A Systems Approach to Medical Device Cleaning

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- B.S. Microbiology
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- ISO 10993 US Delegate and AAMI Representative
1. Topic Overview | Types of Cleaning Overview
   - Industry Standards
   - Test Selection & Limits
   - Impacts to Validated Cleaning
2. What can QTS do to help? | Q&A Session
1 Overview
Cleaning is a broad topic…

- Several variations in how to clean – types, limits, processes, requirements, etc.
- Pros & Cons with each
- Varying viewpoints and approaches

So, how to start?

- Feasibility
- Risk-based approach
- Conservative approach
Where to start?

What is Cleaning?
- Program to negate processing additives and materials

Create a Process Map designed to your Medical Device(s)
- Identify unknown processes & needs
- Construct a detailed process flows with requirements

Integrate Biocompatibility Requirements
- Post-clean
- Assess effectiveness of cleaning
Identifying Ways to Clean

In-Process vs. Terminal Cleaning

• Manual IPA dip or wipe (non-validated)
• Cleaning process utilizing Detergents or Solvents
  – Dip tanks or sprays
  – Complex, multi-step systems

Establish In-Process Cleans to support Final Clean

• Mitigates contamination between processes or materials
• Buffers against Endotoxins/blooms
Multiple, complex manufacturing processes may require different, additional and/or more rigorous specifications

• One size does not always fit all

Business Considerations

• Expense
• Difficulty
• Time
Segregate: Implants vs. Instruments/Delivery Devices

Segregation should be based on…

• Risk to Patient
• Materials
• Processing/Machining Upstream
  – Residues
  – Burrs
  – Oils/lubricants that are needed for the device to work
• Location: Manufacturing site vs. Packaging site
Reusable Cleaning

- Performed separate from Single-use processes
- Governed by own standards
- Viewed separately than single-use device cleaning
- **CAUTION:** limits, markers, standards, etc., for reusable devices **DO NOT** translate to single-use cleaning
2 Technical Overview

Setting Up A System & Validation
How & When to Validate

Best Practice

• **In-process Cleaning**: PQ validation not required
• **For Implants**: final clean OQ/PQ should be validated

Considerations

• What does FDA/notified bodies require?
• Dunnage/coupon parts can be used for validations – but **CAUTION** should be taken when using this method
• Don’t let Pharma criteria dictate your Medical Device requirements
Industry Standards

Currently not one encompassing standard on single-use medical device cleanliness

ASTM Guidance Documents
- Open-ended, no acceptance criteria
- Not necessarily endorsed by FDA

ISO 10993
- Rooted in patient biocompatibility
- Various tests and parts have been applied to cleanliness due to impact on patient safety
## Cleanliness Testing

<table>
<thead>
<tr>
<th>Types of Test</th>
<th>Specifications/Limits</th>
</tr>
</thead>
</table>
| Gravimetric            | • Industry practice is a 2 log reduction or LD50  
  • ASTM F2459 (Specific to Metals)                                                                                                                  |
| FTIR (Fourier Transform Infrared Spectroscopy) | • ISO 10993-18 with USP 32 and/or ASTM F2456  
  • No established match limit  
  • Typical standards need to be 98% or higher match  
  • 95% or higher is considered a match with general libraries  
  • Spectrums between 80%-95% should only be considered a match to material type, i.e. silicone based lubricant, etc.  
  • Any spectrum below 80% is not considered a match                                                                                           |
## Cleanliness Testing

<table>
<thead>
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<tbody>
<tr>
<td>Cytotoxicity</td>
<td>• ≤ 2 per ISO 10993-5</td>
</tr>
<tr>
<td>Bioburden</td>
<td>• ≤ cleanroom/sterility limits</td>
</tr>
</tbody>
</table>
| Endotoxin     | • USP 85  
• Depends on device type/usage; refer to FDA limits |
| Particulates  | • USP 788 – specific to injections but no clinical relevance  
• ISO 8536-4 for infusion sets  
• EN45502 for pacemakers  
• AAMI AT6-2005 for transfusion devices  
• New ISO 10993-22 for Nanomaterials may offer some guidance when released |
## Cleanliness Testing

