Isolator Technology for Aseptic Manufacturing

May 29, 2015

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Definition of Isolator Technology

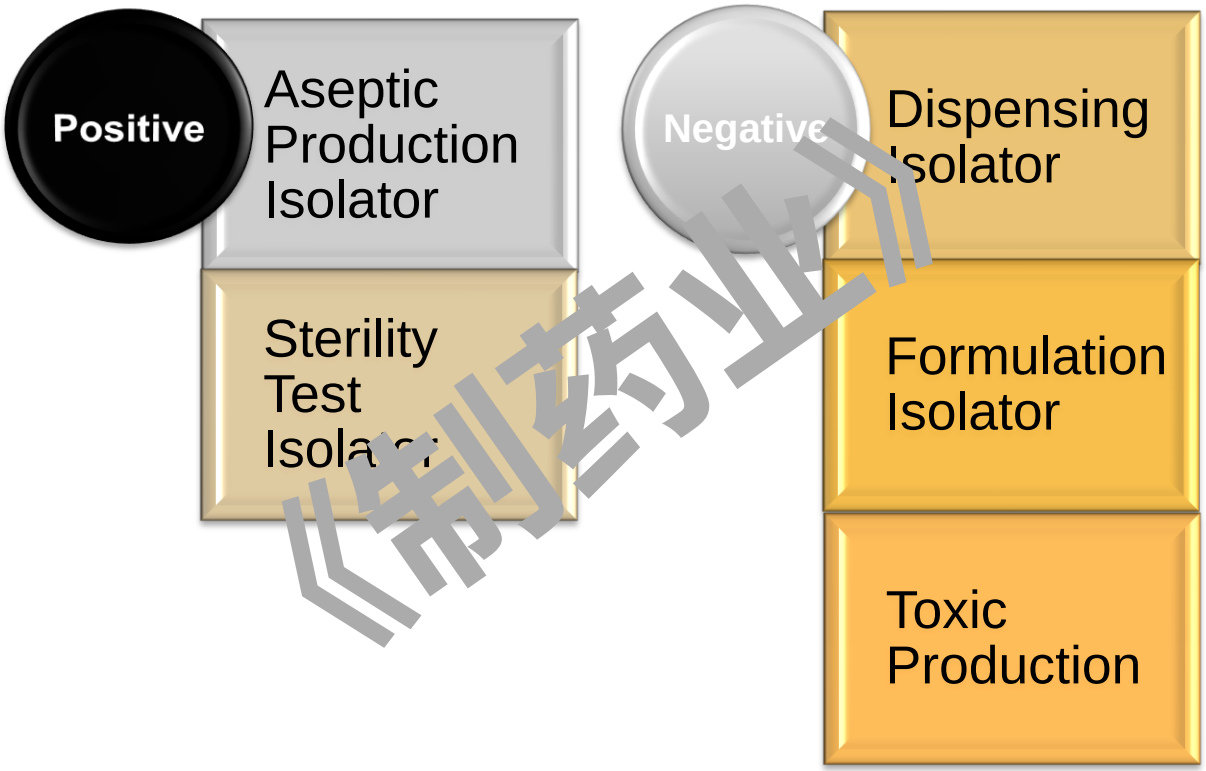
A localized environment created by a sealed enclosure to isolate the product from contamination and/or people.

ISO 14644-7:Separative Enclosure (Clean Air Hoods, Gloveboxes, Isolators, Mini-environments)

"A well-designed positive pressure isolator, supported by adequate procedures for its maintenance, monitoring, and control, offers tangible advantages over traditional aseptic processing, including lower opportunities for microbial contamination during processing. „

Guidance for Industry
Sterile Drug Products Produced by Aseptic Processing
— Current Good Manufacturing Practice

Isolator Types and Applications



Isolator Types and Applications

The routine usage of isolators in the pharmaceutical industry follows the usual steps to produce medications:

- Fine Chemical Production
- Sampling/Dispensing
- Mixing/Compounding
- Aseptic Filling/ Stoppering/Capping
- Lyophilizer Loading/Unloading
- Final testing (Sterility Testing)

