Advancements in Manufacturing - Isolator Technology

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Regional Sales Director

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

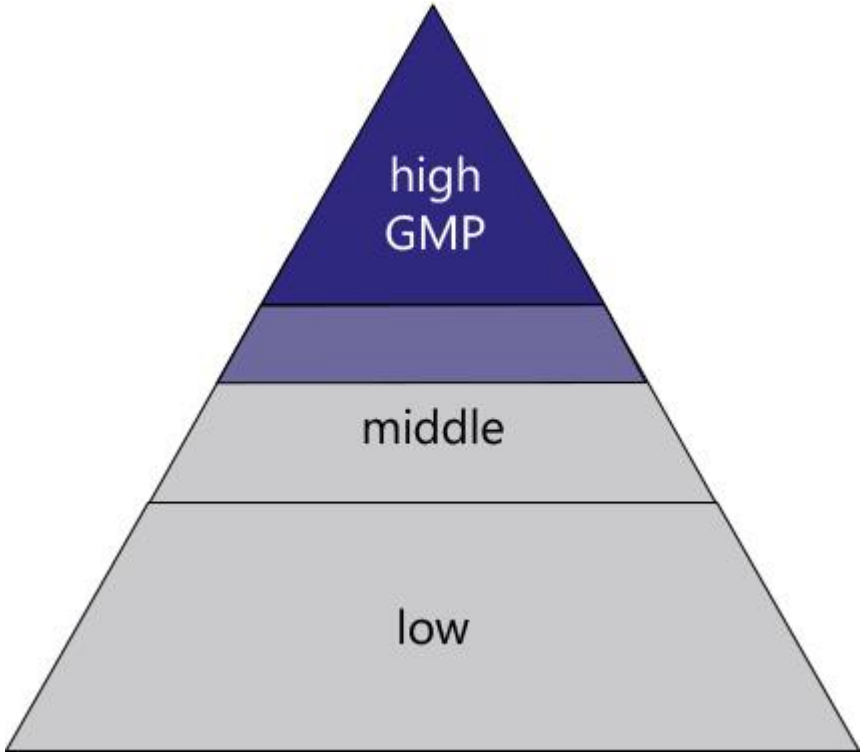
Core competence:

- 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



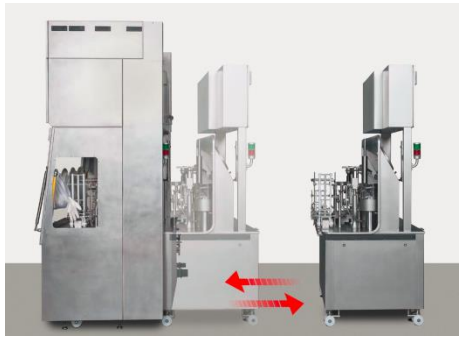
Your Benefit:

Process and validation guarantee

SKAN Core Competences

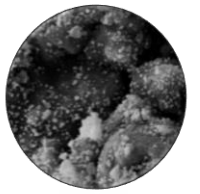
Sterility testing isolators

Transfer airlocks



VARIOSYS® Flexible small and medium scale filling solution

INTEGRA



NANOX® catalytic converter

H_2O_2 Decontamination

- SKANFOG®
- Flash evaporation

Isolators for production filling lines

SKAN E-Beam decontamination

Robotics, special application and oRABS

WGT glove testing

SKAN BI

References Asia

Regulatory Annex 1 Draft 2017 - 2020

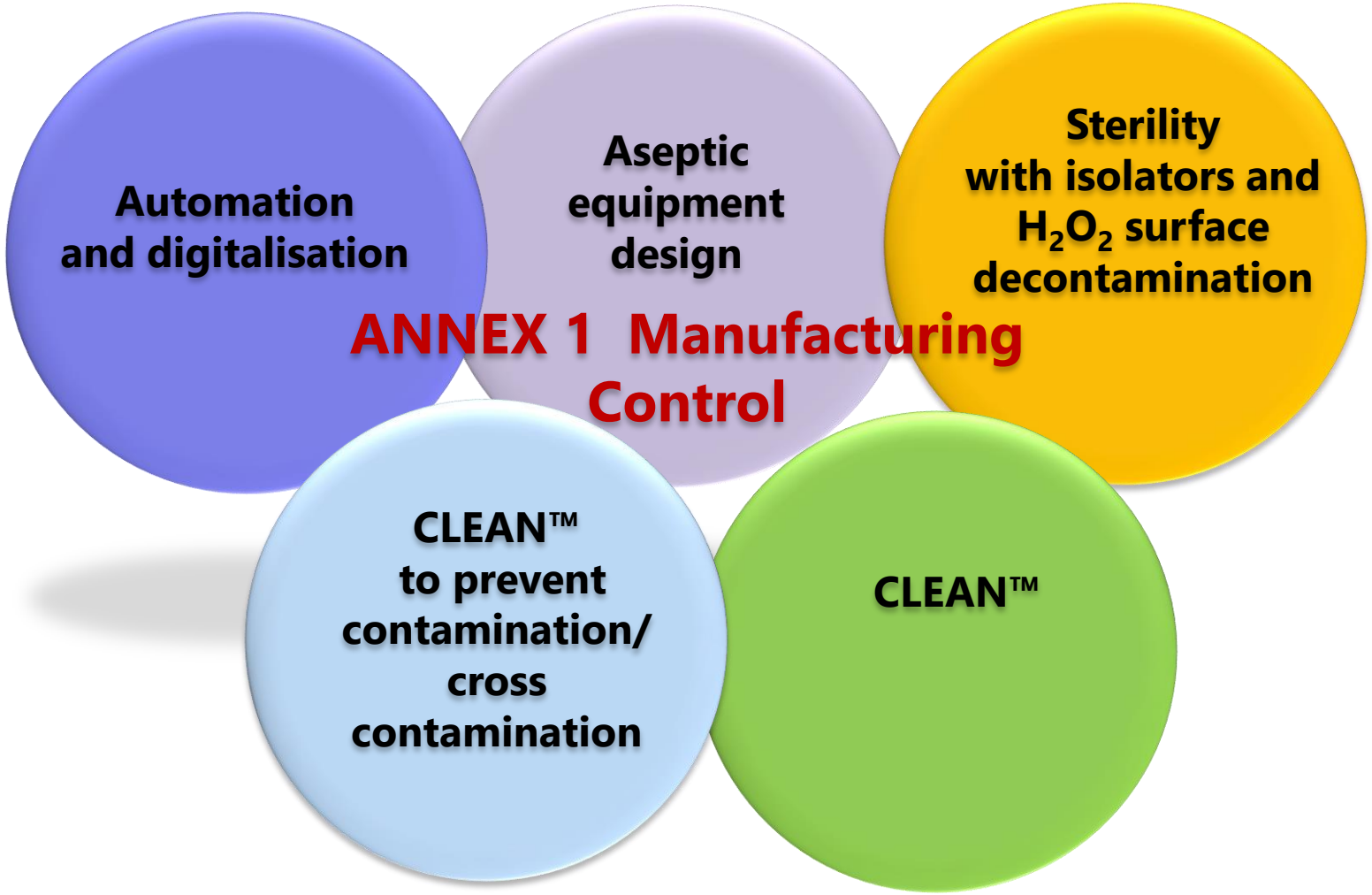
What are the major drivers for the new Annex 1?

- Quality Risk Management QRM
- Contamination Control Strategy CCS

181 4.3 Restricted Access Barrier Systems (RABS) and isolators are beneficial in assuring the required
182 conditions and minimizing the microbial contamination associated with direct human interventions
183 in the critical zone. Their use should be considered in the CCS. Any alternative approaches to the use
184 of RABS or isolators should be justified.

