Advancements in Manufacturing - Isolator Technology

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Overview

▪ Introduction SKAN
▪ Drivers of advancements i.e. Annex 1;
▪ Contamination Control Strategy
▪ Solutions for toxic products
SKAN - Market Leader Aseptic Isolators

- >50 years of experience
- Headquarter in Switzerland: Basel

Core competence:
- Transition of user requirements into high quality equipment that meet **regulatory** requirements, can be **validated and maintained** throughout their life cycle
- Primary markets are **Pharma/Biotech and Healthcare**
- **Technology and market leader** in isolator technology worldwide
Our Experience is your Benefit

Your partner for pharmaceutical processes

- From design to validation
- Worldwide customer support

Your Benefit:
Process and validation guarantee
SKAN Core Competences

- **Sterility testing isolators**
- **Transfer airlocks**
- **VARIOSYS® Flexible small and medium scale filling solution**
- **INTEGRA**

- **Isolators for production filling lines**
- **SKAN E-Beam decontamination**
- **Robotics, special application and oRABS**

**NANOX® catalytic converter**
- **H₂O₂ Decontamination**
- **SKANFOG®**
- **Flash evaporation**

**WGT glove testing**

**SKAN BI**
References Asia
What are the major drivers for the new Annex 1?

- Quality Risk Management QRM
- Contamination Control Strategy CCS

- Keep operators out of critical aseptic operations
- Barrier solutions the preferred technology
Contamination Control Strategy - Elements

- Automation and digitalisation
- Aseptic equipment design
- Sterility with isolators and $H_2O_2$ surface decontamination
- CLEAN™ to prevent contamination/cross contamination
- CLEAN™

ANNEX 1 Manufacturing Control
Contamination Control Strategy - Isolators

- Operators have no direct access to critical areas
- Validated and accepted decontamination system with $\text{H}_2\text{O}_2$
- Reduced clean room requirements outside of the isolator (ISO 7/8 Class C/D)
- Less gowning of the operators
- Suitable for high potent products
Isolator Air Handling System
2 Principle

2.1 The manufacture of sterile products is subject to special requirements in order to minimize risks of microbial, particulate and pyrogen contamination. The following key areas should be considered:

i. Facility, equipment and process design should be optimized, qualified and validated according to the relevant sections of the Good Manufacturing Practices (GMP) guide. The use of appropriate technologies (e.g. Restricted Access Barriers Systems (RABS), isolators, robotic systems, rapid microbial testing and monitoring systems) should be considered to increase the protection of the product from potential extraneous sources of particulate and microbial contamination such as personnel, materials and the surrounding environment, and assist in the rapid detection of potential contaminants in the environment and product.
Contamination Control Strategy - Design

First Air – Refers to filtered air that has not been interrupted by items (such as operators) with the potential to add contamination to the air prior to reaching the critical zone.

**TOPIC 1: ISOLATOR DESIGN ........................................4**

**Q1-1:** What should the pressure differential be between the isolator interior and the surrounding area? ....5

**Q1-2:** What are the design considerations for isolator gloves? ..........................6

**Q1-3:** How should the isolator be designed to minimize risk posed by interventions? ..........................7
Surface decontamination

4.24 For RABS and isolator systems, decontamination methods should be validated and controlled within defined cycle parameters. The cleaning process prior to the disinfection step is essential; any residues that remain may inhibit the effectiveness of the decontamination process:

i. For isolators, the decontamination process should be automated and should include a sporicidal agent in a suitable form (e.g. gaseous, aerosolized or vaporized form) to ensure thorough microbial decontamination of its interior. Decontamination methods (cleaning and sporicidal disinfection) should render the interior surfaces and critical zone of the isolator free of viable microorganisms.
Conventional flash vaporization – Surface decontamination

SKAN decontamination system with > 20 years of experience

- **H₂O₂ vapor**
- **Carrier air (recirculated)**
- **HEPA filter**
- **Peristaltic pump**
- **Hot plate**
- **Ventilator on**
- **H₂O₂ bottle**