Isolator Types and Applications

Containment Isolators

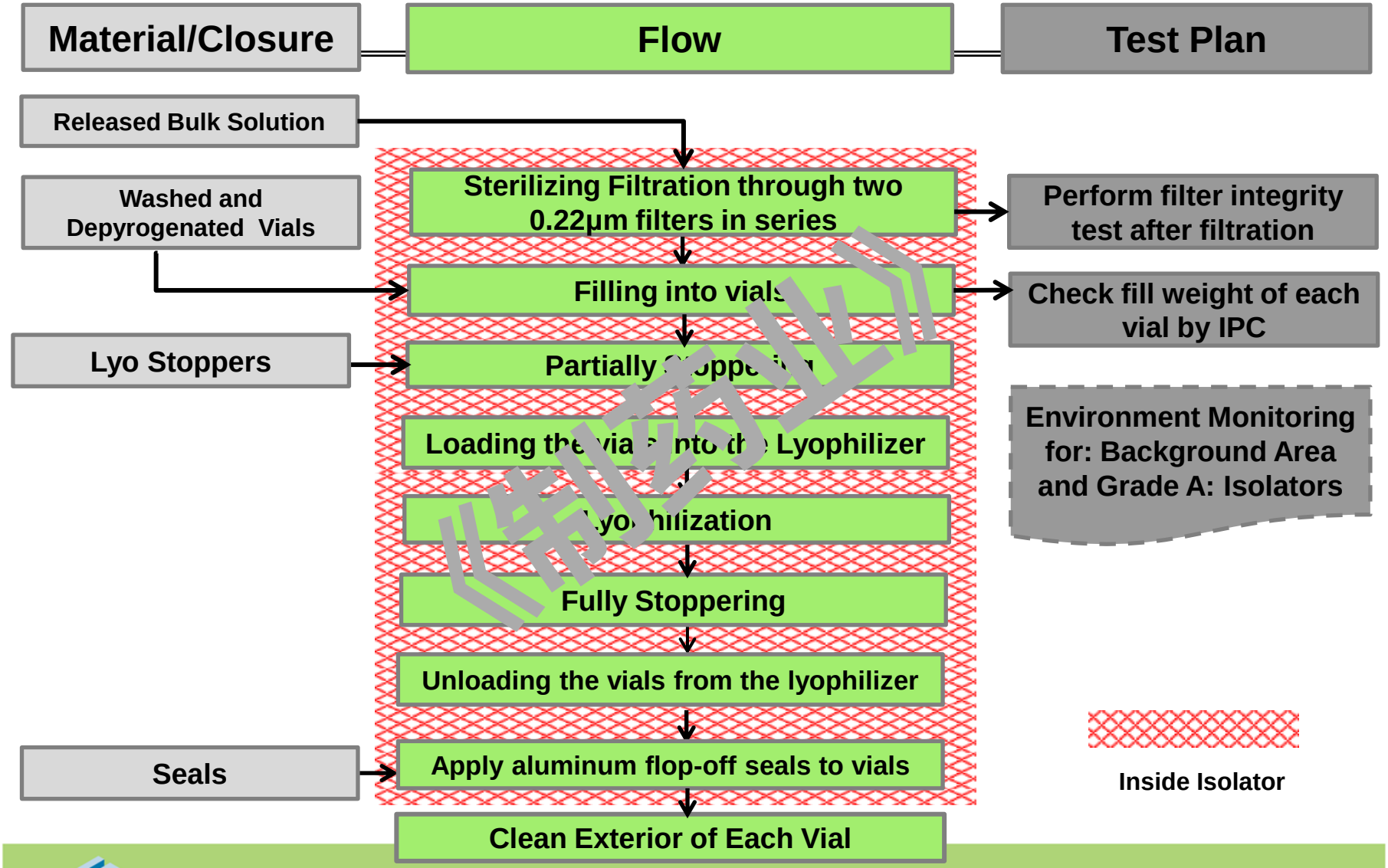
- Generally negative pressure
- Typically ISO 7 (Class 10,000 at rest, Grade C)
- No air exchange with the surrounding environment (except through a HEPA filter)
- Equipped with nitrogen supply if required
- All materials exiting the isolator must be cleaned or contained
- Cleanable in a reproducible and quantifiable manner; swab-tests and tracer substances should be used during qualification