- Keep operators out of critical aseptic operations
- Barrier solutions the preferred technology

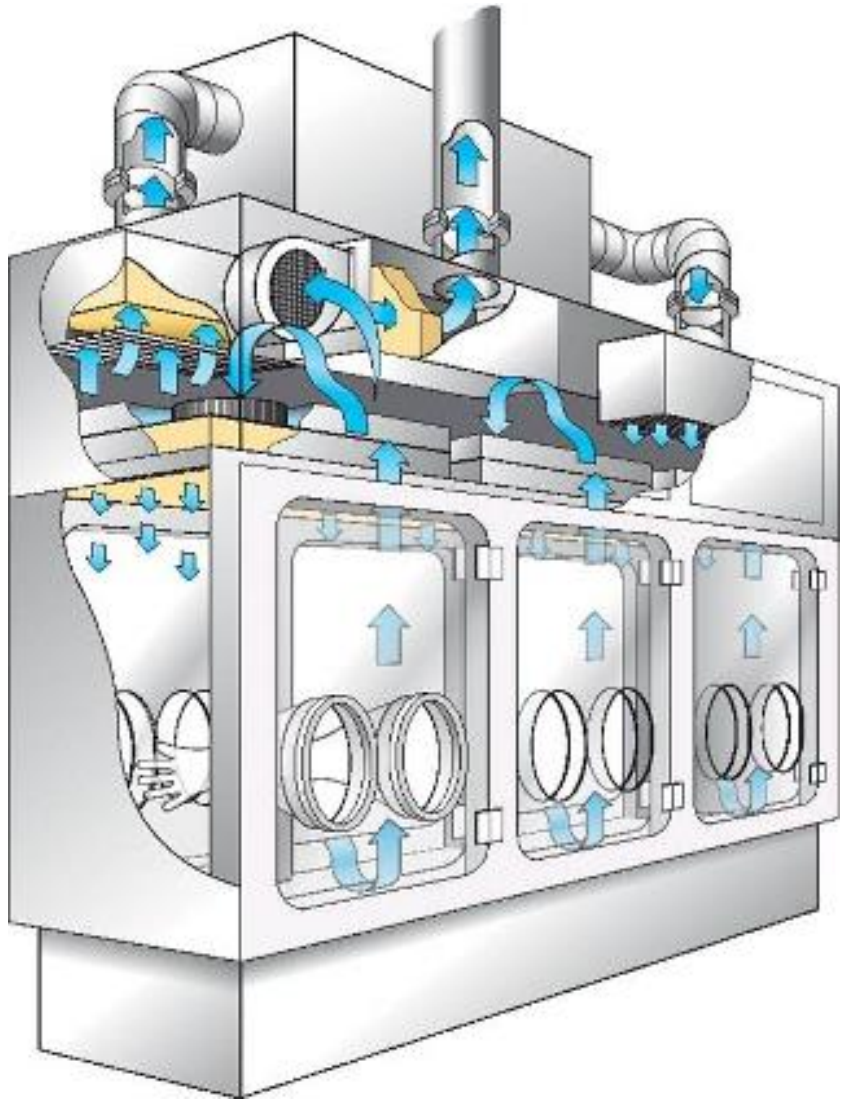
Contamination Control Strategy - Elements



Contamination Control Strategy - Isolators

- Operators have no direct access to critical areas
- Validated and accepted decontamination system with H_2O_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

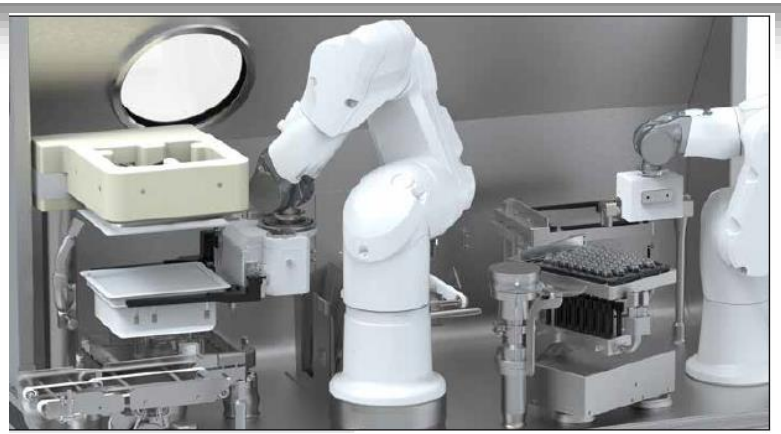


Contamination Control Strategy - Automation

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.