### Types of Test

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<tbody>
<tr>
<td>Moisture Content</td>
<td>• ASTM D789 – Various options</td>
</tr>
<tr>
<td></td>
<td>• ISO 15512 – Plastics</td>
</tr>
<tr>
<td></td>
<td>• USP 921 – Karl Fisher</td>
</tr>
<tr>
<td></td>
<td>• Gravimetric</td>
</tr>
<tr>
<td>TOC (Total Organic Carbon)</td>
<td>• USP 643; No established limit for medical devices</td>
</tr>
<tr>
<td></td>
<td>• Devices require extraction validation</td>
</tr>
<tr>
<td>Extractable &amp; Leachable</td>
<td>• Extraction time, temperature, and solution is critical</td>
</tr>
<tr>
<td></td>
<td>• Utilization of LD50, NOAEL and other toxicological data to establish limits and safety</td>
</tr>
</tbody>
</table>
Other Factors to Consider for Acceptance Criteria

**Understanding Clinical Relevance**

- How the Device is Used
  - Implant
  - Delivery Device
  - Surface Skin or Indirect

- Applying Toxicity Levels
  - LD50 Data – Injected, ingested, etc.
  - Establishing a general acceptance level, e.g. 1.5 PPM
  - NOAEL (no-observed-adverse-effect level)
  - LOAEL (lowest-observed-adverse-effect level)
Making the Perfect Batch (in cleaning)

Image: www.handletheheat.com
Validated Cleaning

Challenge your cleaning system through OQ & PQ portions of validation

Follow Your Master Validation Plan

- **OQ → Operational Qualification**
  - Principle is to challenge the system/equipment at nominal parameters to achieve cleanliness on representative product

- **PQ → Performance Qualification**
  - Challenged or worst-case scenario of your product through the standard production parameters in triplicate (at a minimum)
Risks to Validated Cleaning

Material Inputs
- Change in process or material upstream
- Not changing solutions
- Water systems
- Employee knowledge

Preventative Maintenance
- Cleaning tanks
- Routine equipment inspection & validations
- Distillation units
In Summary…

• Various ways of assessing cleanliness

• Options available – different ways to measure “clean”

• Choosing the right option for you
  – What materials are used in the device composition?
  – How is it fabricated?
  – How is the device utilized?
Choosing Your Path

- Risk based on inputs and outputs of your cleaning system
- Risk, e.g. Class I device vs. Class III device
- Identifying contaminants
  - Requesting **ALL** SDS from **ALL** suppliers
  - **No Unknowns** from the processing materials
- Retesting, monitoring, and requalification plans
How can QTS help?
Risk Mitigation at QTS

Customer-to-customer line clearance
- Protecting from cross-contamination

Tankless water systems
- Endotoxin-free DI water
- Lower risk of biofilm development & contamination

Dedicated cleaning environment
- Attached to our cleanrooms, reduces opportunity for contamination
- Special production team, primary focus is cleaning
QTS Sterilization & Cleaning Services Team

Sopheak Srun
Principal Sterilization Specialist
- BS Genetics, Cell Biology & Development
- MPH with a concentration in Epidemiology
- SM (NRCM), Microbiology Certification
- 10+ years in Medical Device Industry

Molly Swanson
Sterilization Specialist
- BS Genetics, Cell Biology & Development
- 4+ years in Medical Device Industry
- Extensive IQ/OQ/PQ experience
QTS Service & Expertise

1. Start with conversations about the best route for your organization and/or device needs
2. Suggest various cleaning processes
3. Choose applicable markers/tests
4. Verify/validate that the selected processes work
   – Coordinate lab testing & interpret results
5. Perform cleaning assessment(s) or adoptions
   – Biological comparisons
Connect with QTS:

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