Isolator Types and Applications

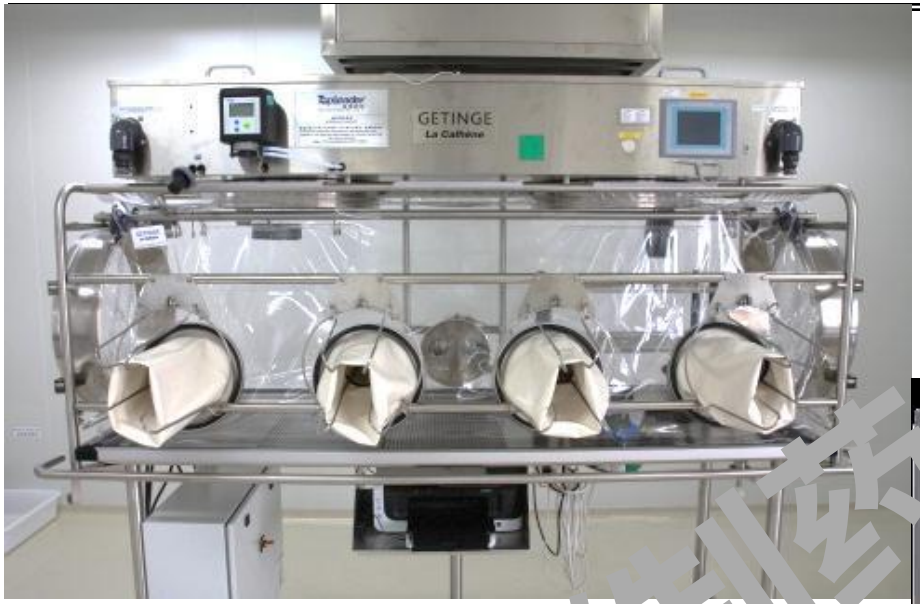
Isolators for Aseptic Processing

- No air exchange with the surrounding environment except when that air passes though a HEPA filter
- Typically classified as ISO 5 (Class 100, Grade A)
- Typically operated under positive pressure/subject to decontamination procedures prior to use
- Decontaminated in a reproducible manner (VHP,ClO_2….)
- All materials that enter the isolator must be sterilized and must enter either directly through a decontaminating or sterilizing system or via a rapid transfer port

