Toxic Material Handling

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High Potent Material Process Overview

Non aseptic Bulk
- Scaling and dispensing
- Formulation
- Sterilization
- Aseptic Filling
- Sterility testing

Aseptic Bulk
- Scaling and dispensing
- Formulation
- Aseptic Filling
- Sterility testing
High Potent Material Process Overview

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High Potent Material Process Overview

- Non aseptic Bulk
  - Scaling and dispensing
  - Sterility testing

- Aseptic Bulk
  - Formulation
  - Aseptic Filling
  - Sterility testing

Containment Solution
Aseptic Solution
High Potent Material Process Overview

Non aseptic Bulk
- Scaling and dispensing
- Formulation
  - Sterilization
  - Aseptic Filling
    - Rubber stopper
    - Environment monitoring etc.
- Sterility testing

Aseptic Bulk
- Scaling and dispensing
- Formulation
  - Container (Syringe vial and etc.)
- Aseptic Filling
  - Rubber stopper
  - Environment monitoring etc.
- Sterility testing
- Material in
- Dilution source
High Potent Material Process Overview

Non aseptic
Bulk

Scaling and dispensing

Formulation

Sterilization

Aseptic Filling

Sterility testing

Aseptic Bulk

Material in

Dilution source

Formulation

Aseptic Filling

Sterility testing

Rubber stopper

Container
(Syringe vial and etc.)

Environment monitoring etc

Dilution source

Material in

Rubber stopper

Environment monitoring etc
High Potent Material Process Overview

Non aseptic Bulk
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  - Environment monitoring etc.
  - Sterility testing

Aseptic Bulk
- Scaling and dispensing
- Formulation
- Aseptic Filling
  - Rubber stopper
  - Environment monitoring etc.
  - Sterility testing
Categorization of toxicity
Toxic Process  Containment Isolator

Non Aseptic and Toxic Bulk

Scaling and dispensing

Formulation

Aseptic Filling

Sterility testing

RTP
Material in/out etc.

Split Valve
Bulk in/out etc.

Filter (Containment) FiPa / FIBO

Liner connection
Material in/out etc.
Aseptic Formulation  Aseptic transfer

- Aseptic Bulk
- Scaling and dispensing
- Formulation
- Aseptic Filling
- Sterility testing

RTP
Environment monitoring / waste etc.

SART connector
WFI or any other sterile liquid

Connecting Isolator
Mobile unit from process to process

Rapid or Super rapid deco. Air lock (SARA)
Bulk Material etc.
Fill Finish

Aseptic Bulk ➔ Scaling and dispensing ➔ Formulation ➔ Aseptic Filling ➔ Sterility testing

Dry Heat Tunnel
Bulk material (Syringe / Vial / Ampule / Cartridge)

E-beam Sterilization
Tub Solution
Fill Finish

- Aseptic Bulk
- Scaling and dispensing
- Formulation
- Aseptic Filling
- Sterility testing

- Process system / Beta bag system
- Rubber stopper supply
- RTP
- Product Transfer
- RTP Tool/Waste etc.
Sterility Test

- Aseptic Bulk
- Scaling and dispensing
- Formulation
- Aseptic Filling

Sterility testing

SARA Tools/Waste etc.
RTP Tool/Waste etc.
ADC Process Storage final Product, Inspection, Packaging

- Aseptic ADC
- Storage final Product
- Inspection
- Packaging

Workshop with a Customer to design an appropriate solution

Isolator for Inspection

Isolator for Packaging
ADC Process Product and Format Change

Aseptic ADC

Off Line Cleaning

Isolator for Cleaning
Isolator
Isolator

- Leak
- Pressure
- Filter
- AHU
- Room
- Critical area
- Decontamination
- Process equipment
- Transfer / Connection
- Cleaning
- Qualification
- Monitoring
- Operator Training
- Maintenance
- Others
### Decision process of isolator leak rate

**Guideline (Internal and external)**

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<td>Erlass der Schweizerrischen Unfallversicherungsanstalt SUVA Grenzwerte am Arbeitsplatz 2003</td>
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<td>6</td>
<td>Power Point Presentation H₂O₂ gas Concentration Measurement</td>
<td>VSL. 31.03.2004</td>
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<td>10</td>
<td>Dichtigkeitsberechnung von Isolatoren</td>
<td>Excel Tabellen Kalkulation</td>
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Outline

- Isolator Analysis (GMP)
- ISO
- Containment Leak test method
- Isolator system risk analysis
- Risk analysis SIS700
- Swiss accident insurance
- Limitation for work station
- H₂O₂ gas concentration measurement
- H₂O₂ sensor calibration method
- Distribution of H₂O₂ gas
- Use of H₂O₂ sensor
- Calculation of isolator leak
Pressure

Differential pressure Only containment

Always negative pressure
Vial line (aseptic only)

Air Flow (by design, depending on phase)
Isolator

- Leak
- Pressure
- Filter
- AHU
- Room
- Critical area
- Decontamination
- Process equipment
- Transfer / Connection
- Cleaning
- Qualification
- Monitoring
- Operator Training
- Maintenance
- Others
- Others

Room

AHU

Filter

Pressure

Leak

Critical area

Decontamination

Process equipment

Transfer / Connection

Cleaning

Qualification

Monitoring

Operator Training

Maintenance

Others

Others

Others

Others
Filter

• BIBO
Filter

**Issues of BIBO solution**

1. Replace the filter in interstitial area (exposure risk)
2. Space required to replace the filter
3. Washing from dedicated exhaust area to BIBO
4. Cleaning validation for the above area
5. High consumption of washing water

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1. Containment solution within isolator (No toxic substances outside isolator)
2. Space for filter replacement can be reduced.
3. Dedicated exhaust area should be out of scope for washing.
4. Cleaning validation can be limited inside isolator.
5. Minimize waste water.
• FIBO
Filter
Filter

FIPA
Filter

FIPA filters
Isolator

Leak
Pressure
Filter
AHU
Room
Critical area
Decontamination
Process equipment
Cleaning
Qualification
Monitoring
Operator Training
Maintenance
Others
Filtration
Sterilization for Bulk and Tub
Transfer

Split Valve

Information by Charge point / Buck
Transfer

RTP
Transfer

Liquid Transport (AT port)
Transfer

Liner
Transfer

Pass box
Summary

**Containment solution**
Select proper containment solution

**Aseptic solution**
Always important to stand both containment and aseptic

**Connection**
Select proper connection based on the process and material handling
Thank you