

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



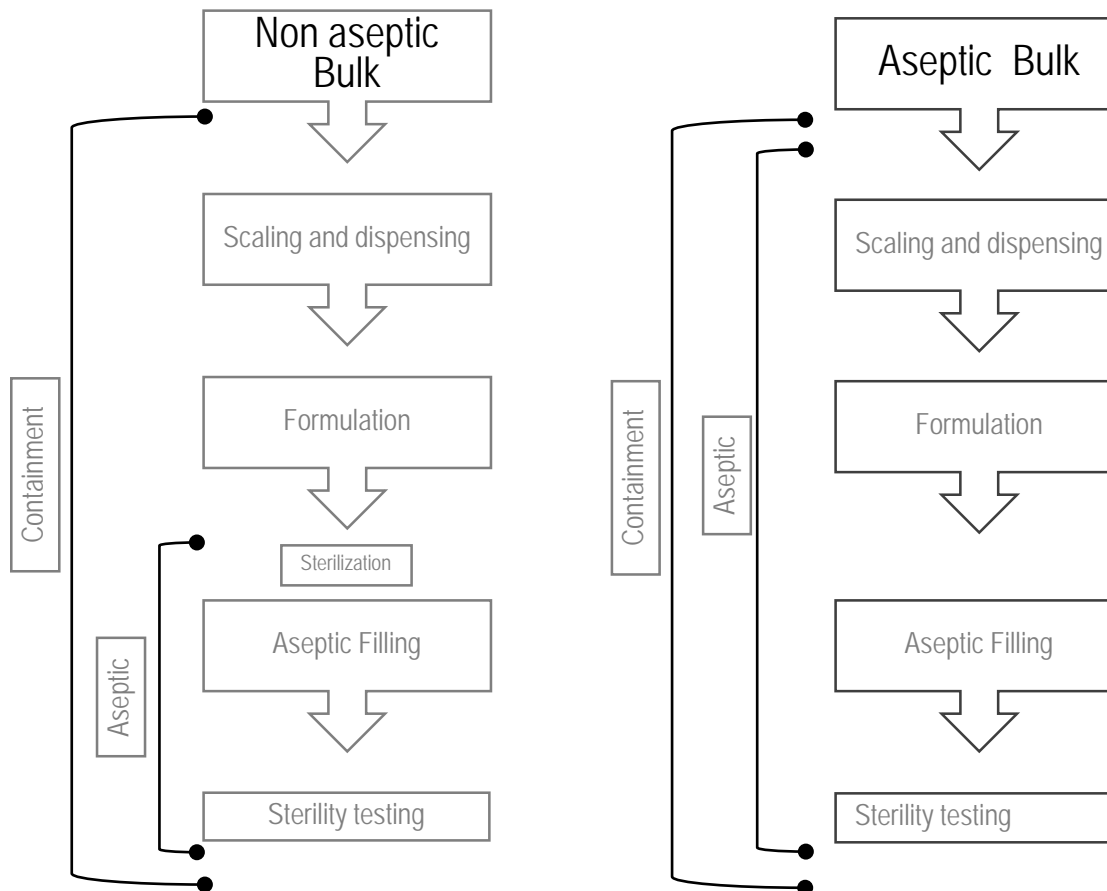
Aseptic Filling



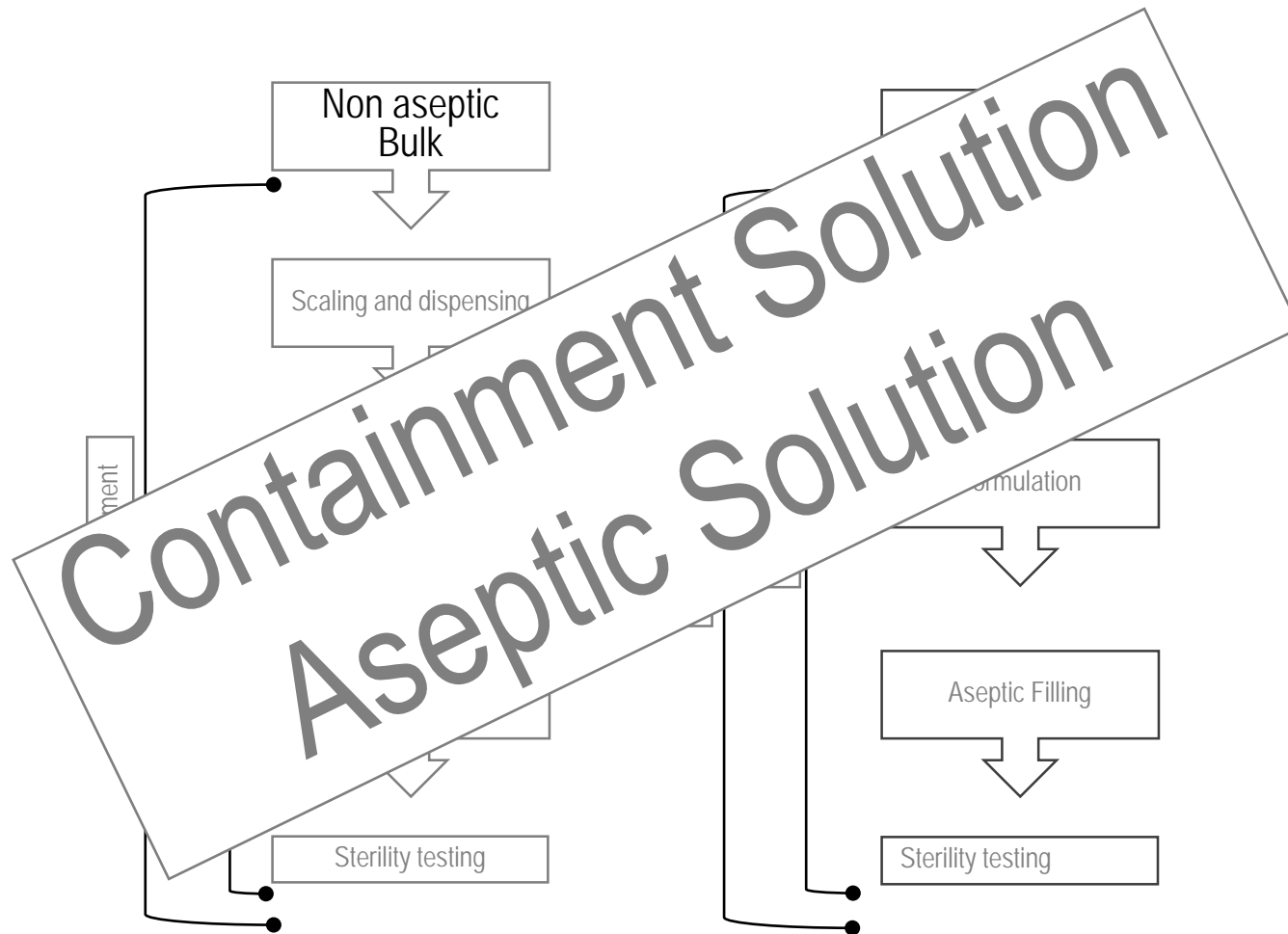