A Typical Aseptic Processing

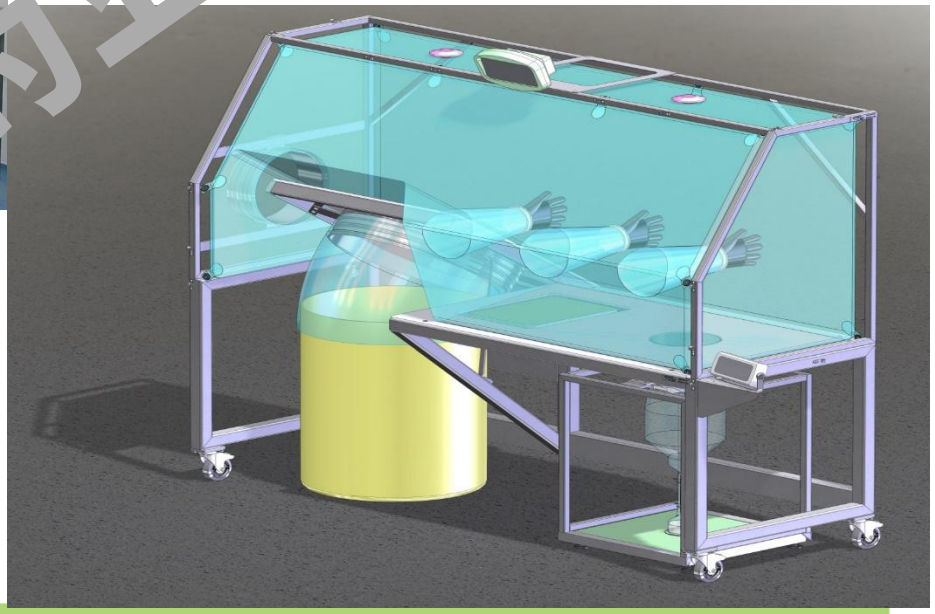


Typical Applications in Aseptic Manufacturing



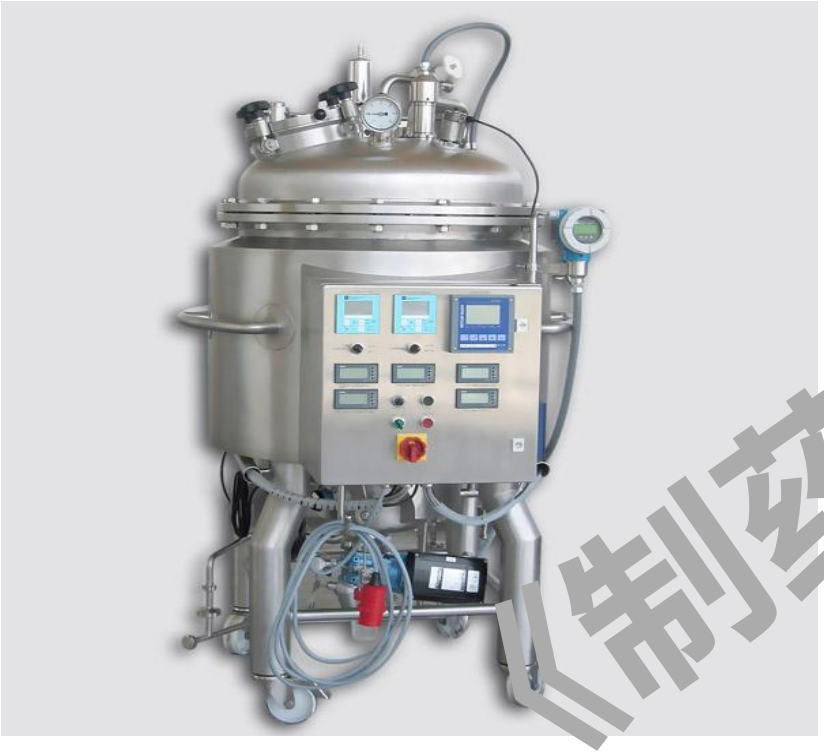
Sterility Test Isolator

Typical Applications in Aseptic Manufacturing



Sampling/Dispensing

Typical Applications in Aseptic Manufacturing



Formulation

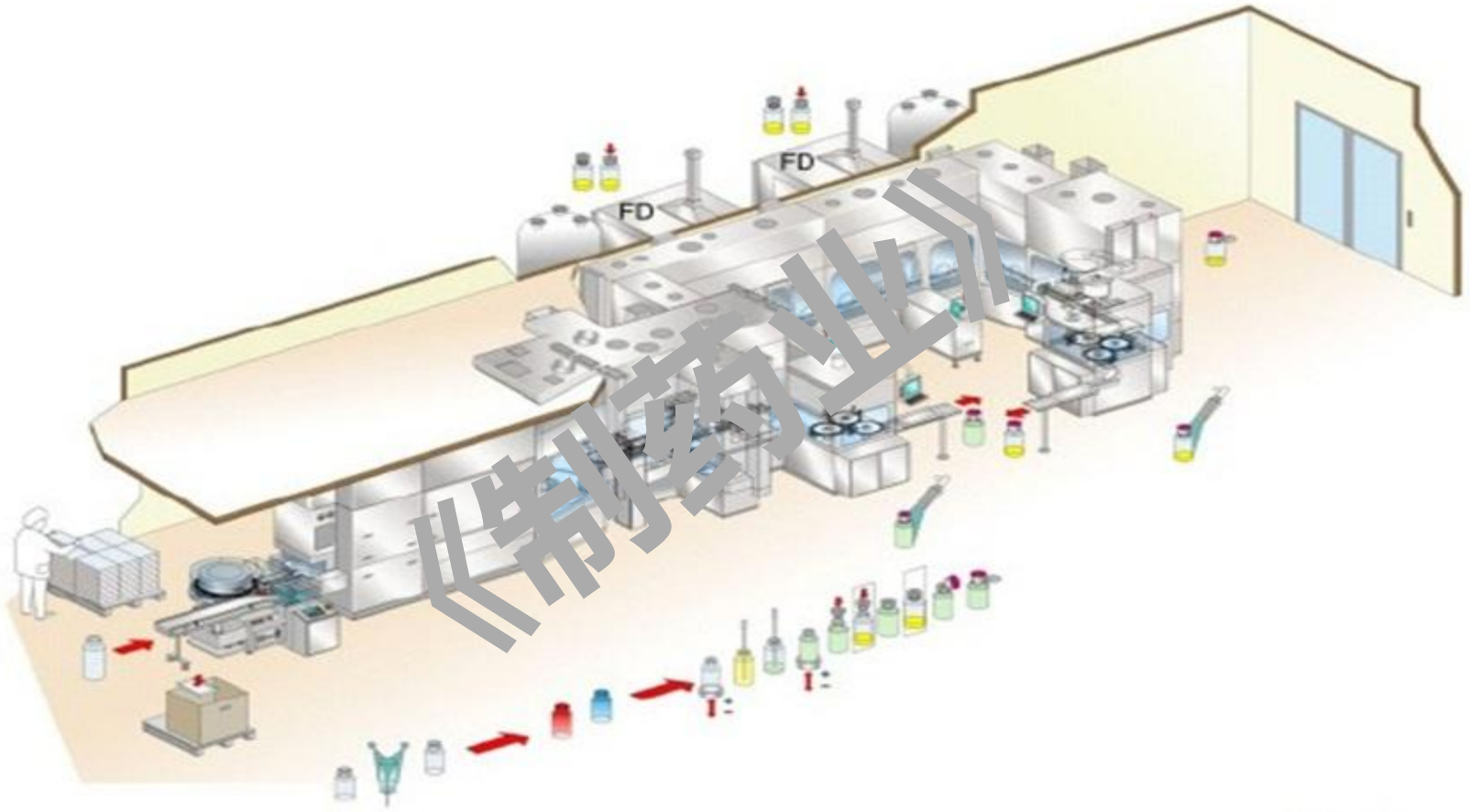
Typical Applications in Aseptic Manufacturing