Automation and digitalisation

Contamination Control Strategy - Design

2467 First Air – Refers to filtered air that has not been interrupted by items (such as operators) with the
2468 potential to add contamination to the air prior to reaching the critical zone.

PDA

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

Aseptic Equipment Design

Surface decontamination

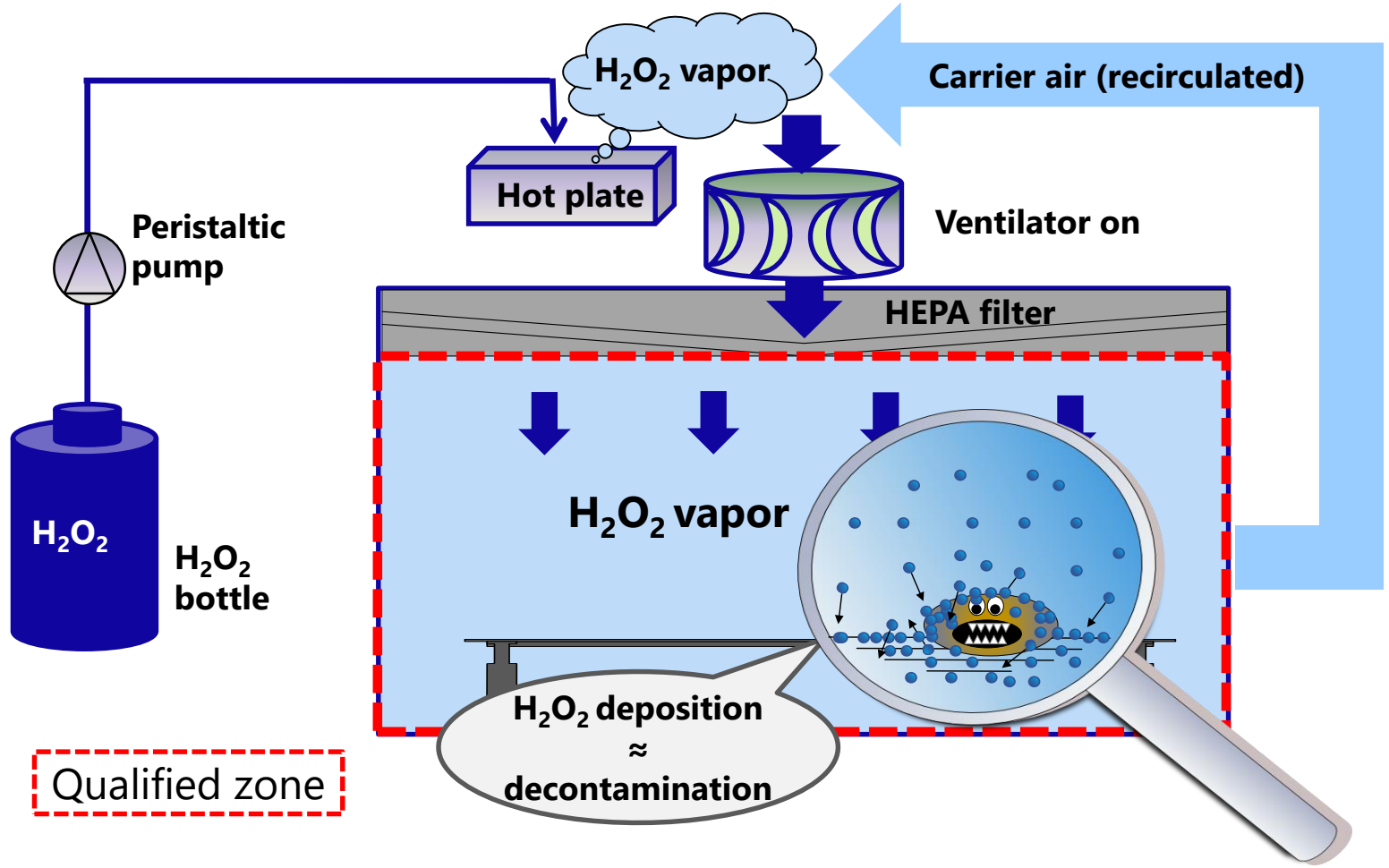
4.24 For RABS and isolator systems, decontamination methods should be validated and controlled within defined cycle parameters. The cleaning process prior to the disinfection step is essential; any residues that remain may inhibit the effectiveness of the decontamination process:

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.

Sterility with isolators and H_2O_2 surface decontamination

Conventional flash vaporization – Surface decontamination

SKAN decontamination system with > 20 years of experience

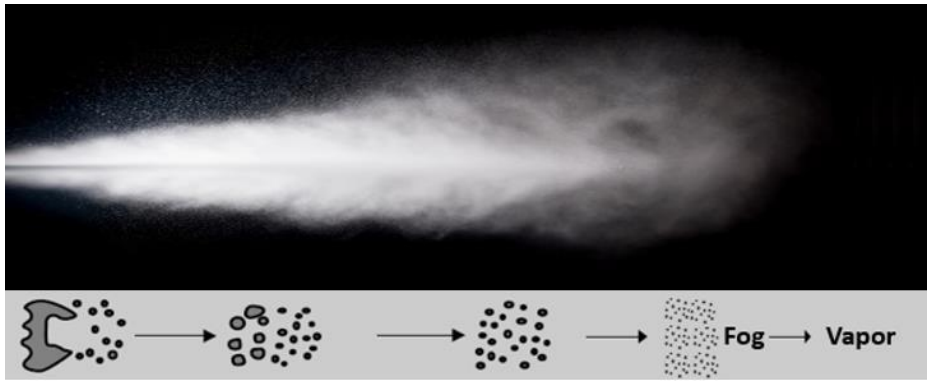


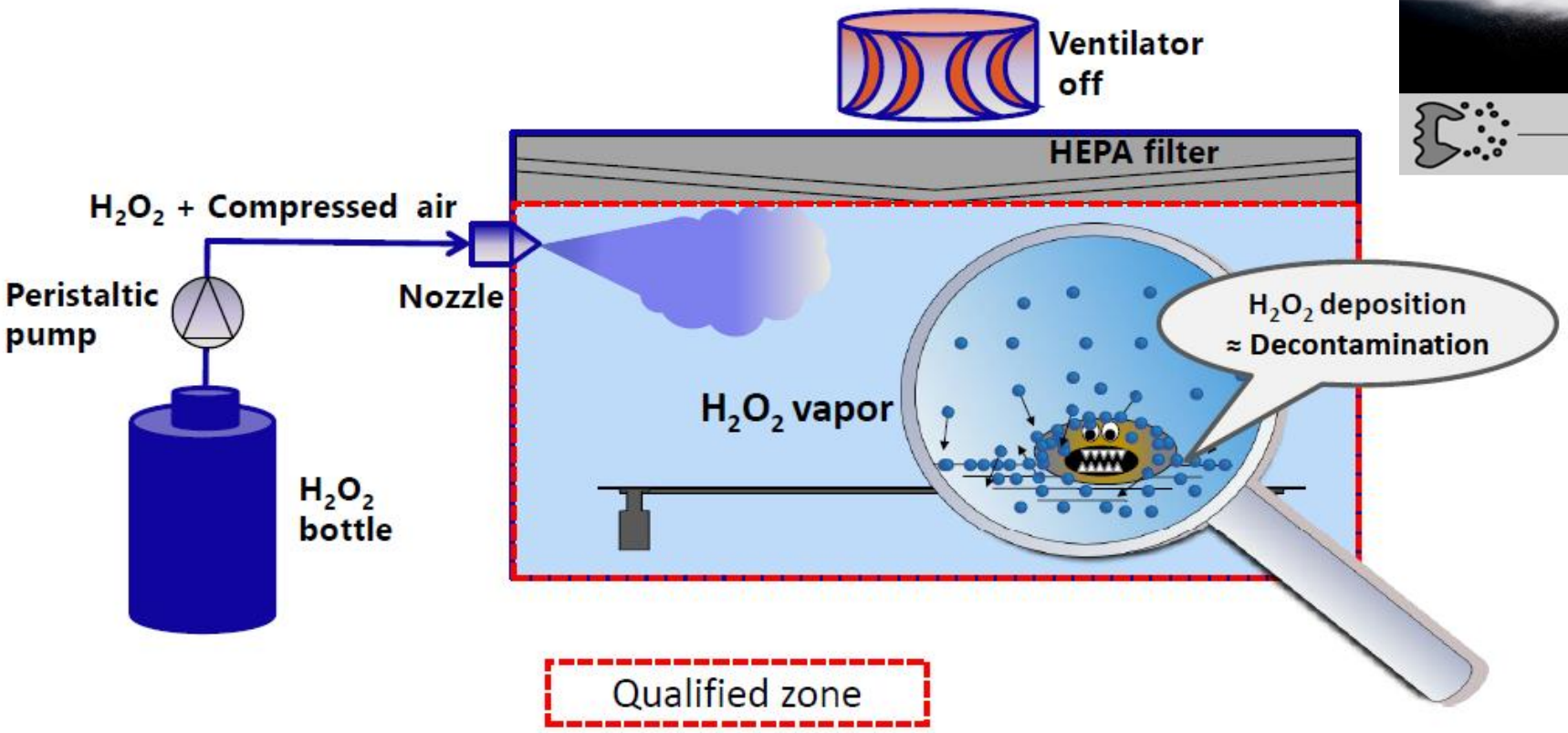
Sterility with isolators and H_2O_2 surface decontamination

Indirect vaporization – Surface decontamination

SKANFOG®: Re-invented fogging technology

Indirect vaporization through micro-nebulization





Sterility with isolators and H_2O_2 surface decontamination

Surface decontamination – Comparison of systems

SKANFOG® vs vaporized H_2O_2

- Latest development based on more than 20 years experience
- SKANFOG® uses less H_2O_2 than flash vaporization
- Aeration phase much faster
- Both systems guarantee a safe 10^6 microbiological reduction

→ SKANFOG ® provides required **decontamination level in less time and with less H_2O_2**

Contamination Control Strategy - Clean™

565 5.4 The cleaning process should be validated to:
566
567 i. Remove any residue or debris that would detrimentally impact the effectiveness of the
568 disinfecting agent used.
569 ii. Minimize chemical, microbial and particulate contamination of the product during the process
570 and prior to disinfection.
571
572 5.5 Direct and indirect contact parts should be sterilized. Direct contact parts are those that the
573 product passes through, such as filling needles or pumps. Indirect product contact parts are
574 equipment parts that come into contact with sterilized critical items and components.

