



OINDP Component and Equipment Cleaning

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Key Sections of IPAC-RS GMP Guideline



- OINDP Components/Sub-components
- Quality Unit
- Change Control Supply & Quality Agreements
- Control of Suppliers and Sub-contractors
- Extractables
- **Cleaning**



Outline

- Why is Cleaning Important for OINDP?
- Environmental Conditions
- Dedicated and Non-Dedicated Equipment
- Component and Equipment Cleaning
- Cleaning Validation
- Packaging & Storage

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3



Why Clean?

- Patient safety
 - Minute quantities of residue can leach into the drug product, exposing patients to compounds with potential safety issues
 - Small particulates can irritate airways, particularly in asthmatics/individuals with compromised respiratory systems
- Product quality
- Impact on OINDP manufacturers' regulatory compliance
 - Potential impact on drug product registration
 - Leachables & extractables testing and specifications
 - Enumeration and characterization of foreign particulates
 - Microbiological testing and specifications

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Contamination Control

- Residues from manufacturing process
 - Mould release agents
 - Lubricants
 - Etc
- Environmental contamination and particulates
- Microbial contamination
- Cross-contamination from other materials
 - Particularly with use of non-dedicated equipment

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Potential Sources of Contamination

- Equipment (both dedicated and non-dedicated)
- Ancillary materials used in manufacture
- New raw materials introduced into the facility
- Other product lines
- Packaging & Storage containers
- Environmental conditions
- Cleaning materials
 - Ensure additional contaminants are not introduced

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Facility & Equipment Design

- Ideally, facilities and equipment should be chosen or designed to minimize contamination and facilitate cleaning
- Segregating work areas, e.g., through walls or barriers
 - May be helpful in avoiding cross-contamination
 - Especially useful for facilities that manufacture multiple products or that manufacture for both pharma and consumer or other markets



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Environmental Conditions

- Categories of environmental conditions are described in detail in the IPAC-RS Guideline (PS 9000 9.2)
 - Minimum conditions
 - Environment
 - Transit Packaging
 - Standard conditions
 - ISO Clean Room Conditions
 - Grade 5 →8 (Class 100 → 100,000)
 - Enhanced conditions
 - Microbial Control
 - Special Packaging

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Environmental Conditions

- Required conditions should be discussed and agreed on by the OINDP manufacturer and supplier for
 - Component manufacturing
 - Air used for product drying
 - Storage/packaging



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Dedicated/Non-Dedicated Equipment

- Dedicated equipment
 - Reduces risk of cross-contamination between materials
 - Does not eliminate risk of contamination
 - **Process should be considered:**
 - Complete tear down?
 - What cleaning agent?
- Non-dedicated equipment
 - Requires cleaning between materials
 - Nature and extent of cleaning should be determined based on risk assessment that considers the equipment, process, material, and component type
 - **Cleaning & Validation**
 - **Purge Cycle**

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Equipment and Component Cleaning

- Customer and supplier should discuss, agree, and document in the Quality Agreement
 - “What” you are removing
 - Requirements for cleaning
- Cleaning processes should be documented in SOPs, including
 - Materials
 - Maintenance
 - Verification checks/validation/re-validation requirements
 - Specifications
 - Process parameters
 - Reworking requirements (where appropriate)
- Cleaning activities should be recorded
 - Checklist



Equipment Cleaning / Validation & Verification

- Ensures that the cleaning process will result in an acceptably low level of contamination/material carryover
 - Agree on the level with your customer and documented
- Suppliers and customers should discuss validation requirements
 - Drug product contact components generally have more stringent requirements
 - Required where cleaning is to remove material to known/qualified level
- Validation protocol should be carefully defined and might include:
 - Cleaning materials/agents
 - Sampling sites & Methods for measuring contamination
 - Acceptable levels of contamination
 - Spiked recovery studies
 - Expiration date of cleaning
 - Revalidation requirements



Cleaning Validation

- When do I revalidate?
 - If there is any change to the cleaning process, materials, or equipment
 - Consult with and notifying customer to assess need for revalidation
- Following validation, the process should be monitored to ensure that cleaning continues to be effective during routine production

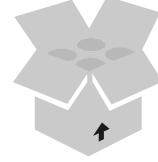


Component Cleaning

- Requirements for component cleaning should be discussed and agreed between the customer and supplier
 - particulates
 - microbial contamination
 - processing aids
- If the components are cleaned, cleaning should be verified, through, e.g., regular checks
 - Ensure that cleaning is effective
 - Ensure that ancillary materials are removed
 - Fully document



Packaging/Storage



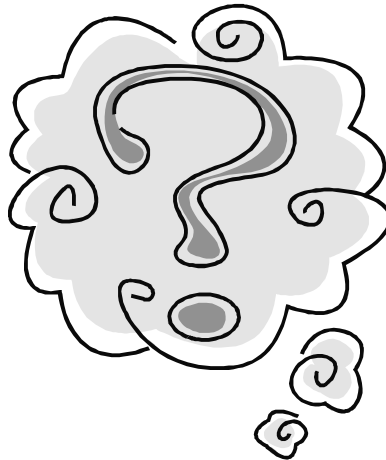
- Reusable containers used for raw material or product storage should be cleaned
 - Define cleaning process with customer
 - Agree on frequency
- Packaging materials can introduce contaminants and/or particulate matter
 - Packaging should be carefully selected in consultation with customer
- Packaging materials should
 - Not introduce contaminants or foreign particulates
 - Create an effective barrier to prevent contamination from external environment

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Questions?



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16