Small Scale Filling Isolator

Typical Applications in Aseptic Manufacturing

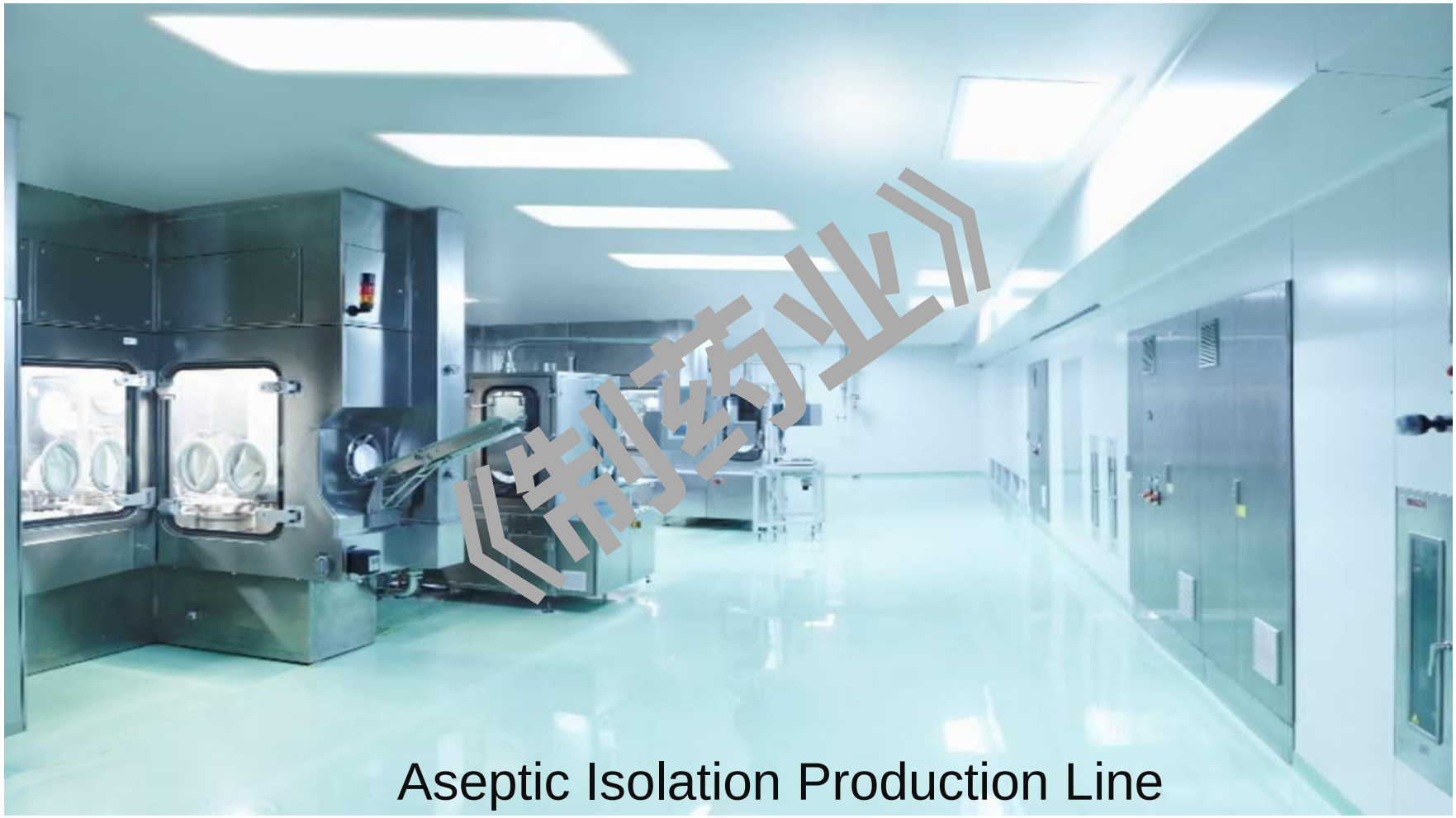
Large Scale Filling Isolator

Typical Applications in Aseptic Manufacturing



Integrated Isolation Production Line

Typical Applications in Aseptic Manufacturing



Aseptic Isolation Production Line

Typical Applications in Aseptic Manufacturing