Sterility testing



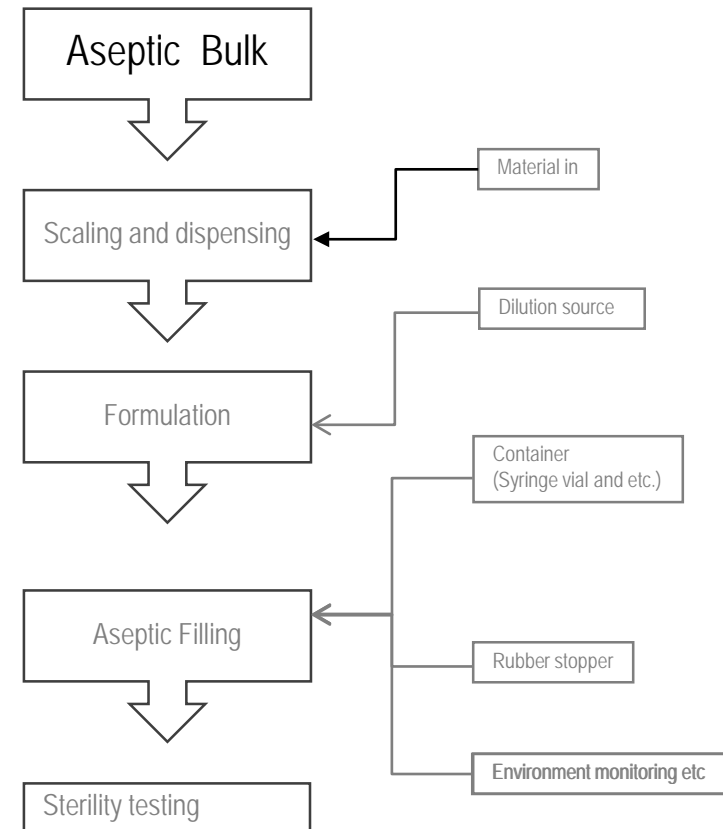
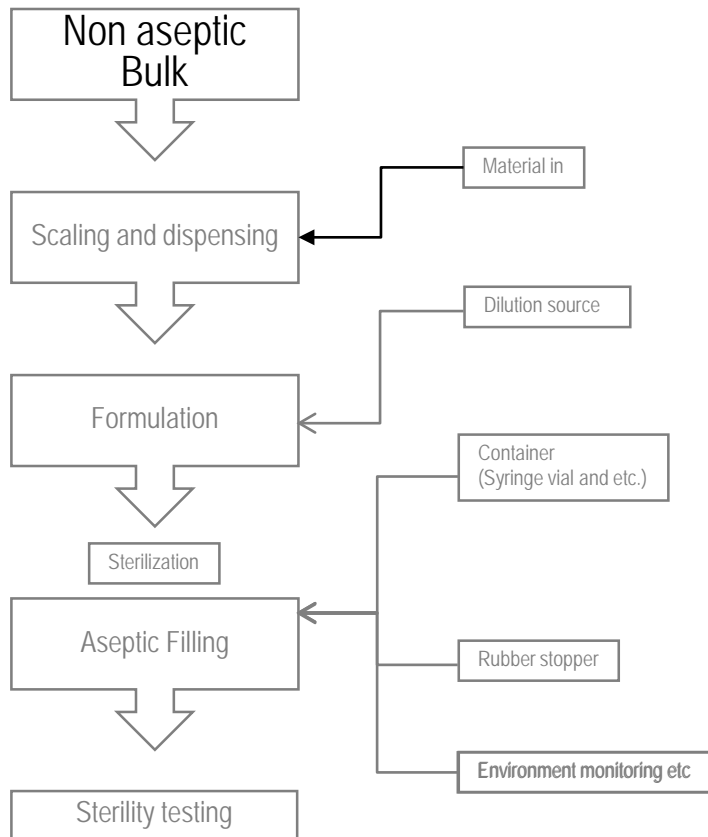
High Potent Material Process Overview