Qualified zone

**Sterility with isolators and H₂O₂ surface decontamination**
Indirect vaporization – Surface decontamination

SKANFOG®: Re-invented fogging technology
Indirect vaporization through micro-nebulization

Sterility with isolators and H₂O₂ surface decontamination
Surface decontamination – Comparison of systems

SKANFOG® vs vaporized H₂O₂

- Latest development based on more than 20 years experience
- SKANFOG® uses less H₂O₂ than flash vaporization
- Aeration phase much faster
- Both systems guarantee a safe 10⁶ microbiological reduction

→ SKANFOG® provides required **decontamination level** in less time and with less H₂O₂
Contamination Control Strategy - Clean™

5.4 The cleaning process should be validated to:

i. Remove any residue or debris that would detrimentally impact the effectiveness of the disinfecting agent used.

ii. Minimize chemical, microbial and particulate contamination of the product during the process and prior to disinfection.

5.5 Direct and indirect contact parts should be sterilized. Direct contact parts are those that the product passes through, such as filling needles or pumps. Indirect product contact parts are equipment parts that come into contact with sterilized critical items and components.

Points to Consider for the Aseptic Processing of Sterile Pharmaceutical Products in Isolators

TOPIC 7: CLEANING, DISINFECTION, DECONTAMINATION: CYCLE DEVELOPMENT AND VALIDATION

Q7-1: What are the special considerations for cleaning and disinfecting isolator interiors (nonproduct contact surfaces) prior to decontamination? ....40

Q7-2: What are the current options for isolator interior decontamination? .............................................43

Q7-3: Should empty isolator mapping of temperature and humidity be performed as part of decontamination qualification studies? ..........45

Q7-4: What conditions and configurations should be considered during decontamination cycle development and validation? ..................................46

CLEAN™ to prevent contamination/cross contamination
Isolator glove integrity testing

4.23 The materials used for glove systems (for both RABS and isolators), as well as other parts of an isolator, should be demonstrated to have good mechanical and chemical resistance. Integrity testing of the barrier systems, and leak testing of the glove system and the isolator should be performed using a methodology demonstrated to be suitable for the task and criticality. The testing should be performed at defined periods, at a minimum at the beginning and end of each batch, and should include a visual inspection following any intervention that may affect the integrity of the system. For single unit batch sizes, integrity may be verified based on other criteria, such as the beginning and end of each manufacturing session. RABS gloves used in Grade A zone should be sterilized before installation and sterilized (or effectively decontaminated by a validated method which achieves the same objective) prior to each manufacturing campaign. The frequency of glove replacement should be defined within the CCS.

SKAN Version 2 coming up soon:
- Enhanced DI function
- Even more hygienic design
- Latest battery management
Solutions for Toxic Products

Containment Classification

6 extremely hazardous
5 very highly hazardous
4 highly hazardous
3 hazardous
2 moderately hazardous
1 low hazard

OEB Occupational Exposure Band

OEL Occupational Exposure Limit (mg/m³)

PDE Permissible Daily Exposure (mg)

ADE Acceptable Daily Exposure (mg)

1000 - 5000
100 - 1000
10 - 100
0.1 - 1
< 0.1
Developments in Isolator Technology for Toxic Application

2000 - today

2015 - today

2020
Safe Change Filter System (FIPA) for Toxic Application

Cartridge HEPA - Safe Change filter system FIPA:

- no extra space in technical area needed
- return air ducts protected with cartridge filters (no wash down required)
- Safe change filter system located next to filling area
Aseptic Toxic Isolators
Highly Potent Process: Sterility Test
SKANs Solution with CLEAN™

- Development of a suitable cleaning strategy with risk assessment
- How does the active substance spread inside the isolator?
- What is the recovery from different materials?
- How effective is the applied cleaning procedure?

Cleaning validation visualized with Riboflavin
Questions?

Thank you!

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