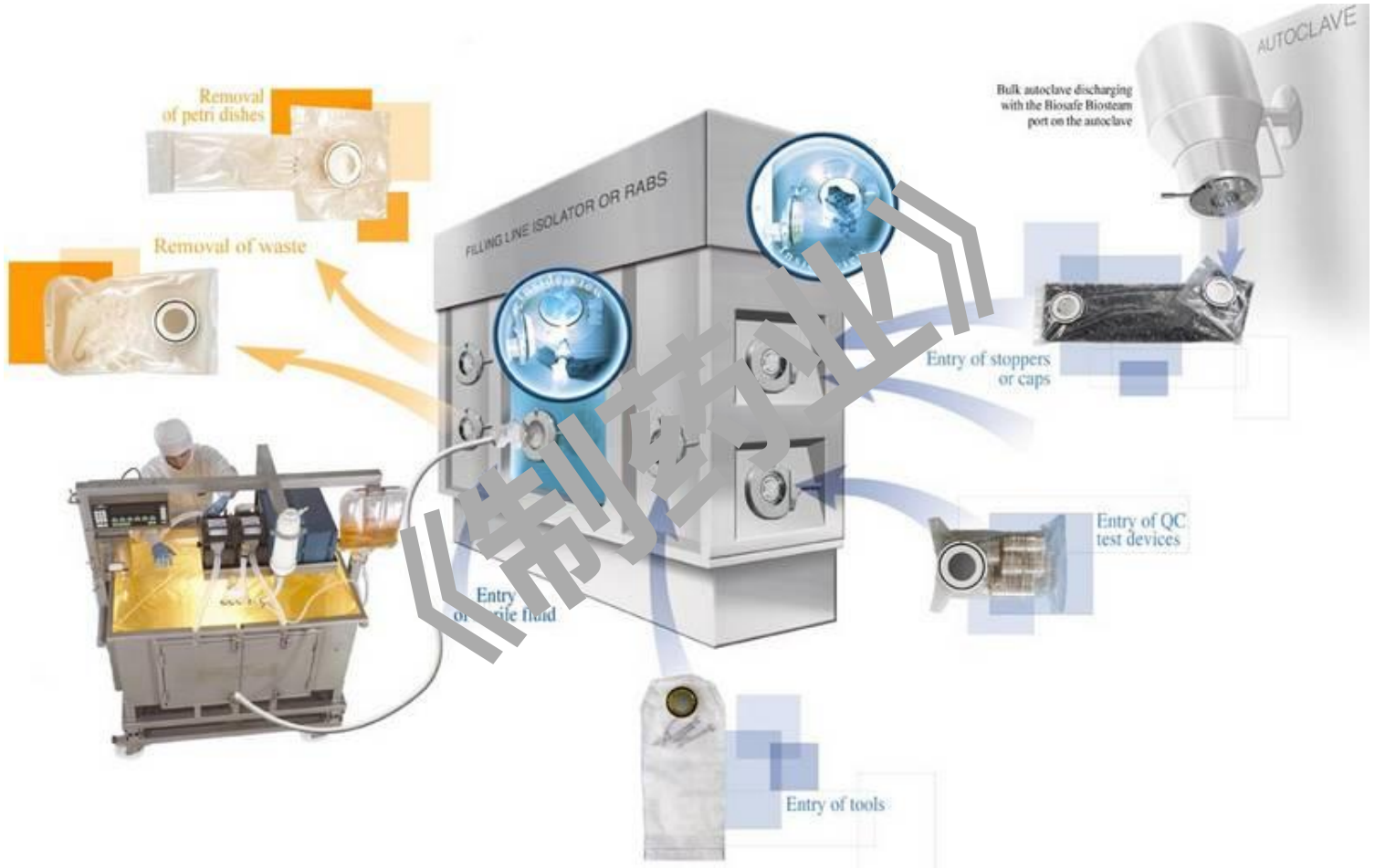
Aseptic Filling Operation

Typical Applications in Aseptic Manufacturing

Capping Station

ALUS

Critical Design Considerations



Critical Design Considerations

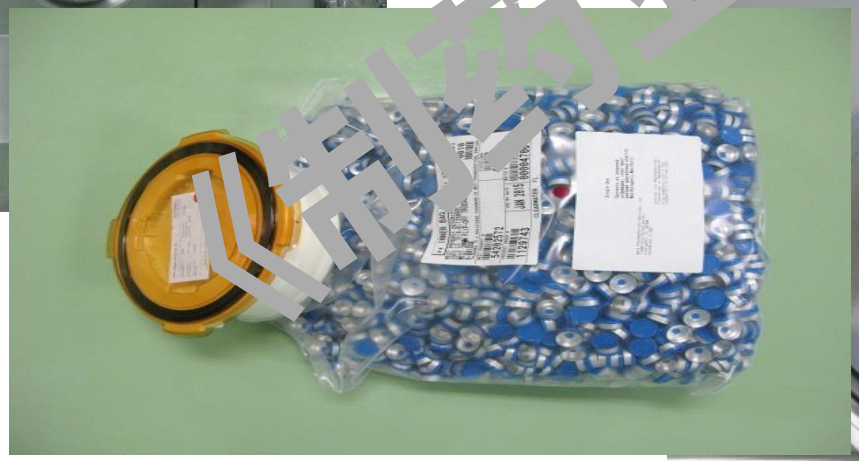
- Gloves/Gauntlets
- RTP(Rapid Transfer Port)
- RTA(Rapid Transfer Airlock)
- ART(Aseptic Rapid Transfer)
- Mouse Hole
- FIPA/BIBO
- ……..