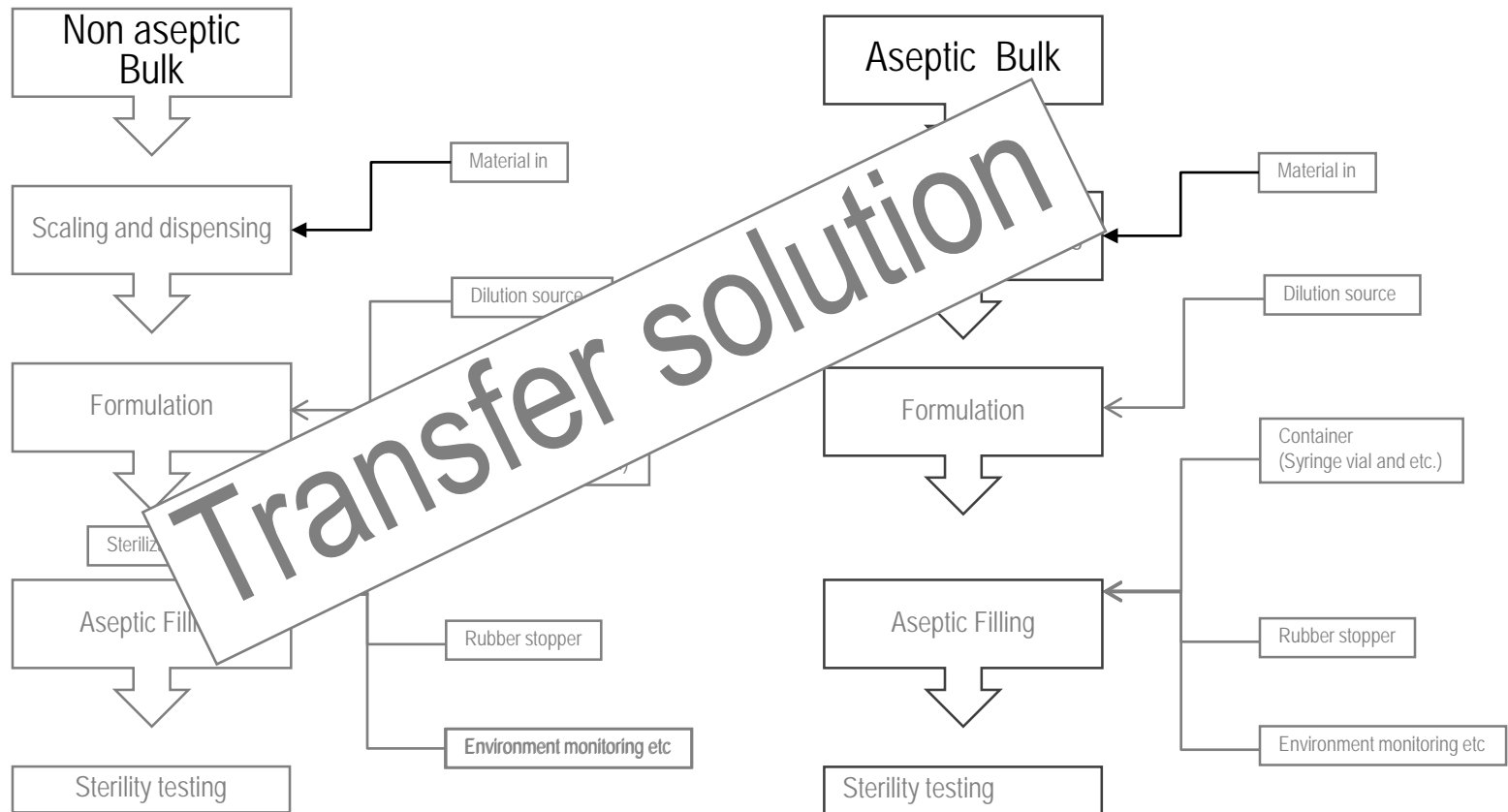
High Potent Material Process Overview



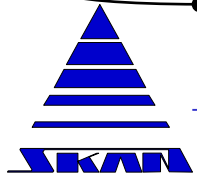
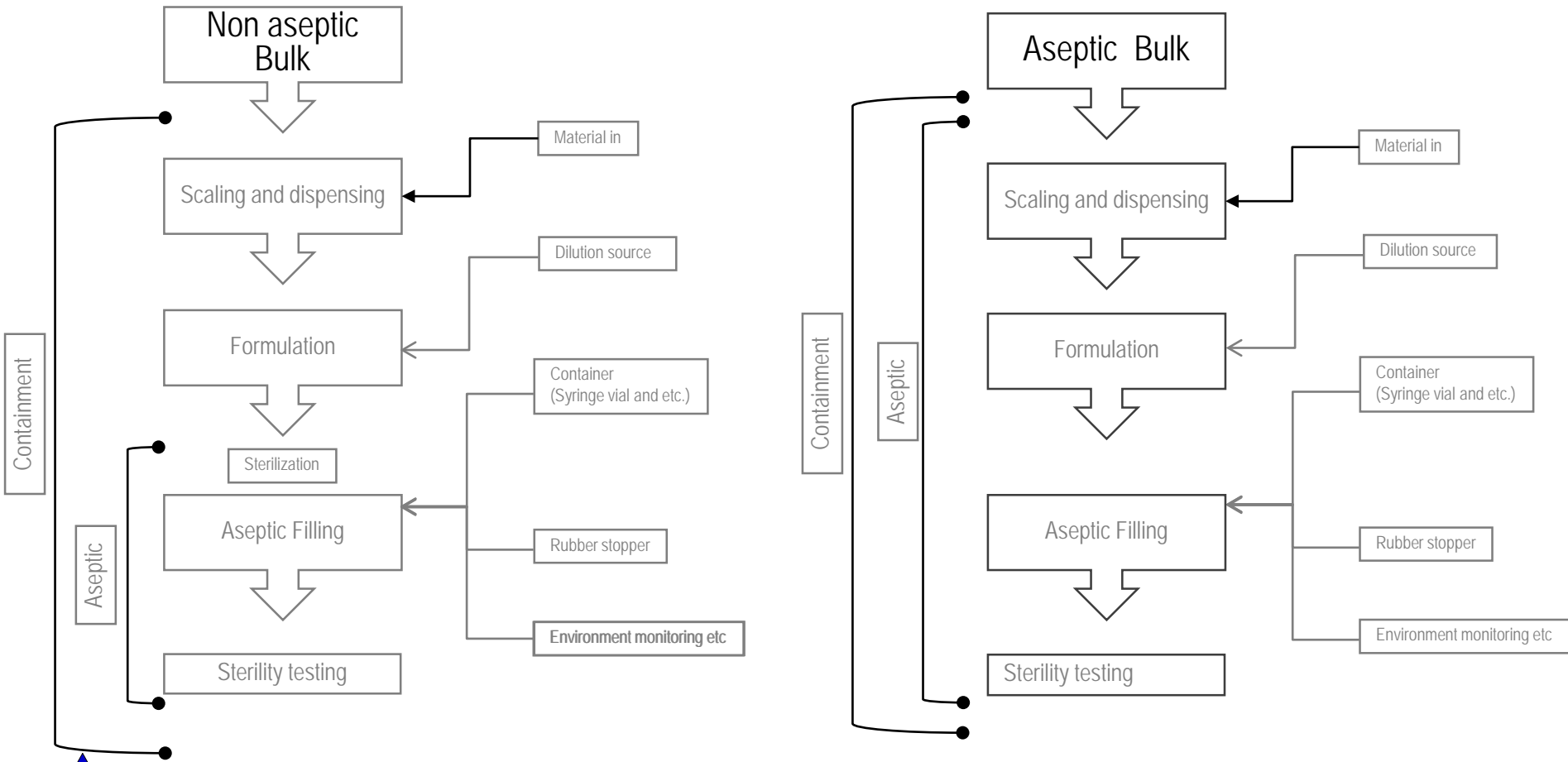
High Potent Material Process Overview



