings
Liver Injury	• Range of doses tested demonstrating significant survival benefit and reduction in hemorrhage rate relative to control • Survival benefit improved with increasing dose • Similar level of organ contact observed with all doses
Iliac Artery Injury	• Foam resulted in a significant survival benefit and reduction in hemorrhage rate relative to control
Spleen Injury Survival	• Demonstrated long-term viability of foam treatment

Duggan et al., J. Trauma, 2013
Duggan et al, JSR, 2013
Peev et al., J. Trauma, 2014
Rago et al, J. Trauma, 2014
Rago et al., J. Trauma, 2014
Duggan et al, JSR, 2014

Additional discussion of swine studies in tomorrow's session

Recently Deceased Study (RDS) in Humans

Objective	Confirm appropriate human dose in recently deceased subjects
Study Population	Subjects within three hours of death *Minimize any post-mortem changes in tissue compliance*
Sites	Massachusetts General Hospital University of Texas Health Science Center – Houston Oregon Health and Science University
Outcome	Foam performance as compared to swine results

Additional discussion of RDS in tomorrow's session

Arsenal Trauma Foam is Moderate Risk

- Patients will die without immediate control of bleeding
  - Lack of alternative treatments for intra-abdominal hemorrhage
  - Surgical control not immediately available
- Probable benefit outweighs probable risk for its intended use
  - Pre-clinical data will be used to demonstrate safety and effectiveness
- Device design for simple application by trained personnel

Post-market surveillance planned

Regulatory Pathways Considered

Pathway	Risk	Arsenal Considerations
510(k)	Low/Moderate (Class 2)	Requires substantially equivalent legally marketed device

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De novo 510(k)	Low/Moderate (Class 2)	Special controls can be written to provide a reasonable assurance of safety and effectiveness – **PROPOSED PATHWAY** • **Least burdensome approach**

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Expedited access PMA	High (Class 3)	• Likely requires pre-market clinical study • Longer review times likely for Class 3 device • Guidance document established 4 months ago; no experience with pathway • Requirement of FDA review for post-market manufacturing changes → burdensome for low volume products • **NOT the least burdensome approach**

De Novo 510(k) Proposed Special Controls

Key Risks	Mitigations
Patient diagnosis	• Indication to ensure only high risk patients receive treatment • Robust training and certification program
Safety & efficacy	• Two acute lethal, large animal models (arterial and venous injuries) • One survival, large animal model • Conformity to ISO-10993
Dose translation	• Recently deceased study to translate swine dose to human dose
Product reliability	• Bench and analytical testing to confirm product specifications and performance (delivery system and formulation)
Device usability	• IFU / labeling • Usability testing
Safety monitoring	• Post-market surveillance including medical device reporting and registration on clinicaltrials.gov

Proposed special controls provide reasonable assurance of safety and efficacy

Pre-Market vs. Post-Market: Considerations

	Pre-market IDE	Post-market
Study population	Research based, narrowly defined eligibility criteria	Observational or registry based study, more consistent with trauma population
Endpoint	Primary endpoint with statistical power	Observational study – statistically powered endpoint not required
Time to first patient	+6 months	
Time to full launch	+2 years	
Protocol Flexibility	Protocol modifications require FDA review/IDE supplement & IRB ***Protocol Change = 90 - 120 Days***	Generalized "open ended" protocol could enable changes to be made without FDA involvement or IRB changes ***Protocol Change = 0 Days***

Summary

- Reasonable assurance of safety and effectiveness based on work in 600+ swine and RDS study
  - Performance in two large animal models of lethal hemorrhage and one survival model; confirmed biocompatibility
  - Groundbreaking study for human dose translation in recently deceased subjects
  - Six peer reviewed publications and eight presentations at national meetings
- Ongoing development of robust training/certification plan
- Post-market surveillance planned
- Proposed regulatory pathway: *De novo* 510(k)

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Statistics on Medical Device Development

- Survey conducted of 204 companies developing "innovative new technologies" (20% of total number of companies in this space)

Pathway	Average time to clearance	Average cost to clearance / approval
510K	10 months from first filing	$31M
510K + clinical trial	31 months from first communication	
PMA	54 months from first communication	$94M

Report "FDA Impact on U.S. Medical Technology Innovation: A Survey of Over 200 Medical Technology Companies" November 2010 (published by Stanford professor)

Proposed Post-Market Plan

Initial human experience – Level 1 trauma

- Post-market observational study
- Training and certification
- Executive committee review
- ~20 cases across sites
- Commercial distribution - SOCOM only

Expanded human experience

- Post-market observational study
- Training and certification
- Executive committee review
- ~20 additional cases

Full commercial launch

- Training and certification
- Ongoing data registry

Controlled post-market study to confirm labeling and gather data to drive market adoption