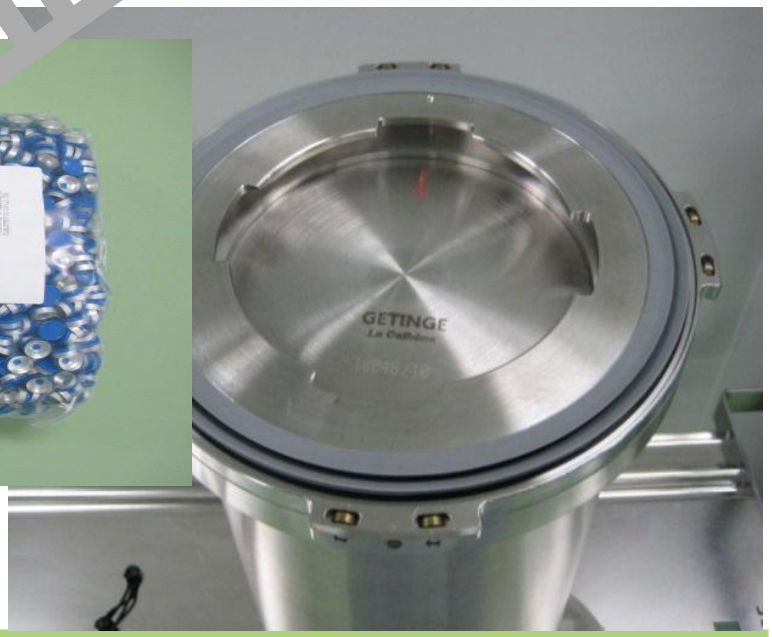
Critical Design Considerations

Gloves & Integrity Testing

Critical Design Considerations

Rapid Transfer Port





Critical Design Considerations

Rapid Transfer Port

Critical Design Considerations

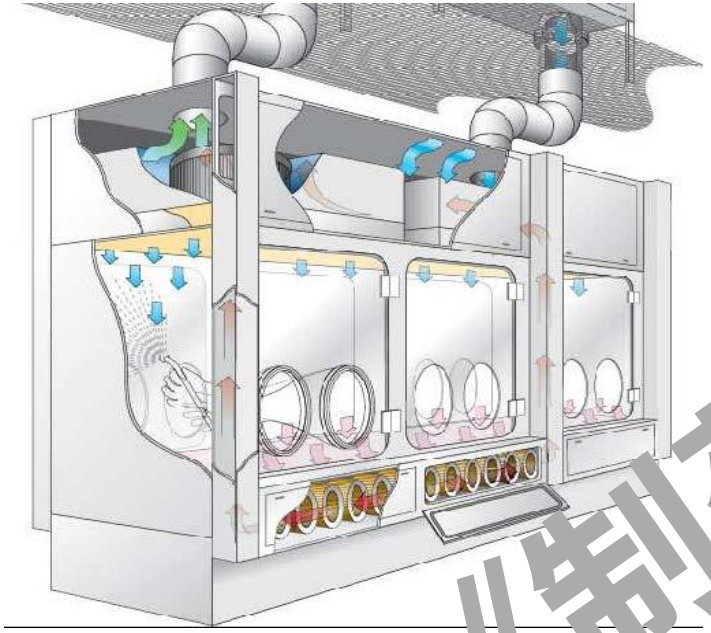
Disposable vs Reusable

Critical Design Considerations

Mouse Hole vs RTA

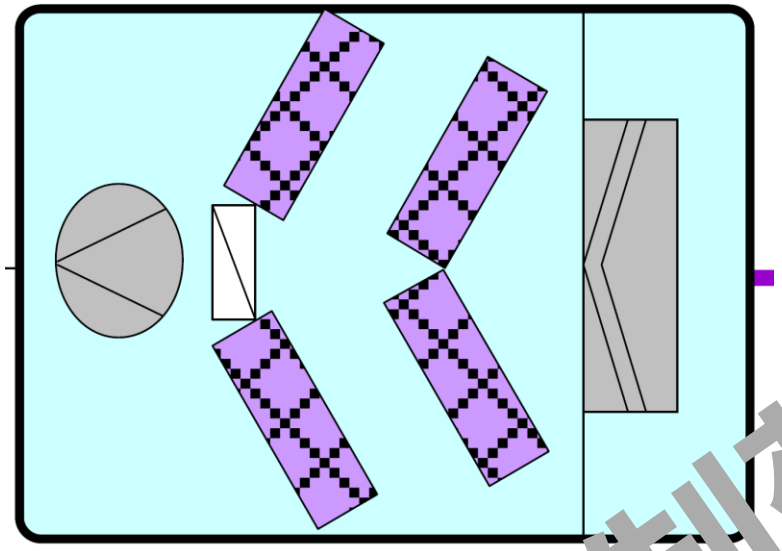
Standalone or Integrated

Critical Design Considerations



FIPA vs BIBO

Critical Design Considerations



AHU with Catalytic Converter Unit vs Conventional Ones

Critical Design Considerations

Intake Air from the Background Clean Area vs Other Area

Biodecontamination

Biodecontamination of the Isolator and Internal Equipment Surfaces Decontamination is a more reasonable objective than sterilization for the non-product contact surfaces of isolators. A 5 to 6 log reduction of resistant BIs is certainly sufficient (the complete kill of indicators with a population of 10^6 spores).