High Potent Material Process Overview



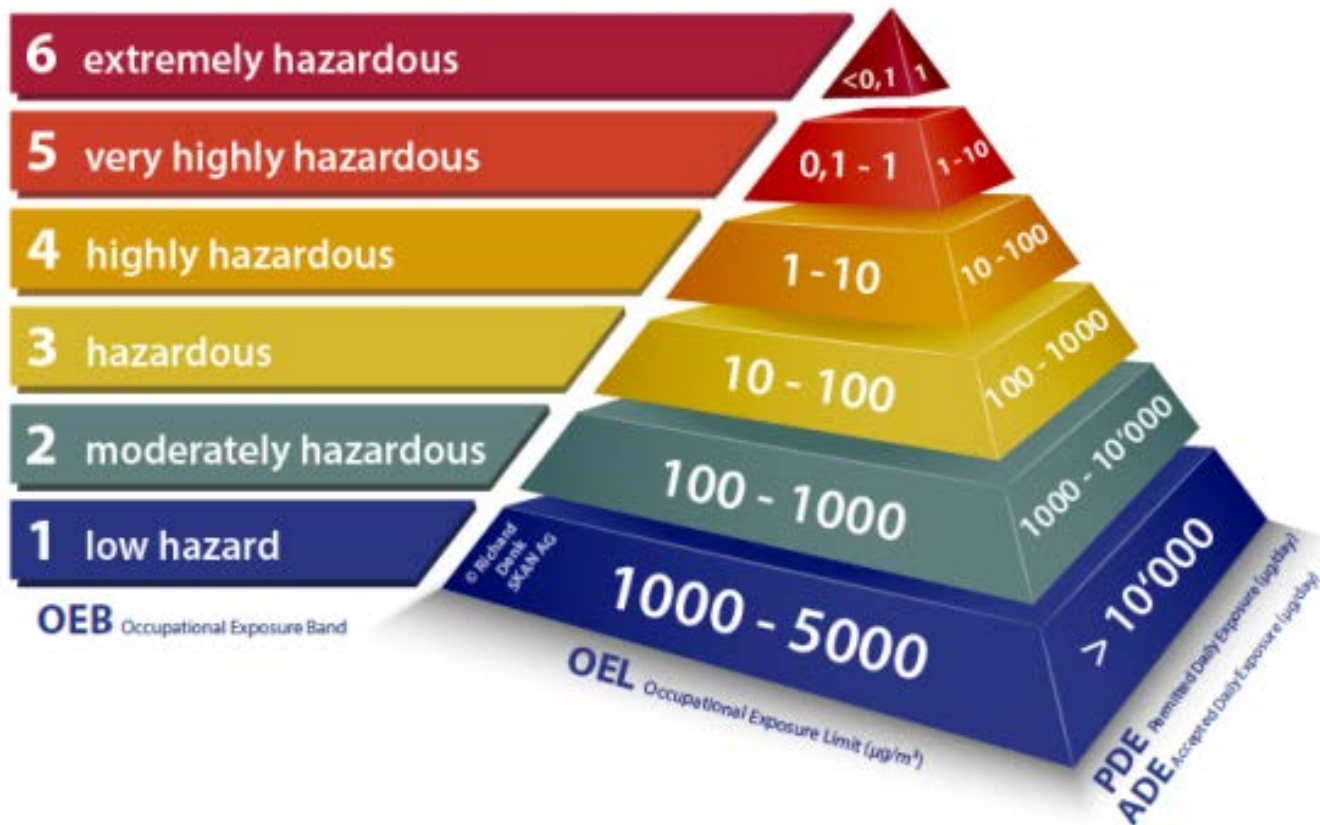
High Potent Material Process Overview



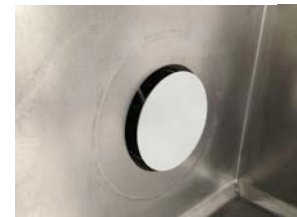
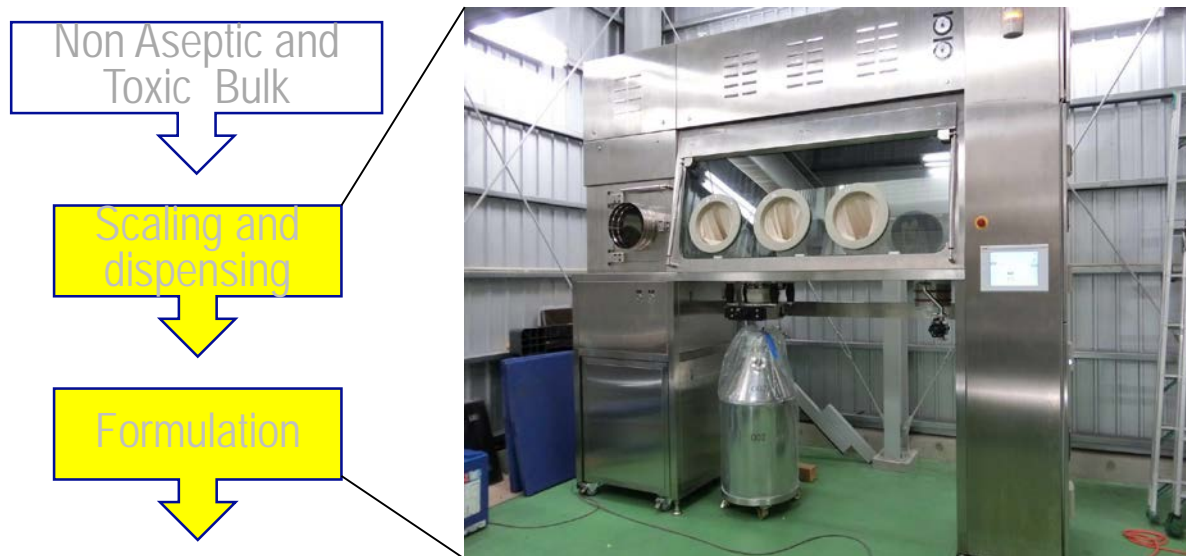
Categorization of toxicity



Containment Classification



Toxic Process Containment Isolator



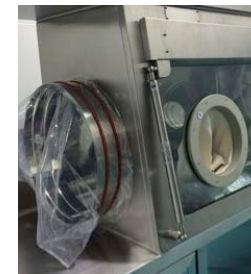
Filter (Containment)
FiPa / FIBO



RTP
Material in/out etc.



