Developing a method to quantitatively assess residual patient material in reusable medical devices

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The comments and opinions expressed in this presentation are those of the speaker, and do not necessarily reflect the formal position of the FDA.
Overview of Project

FDA has received reports of reusable medical devices that contain residual patient material even after being cleaned, which poses a risk for infection.

Goals:

1. To develop an assay for assessing residual debris in reusable medical devices

2. To quantitatively determine the impact of different device designs on the ability to remove organic material from reusable medical devices
Background

- Cleaning is an important first step in reprocessing for effective disinfection and/or sterilization of reusable devices.

- Organic material has been found to compromise the effectiveness of certain sterilization processes.

- Improper cleaning of reusable devices (e.g., endoscopes) increases the possibility of infection for patients.
  - Patient to patient transmission (Hepatitis)
  - Environmental transmission (*Pseudomonas*)

Endoscopes
Arthroscopic Shaver Handles

Ongoing Safety Review of Arthroscopic Shavers

FDA has become aware of instances in which pieces of tissue have remained within certain arthroscopic shavers, a device used in some orthopedic surgical procedures, even after the cleaning process was believed to have been completed according to the manufacturer's instructions. Reports submitted to FDA suggested that the tissue retained was not evident to the naked eye. Multiple manufacturers of these devices recently informed their customers of this situation and reiterated the importance of proper cleaning procedures.

We are concerned about this because retained tissue in these devices can compromise the entire sterilization process. We are actively working with the manufacturers of these devices to gather more data about this situation and to understand its potential public health impact. As the FDA obtains more information that better defines the situation and determines whether there are specific risks, we will provide that information to facilities, health care providers and the public.

The FDA encourages facilities that use any of these types of devices to evaluate the adequacy of their cleaning procedures. Hospitals should consider taking the following steps to minimize any potential risk to patients:

- Be sure that all personnel responsible for device cleaning and sterilization at your facility are aware of and comply with all steps in the manufacturer's instructions for thoroughly cleaning these devices prior to sterilization. Please refer to the specific instructions provided in the labeling or user manual for each brand and/or model of shaver your facility uses.
- Consider inspecting the inside of the devices following cleaning to ensure that they have been cleaned of any tissue or fluids. There may be multiple ways to accomplish this. As one example, the facility that brought this situation to our attention uses a thin video scope to inspect the channels of the shaver handle.

Background

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- During an investigation of an outbreak of Pseudomonas infections, a hospital found that some of their orthopedic surgical devices contained residual bits of patient material even after being cleaned
- residual organic material has been found to compromise the effectiveness of certain sterilization processes
Regulatory Relevance

• FDA has become aware of other types of reusable devices that retained patient debris after cleaning, indicating that this issue is not limited to a particular device or facility

• Manufacturers of reusable medical devices must provide users with reprocessing instructions, including cleaning instructions
  – cleaning instructions must be validated by the manufacturer as being effective to remove soil
  – manufacturers validate cleaning by performing simulated soiling and cleaning of the device, followed by some measurement of residual debris

• Any device that is found to have residual debris after performing the manufacturer-recommended cleaning steps should be reassessed to determine which aspect of the cleaning validation failed

Factors that must be considered for validation of cleaning

• type of test soil used (clinically relevant)
• location of the soil in device (inside device; under sheaths, etc.)
• method of inoculation of test soil
• length of time for the soil to dry on the device (to simulate worse case conditions)
• assessment of soil removal
• quantitative endpoints of “cleaned” device
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The ideal assessments for residue will be:

- Accurate
- Sensitive
- Quantitative
- Fast
- Easy
- Inexpensive

Can be used by manufacturers and users (using a test soil or clinical soil)
Methods that have been used to assay for residues

Direct

- Scanning electron microscopy, surface chemistry analysis, photoelectron analysis staining
- Radionuclide tracers

Indirect

- Liquid Extraction
  - Protein (Bradford, ninhydrin, autoanalyzer, etc.)
  - Lipids and oils (Nile Red Dye)
  - Carbohydrates (phenol-sulfuric acid protocol)
  - Endotoxin (limulus amoebocyte lysate assay)
  - Hemoglobin
  - Total organic carbon
  - Viable microorganisms