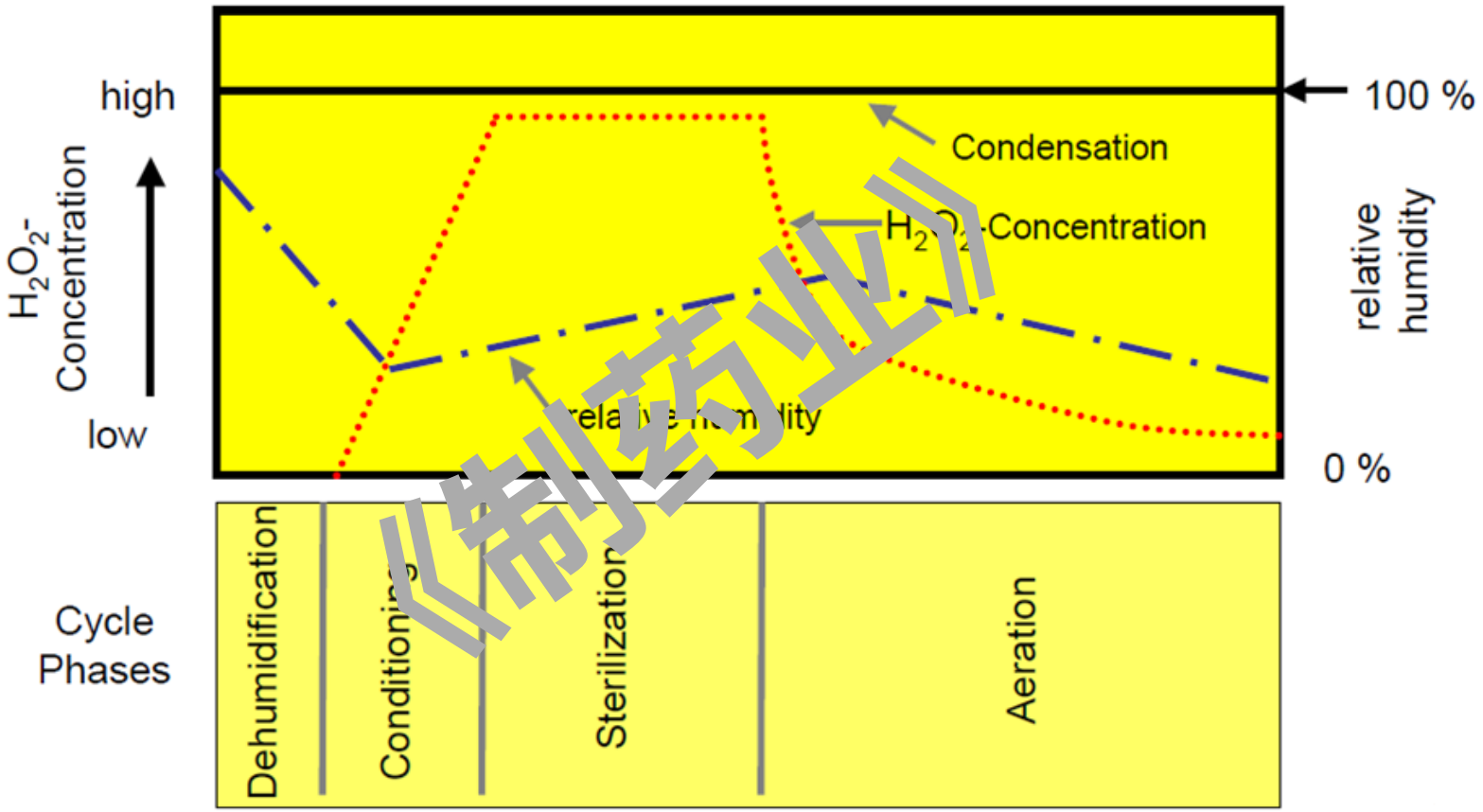
SGM Strip™ / Mesa Strip™
(Spore Strip Biological Indicators)

Biodecontamination

Decontamination Agent

- H_2O_2 (Most preferable)
- ClO2
- O_3
- Peracetic acid (CH_3COOOH)

Biodecontamination



Typical VHP Process Steps

Biodecontamination

Critical Aspects of Decontamination

- Dosage of the Decontamination Agent
- Relative Humidity
- Temperature
- Uniformity of Conditions
- Biological Indicators
- Decontamination Agent Residuals
- Aeration and Outgassing

Conclusion & Summary



- Improvement in product quality!
- Improvement in operator safety!
- Reduction manufacturing space!
- Reduction in capital cost!

SAGENT

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Thank you for your attention!

Questions?

The 7th Vogel Pharmaceutical Engineering International Forum 2015

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