Potential Workshop Outcomes

- Workshop report to summarize findings & discussion
  - Include survey results: “measurements most in need of improvement”
- Formation of a working group to write an “ASTM Standard Guide for Characterizing Fiber-Based Scaffolds”
  - Address top 20 measurements with a couple of paragraphs (why do it, caveats, best practices)

- Formation of working groups:
  - Porosity
  - Diffusivity

- May include teleconferences to discuss
  - how the measurement is currently conducted
  - problems with current practice
  - what could be done to improve things
- May result in
  - White paper
  - Research
  - Proposal writing
  - ASTM standards
**Scope**
- not intended to address meshes for orthopedic or dental
- covers surgical mesh for general surgical uses such as implantation to reinforce soft tissue where weakness exists (hernia repair, suture line/staple line reinforcement, muscle flap reinforcement, gastric banding, etc.).

<table>
<thead>
<tr>
<th>Section 2. Product Characterization</th>
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<tbody>
<tr>
<td>• Mesh thickness</td>
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<td>• Mesh weave characteristics</td>
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<td>• Pore size</td>
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<td>• Mesh density</td>
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<tr>
<td>• Tensile strength</td>
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<td>• Device stiffness</td>
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<td>• Suture pullout strength</td>
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<td>• Burst strength</td>
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<td>• Tear resistance</td>
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<th>Section 3. Final Product Specification</th>
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<td>Examples of in-process and final product tests:</td>
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<tr>
<td>• Device Thickness</td>
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<td>• Pore Size</td>
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<tr>
<td>• Bursting Strength</td>
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<tr>
<td>• Residual levels of manufacturing reagents</td>
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<td>• Residual levels of heavy metals</td>
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<td>• Pyrogen levels</td>
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<td>• Sterility</td>
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<td>• For biodegradable devices: document rate of product resorption &amp; how device properties (suture pullout strength, burst strength and/or tear resistance) change over time</td>
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List of All Measurements

- Fiber Diameter: scanning electron microscopy
  - Uniformity of fiber diameter along fiber length
  - Fiber cross-section: cylindrical or flat ribbon
- Porosity:
  - Gravimetric using scale and calipers (or profilometer)
  - Scanning electron microscopy (“pseudoporosity”)
  - Imaging: confocal, X-ray CT
    - spike with fluor and do confocal
    - spike with contrast agent & do X-ray CT
- Pore size/shape: mercury porosimetry, porometry, permeability, scanning electron microscopy, confocal, X-ray CT
- Scaffold thickness: scanning electron microscopy, caliper, profilometer
- Fiber orientation: scanning electron microscopy, confocal, X-ray CT
- Mechanical properties: tensile strength, lifecycle, suture retention, DMA, tube expansion, burst strength
- Surface wettability
- Diffusivity
- Bubble point test (permeability): ASTM F316 - Standard Test Methods for Pore Size Characteristics of Membrane Filters by Bubble Point and Mean Flow Pore Test
- Permeability: F2952 - Standard Guide for Determining the Mean Darcy Permeability Coefficient for a Porous Tissue Scaffold
- Wickability
- Molecular Mass: GPC
- Degradation rate
  - By products of degradation
- Surface chemistry
- Surface characterization (if functionalized): FTIR, XPS, Raman, TOF-MS
- Residual solvent: GCMS, sensitive to 10 parts in a million
- Fiber charge, scaffold charge
- Cell culture tests: cell adhesion to scaffold, biocompatibility, viability, proliferation on scaffold, penetration into scaffold
Results from an Informal Survey (21 Stakeholders): “three measurements most in need of improvement”

- 12 of 21 respondents listed porosity
- 18 of 21 respondents listed porosity or pore size
- 9 of 21 listed fiber diameter
- 6 of 21 listed diffusivity