Split Valve
Bulk in/out etc.



Liner connection
Material in/out etc.

Aseptic Formulation Aseptic transfer



Connecting Isolator
Mobile unit from process to process



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

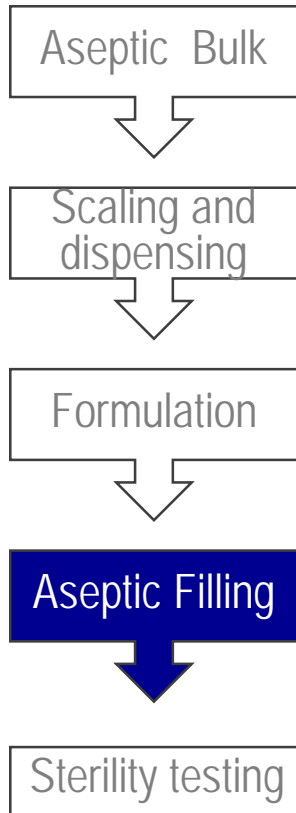


RTP
Environment monitoring / waste etc.



SART connector
WFI or any other sterile liquid

Fill Finish

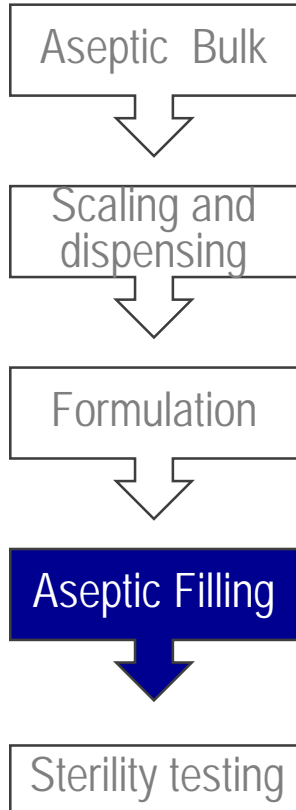


E-beam Sterilization
Tub Solution



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

Fill Finish



Process system / Beta bag system
Rubber stopper supply



RTP
Product Transfer

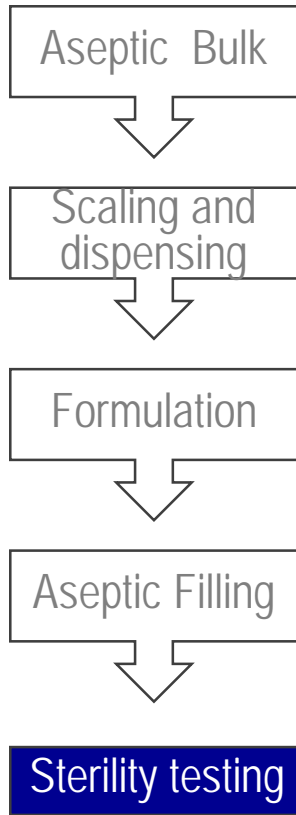


RTP
Tool/Waste etc.



SARA
Tools / Waste etc.

Sterility Test



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

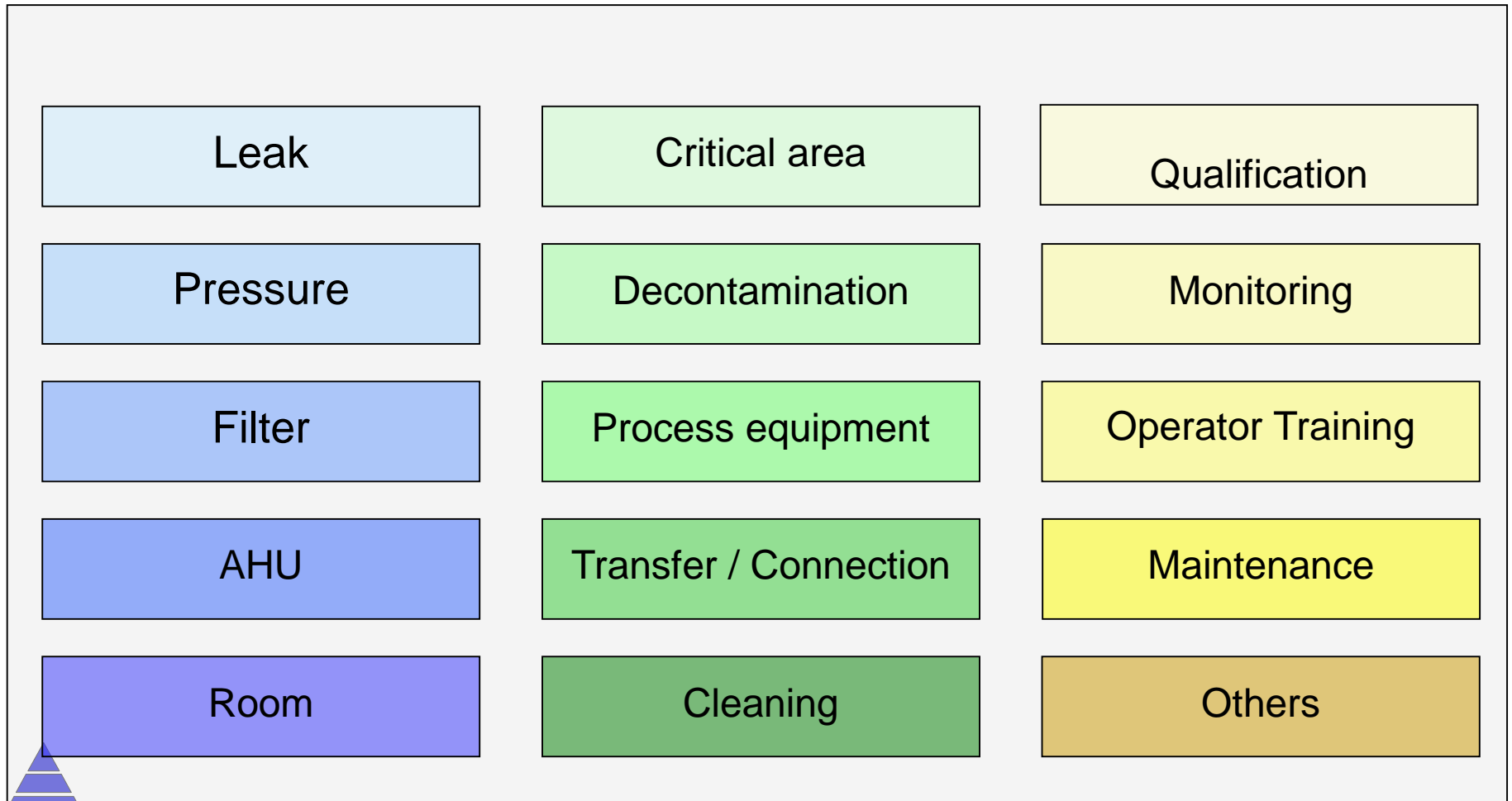


Isolator for Cleaning

Isolator



Isolator



Decision process of isolator leak rate

Guideline (Internal and external)