- Swab
  - Protein
  - ATP fluorescence assay
  - Viable microorganisms
The problems with solid debris in liquid eluate:

- Sampling error
- Inaccuracy

General Protocol

1. Apply test soil to device
2. Allow test soil to dry for defined time periods
3. Clean devices
4. Assess residual debris
Test soil and inoculation

Coagulated blood test soil
- Purified blood proteins (hemoglobin, albumin, fibrinogen, thrombin)
- Forms a jello-like substance

- Dispense test soil directly into lumen of device
- Invert to mix, ensuring that all interior surfaces are coated with test soil
- Set down horizontally
- Allow to dry

Devices Tested

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<th>Cross-section</th>
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Not to scale
General Protocol

1. Apply test soil to device
2. Allow test soil to dry for defined time periods
3. Clean devices
4. Assess residual debris

Assessments for debris

Swab – followed by Bradford assay for protein

Liquid extraction – followed by Bradford assay

HPLC analysis

Mass spectrometry

Quantitative imaging analysis (FTIR/Raman spectroscopy)
Filter-weighing approach to assess residual debris in medical devices

Equipment:
- Nylon filters (0.2 micron pore size)
- Microbalance (or analytical balance)
- Filtered water
- Container for device
- Filtering equipment

Pre-weigh filter

Extract debris

Filter extraction liquid (can save filtered liquid for further analysis)

Dry filter and weigh

Filter-weighing method to assess residual debris

Sensitive
Quantitative
Requires few pieces of specialized equipment
Relatively straightforward to perform
Saved filtrate can be used in downstream applications
Entire sample is filtered – no sampling error
Accurately quantifies insoluble material
Summary of filter-weighing approach to assess residual debris

- Water control
- Device A
- Device B
- Device C
- Device D
- Device E
- Shaver Handle

* = Median
**Summary of filter-weighing approach to assess residual debris**

The filter-weighing approach to assess residual debris in devices reveals a trend of increasing debris with increasing device complexity.

These preliminary data support the continued development of the filter-weighing method to assess residual debris in reusable medical devices.
Future Experimental Directions

Repeat experiments with microbalance
  Greater sensitivity – may more precisely define contributions from designs

Use imaging technology (with Division of Physics)
  Characterize debris on filters using Fourier Transfer Infrared technology
  Characterize debris inside devices using Raman spectroscopy with a microprobe

Purchasing additional medical devices
  More data possibly relating debris retention to device design
  Ability to see the range of debris found in these devices

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FDA Commissioner’s Fellowship
Sampling error

Using the Bradford assay to sample a solution with insoluble protein will yield inaccurate results.

- No thrombin
  - Dilute with 0.5 mL water
  - Divide into 5 samples
  - Assay all five samples

- + thrombin
  - Dilute with 0.5 mL water
  - (wait 5 min to coagulate)
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- Hemoglobin, albumin, fibrinogen

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- Hemoglobin, albumin, fibrinogen
Bone cannot be accurately measured using a Bradford assay

Bone is ~30% protein

Mineralization of tissue can be detected with dyes (Alizarin red S for Calcium, Von Kossa for Phosphate), semi-quantitatively.

Bone is often quantified by mass or density

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Debris found in arthroscopic shaver handles

Blade Port
Blade Port - Closeup
Suction Lumen - Clean
Suction Lumen - Debris
Suction Lumen - Debris
Efficacy of debris extraction method

16 milligrams  →  200 micrograms

Appearance of filters
Cleaning Protocol

- Rinse/Clean ASAP
- Excess soil removal
- Rinse device
- Do not soak device
- Soak device (enz, deterg)
- Scrub (Brush burr, lumen 5X from one side)
- Repeat a step
- Rinse
- Repeat until clean / Inspect
- Dry (shake, wipe)

Appearance of coagulated blood test soil
### Variables in cleaning procedure

- **Device**
- **Test soil**
- **Application**
- **Dry time**
- **Cleaning**
- **Assessment**