- Porosity (void volume, density, porosity uniformity across thickness) (dry & wet)
- Pore Size (shape, interconnectivity, geometry, distribution, pore uniformity across thickness)
- Fiber Diameter (dry & wet)
- Diffusivity (Permeability)
- Fiber Orientation (anisotropy, fiber spatial distribution)
- Mechanical Properties (wet & dry)
- Fiber Cross-Sectional Profile
- Scaffold Thickness
- Fiber Charge
- Other (degradation, surface chemistry, surface wettability, composition, residual solvent, cytocompatibility, cell penetration)
Breakout Sessions

**Goal:** collect information on how the measurements are currently being made & the problems with these approaches

- **We aren’t trying to achieve consensus**
- Information gathering
- Lead generation (for future research)
  - What could be done to address these issues?
  - Is there a research project that could be developed or a working group that could be formed to advance the measurement?
- Topics:
  - Porosity (Tom Bollenbach, Markus Reiterer)
  - Diffusivity (Esmaiel Jabbari, Ramon Montero, Hai Yao)
# Schedule

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
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<tr>
<td>1:00 - 1:10</td>
<td>Breakout overview, responses from stakeholders for “measurements most in need of improvement”</td>
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<tr>
<td>1:10 - 1:25</td>
<td>Porosity Introduction (15 min) Disc. Leaders: Thomas Bollenbach (ARMI), Markus Reiterer (Medtronic)</td>
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<td>1:25 - 1:40</td>
<td>Diffusivity Introduction (15 min) Disc. Leaders: Esmaiel Jabbari (S. Carolina Univ.), Ramon Montero (Akron Biotech), Hai Yao (Clemson)</td>
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<td>1:40 - 2:55</td>
<td>Concurrent Breakout Sessions (1 h 15 min) Porosity (break into 2 groups) Diffusivity (break into 2 groups)</td>
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<td>2:55 - 3:35</td>
<td>Networking computer-poster session (40 min)</td>
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<td>3:35 - 4:35</td>
<td>Report-Outs (1 hour) Porosity 1 report-out (15 min) Porosity 1 report-out (15 min) Diffusivity 1 report-out (15 min) Diffusivity 2 report-out (15 min)</td>
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<tr>
<td>4:35 - 5:00</td>
<td>Discussion &amp; Wrap-Up: workshop report, ASTM standards, formation of working groups</td>
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<td>5:00</td>
<td>Adjourn</td>
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Porosity Focus Questions

1. How do you currently measure porosity?
2. What are the challenges you face in measuring porosity?
3. What do you use for controls in your porosity measurements?
   a) Empty chamber gives 100% porosity
   b) A solid block gives 0% porosity
   c) Is there something that can serve as a reference material that gives a consistent response and has a well-known porosity?
4. How can comparability of porosity measurements be achieved between labs to improve consistency of manufacturing?
5. What properties of fiber-based scaffolds should be characterized for release criteria?
6. Are there clinically relevant specifications that should be characterized to ensure desirable patient outcomes?
Diffusivity Focus Questions

1. How do you currently measure diffusivity?
2. What are the challenges you face in measuring diffusivity?
3. What do you use for controls in your diffusivity measurements?
   a) Empty chamber gives 100% diffusivity
   b) A nonporous membrane gives 0% diffusivity
   c) Is there something that can serve as a reference material that gives a consistent response and has a well-known diffusivity (0.2 µm dia. filter?)
4. How can comparability of diffusivity measurements be achieved between labs to improve consistency of manufacturing?
5. What properties of fiber-based scaffolds should be characterized for release criteria?
6. Are there clinically relevant specifications that should be characterized to ensure desirable patient outcomes?
Importance vs. Difficulty Matrix

Relative Difficulty/Cost

Relative Importance/Impact

Low

High

Low

High
Directions

1. Please discuss the questions in the template

2. Have someone in your group with a laptop prepare a few slides (3 to 5?) to summarize your key discussion points.

3. It is ok if you don’t get to everything

4. Try to capture the most important points

5. Please identify someone to do the report out for your group (15 min presentation to summarize the discussion)

6. This information to write the workshop report