| Pos | Title | Dokumenten ID | |
|-----|--|---|---|
| 1 | Analyse der GMP Anforderungen an Isolatorsysteme | 4-04-800-013513A04 | Outline Isolator Analysis (GMP) |
| 2 | ISO 10648-2(1994) Containment enclosures – part2: classification according to leak tightness and associated checking methods. | ISO 10648-2(1994) | ISO Containment Leak test method |
| 3 | Risikoanalyse Isolatorsysteme | 015287_A | Isolator system risk analysis |
| 4 | Risikoanalyse SIS 700 | 015293_A | Risk analysis SIS700 |
| 5 | Erlass der Schweizerrischen Unfallversicherungsanstalt SUVA Grenzwerte am Arbeitsplatz 2003 | SUVA; 1903.d | Swiss accident insurance Limitation for work station |
| 6 | Power Point Presentation H2O2 gas Concentration Measurement | VSI, 31.03.2004 | H2O2 gas concentration measurement |
| 7 | A validated Calibration Method for Hydrogen Peroxide Gas | PDA Journal, Vol.55, No.1, Jan./Feb.2001 | H2O2 sensor calibration method |
| 8 | Theoretical Analysis of the Condensation of Hydrogen Peroxide Gas and Water Vapour as Used in Surface Decontamination | PDA Journal, Vol.56, No.6, Nov./Dec.2002 | Distribution of H2O2 gas |
| 9 | Application of a Newly Developed Hydrogen Peroxide Vapour Phase Sensor to HPV Sterilizer | PDA Journal, Vol.52, No.1, Jan./Feb.1998 | Use of H2O2 sensor |
| 10 | Dichtigkeitsberechnung von Isolatoren | Excel Tabellen Kalkulation | Calculation of isolator leak |

Isolator

Leak

Critical area

Qualification

Pressure

Decontamination

Monitoring

Filter

Process equipment

Operator Training

AHU

Transfer / Connection

Maintenance

Room

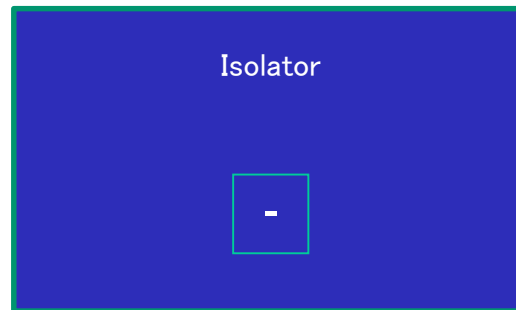
Cleaning

Others



Pressure

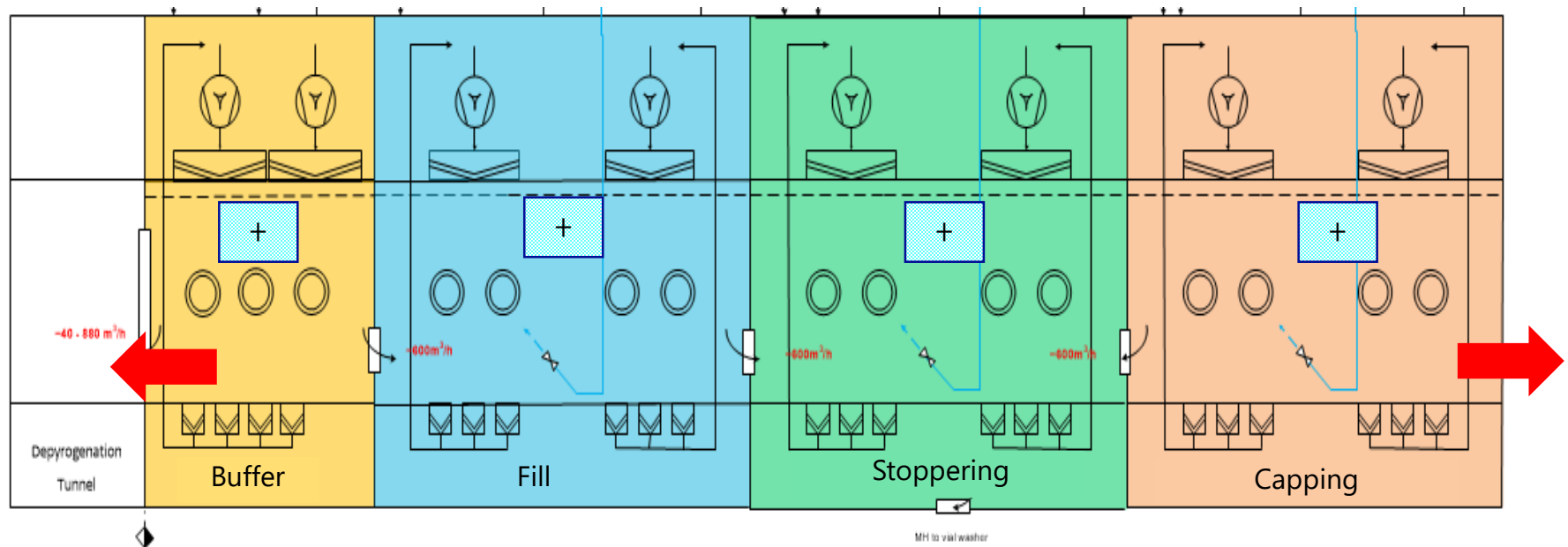
Differential pressure Only containment



Always negative pressure

Pressure

Vial line (aseptic only)



