Arsenal Trauma Foam System

Overview for FDA workshop

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

- **Cartridge**: Contains polyol and isocyanate phases.
- **Nozzle**: Mixes liquid phases & disperses into abdomen.
- **Aeration Mechanism**: With ready indicator.
- **Friction Drive & Piston Rods**: Dispense in <30 sec.
- **Pistol Grip**: Allows one handed operation; Detachable.
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

<table>
<thead>
<tr>
<th>Study</th>
<th>Key Findings</th>
</tr>
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</table>
| **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*  
*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

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

**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

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<tr>
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<th>Risk</th>
<th>Arsenal Considerations</th>
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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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| **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 |
| 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

<table>
<thead>
<tr>
<th>Key Risks</th>
<th>Mitigations</th>
</tr>
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<tr>
<td><strong>Patient diagnosis</strong></td>
<td>• Indication to ensure only high risk patients receive treatment</td>
</tr>
<tr>
<td></td>
<td>• Robust training and certification program</td>
</tr>
<tr>
<td><strong>Safety &amp; efficacy</strong></td>
<td>• Two acute lethal, large animal models (arterial and venous injuries)</td>
</tr>
<tr>
<td></td>
<td>• One survival, large animal model</td>
</tr>
<tr>
<td></td>
<td>• Conformity to ISO-10993</td>
</tr>
<tr>
<td><strong>Dose translation</strong></td>
<td>• Recently deceased study to translate swine dose to human dose</td>
</tr>
<tr>
<td><strong>Product reliability</strong></td>
<td>• Bench and analytical testing to confirm product specifications and</td>
</tr>
<tr>
<td></td>
<td>performance (delivery system and formulation)</td>
</tr>
<tr>
<td><strong>Device usability</strong></td>
<td>• IFU / labeling</td>
</tr>
<tr>
<td></td>
<td>• Usability testing</td>
</tr>
<tr>
<td><strong>Safety monitoring</strong></td>
<td>• Post-market surveillance including medical device reporting and</td>
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<tr>
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<td>registration on clinicaltrials.gov</td>
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**Proposed special controls provide reasonable assurance of safety and efficacy**
<table>
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<tr>
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<th>Pre-market IDE</th>
<th>Post-market</th>
</tr>
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<tbody>
<tr>
<td>Study population</td>
<td>Research based, narrowly defined eligibility criteria</td>
<td>Observational or registry based study, more consistent with trauma population</td>
</tr>
<tr>
<td>Endpoint</td>
<td>Primary endpoint with statistical power</td>
<td>Observational study – statistically powered endpoint not required</td>
</tr>
<tr>
<td>Time to first patient</td>
<td>+6 months</td>
<td></td>
</tr>
<tr>
<td>Time to full launch</td>
<td>+2 years</td>
<td></td>
</tr>
<tr>
<td>Protocol Flexibility</td>
<td>Protocol modifications require FDA review/IDE supplement &amp; IRB&lt;br&gt;&lt;i&gt;Protocol Change = 90 - 120 Days&lt;/i&gt;</td>
<td>Generalized “open ended” protocol could enable changes to be made without FDA involvement or IRB changes&lt;br&gt;&lt;i&gt;Protocol Change = 0 Days&lt;/i&gt;</td>
</tr>
</tbody>
</table>
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)
Arsenal Trauma Foam System

Overview for FDA workshop

September 3, 2014
Statistics on Medical Device Development

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

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<thead>
<tr>
<th>Pathway</th>
<th>Average time to clearance</th>
<th>Average cost to clearance / approval</th>
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<tbody>
<tr>
<td>510K</td>
<td>10 months from first filing</td>
<td>$31M</td>
</tr>
<tr>
<td>510K + clinical trial</td>
<td>31 months from first communication</td>
<td>$31M</td>
</tr>
<tr>
<td>PMA</td>
<td>54 months from first communication</td>
<td>$94M</td>
</tr>
</tbody>
</table>

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

September 3, 2014