← Air Flow (by design, depending on phase)



Isolator

Leak

Critical area

Qualification

Pressure

Decontamination

Monitoring

Filter

Process equipment

Operator Training

AHU

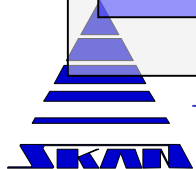
Transfer / Connection

Maintenance

Room

Cleaning

Others

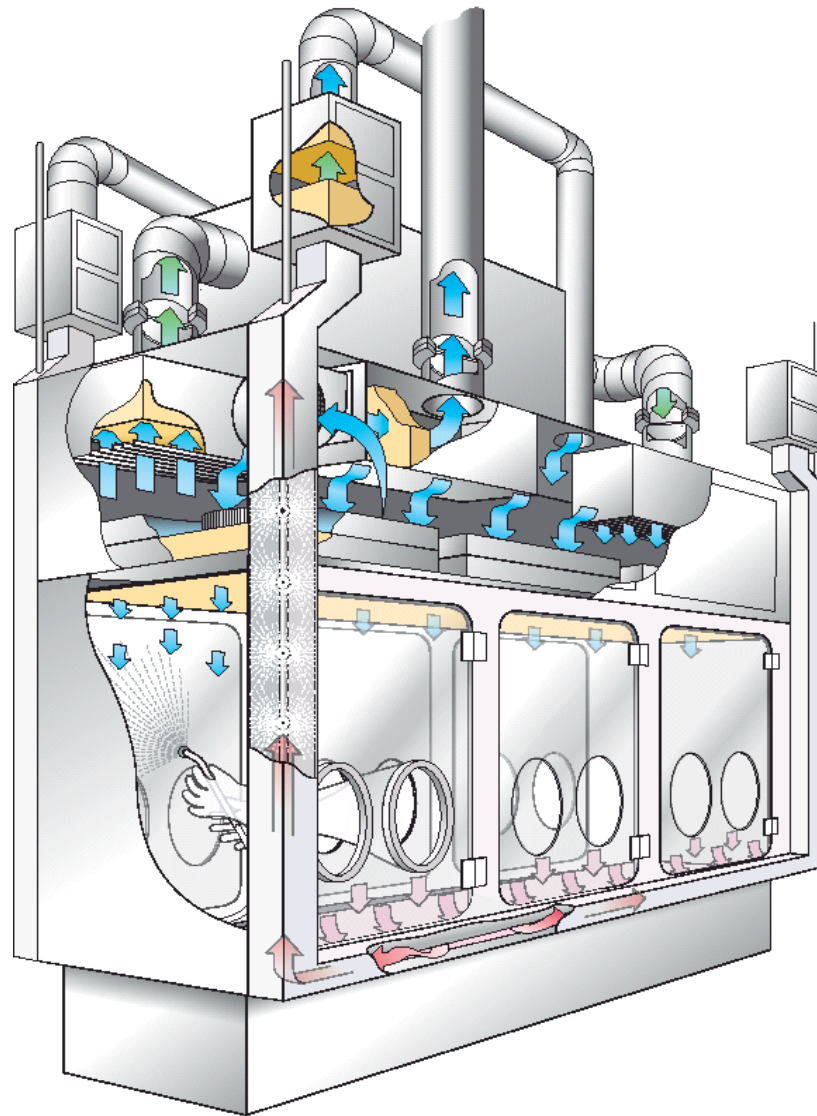


Filter

- BIBO



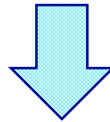
Filter



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



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

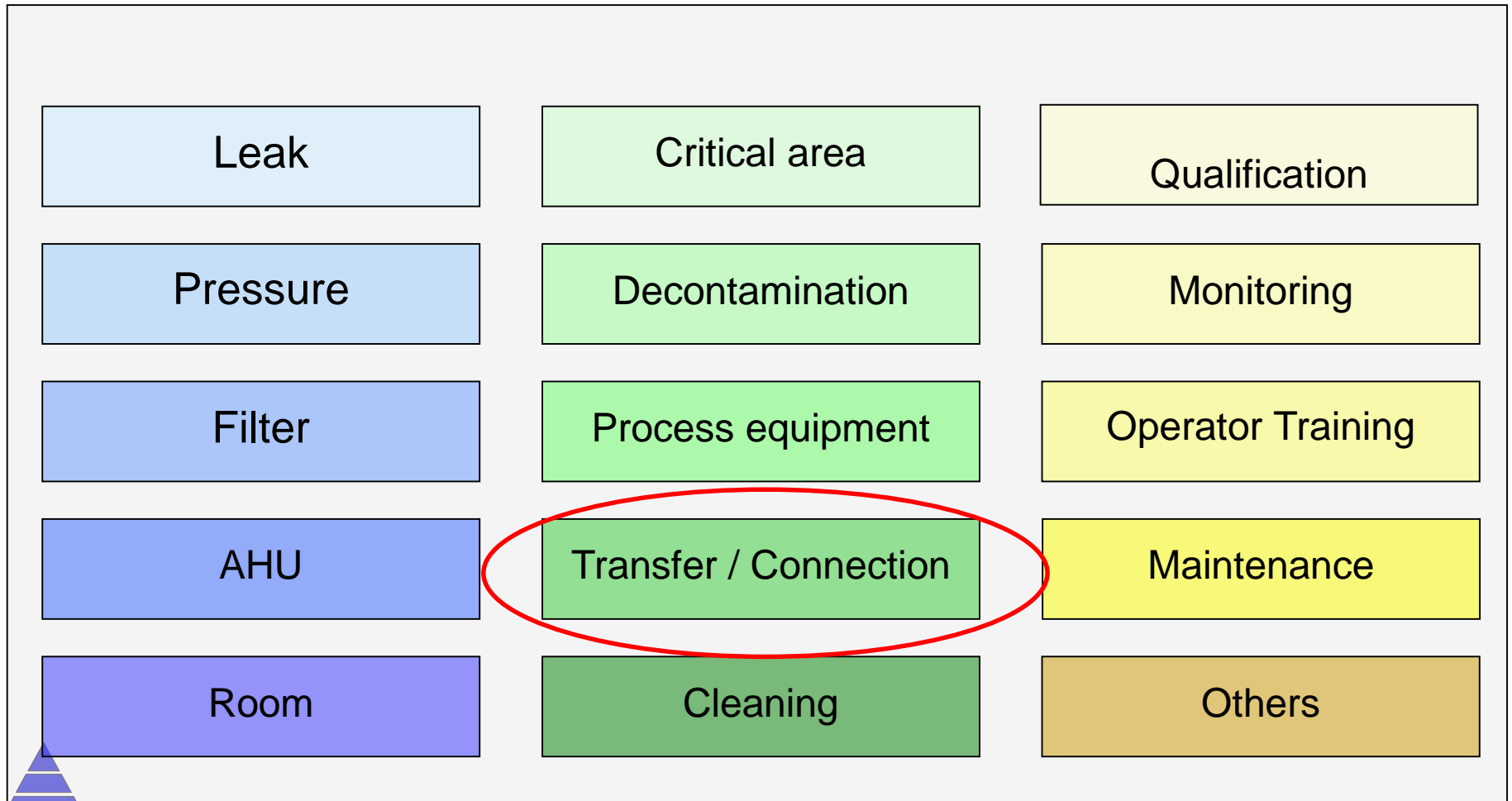


Filter

FIPA filters



Isolator



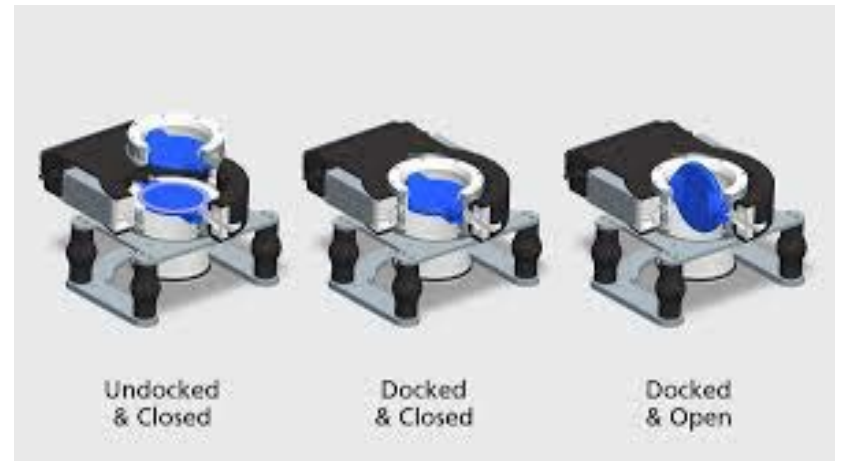
Filtration

Sterilization for Bulk and Tub



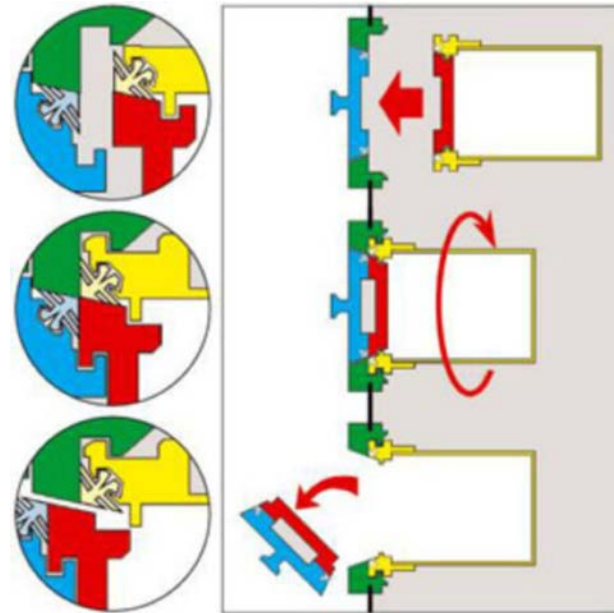
Transfer

Split Valve



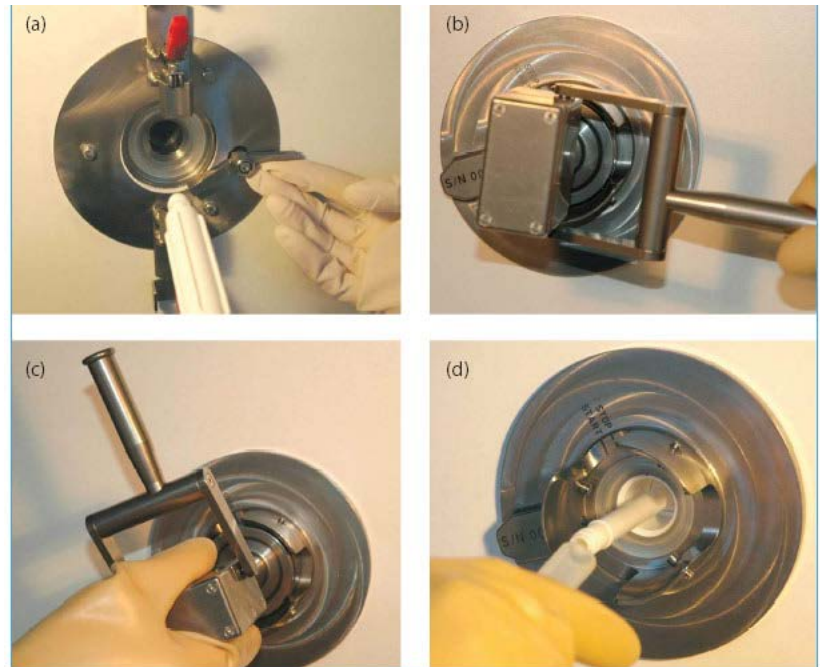
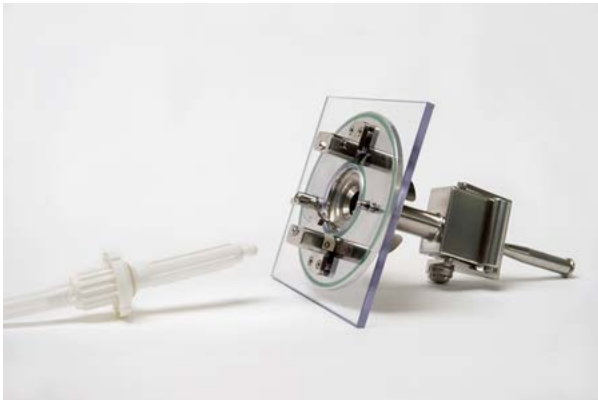
Transfer

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