CLEAN™ to prevent contamination/ cross contamination

PDA

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

Contamination Control Strategy – Glove Integrity Testing

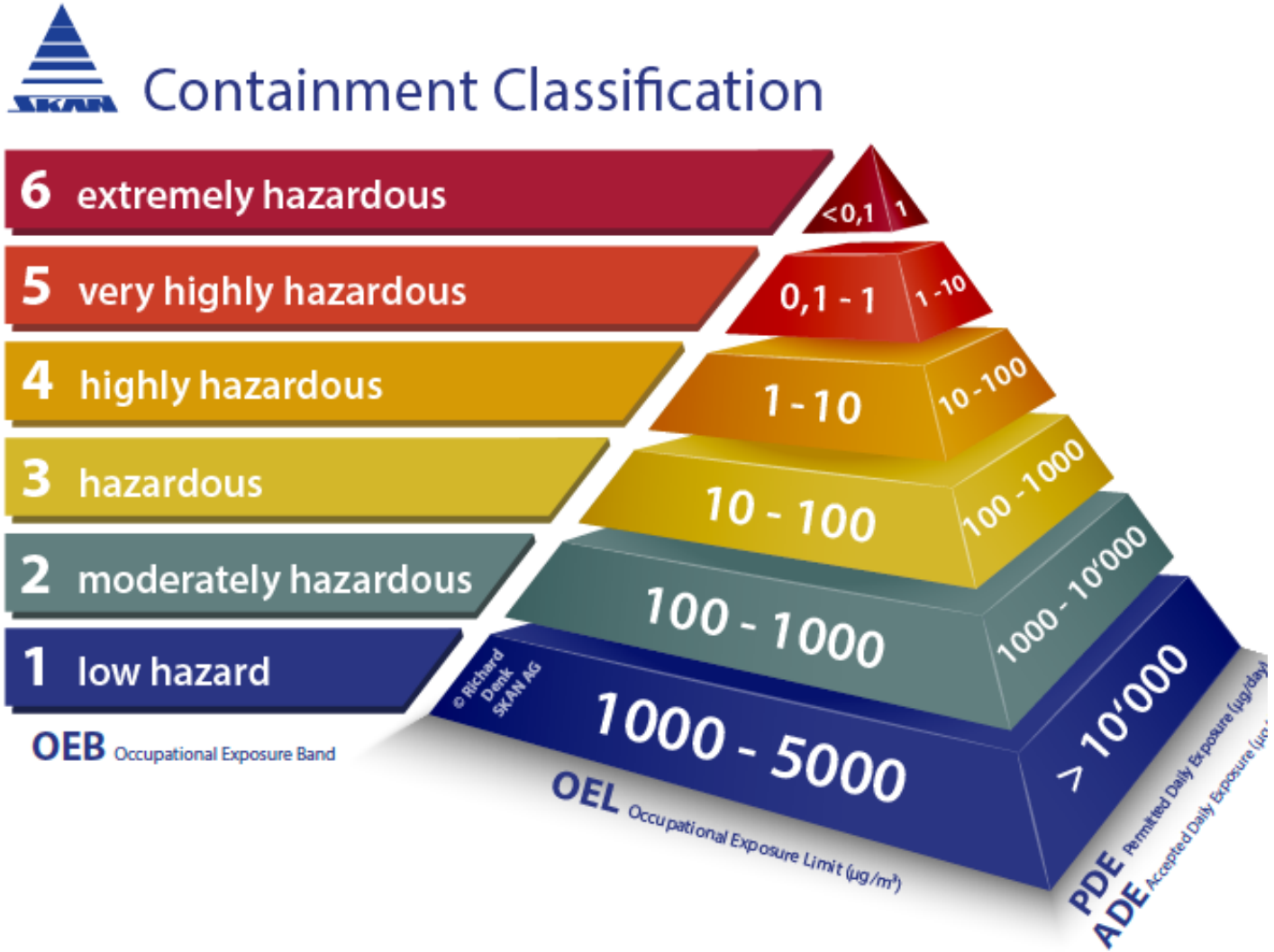
Isolator glove integrity testing

353 4.23 The materials used for glove systems (for both RABS and isolators), as well as other parts of an
354 isolator, should be demonstrated to have good mechanical and chemical resistance. Integrity testing of
355 the barrier systems, and leak testing of the glove system and the isolator should be performed using a
356 methodology demonstrated to be suitable for the task and criticality. The testing should be performed
357 at defined periods, at a minimum at the beginning and end of each batch, and should include a visual
358 inspection following any intervention that may affect the integrity of the system. For single unit batch
359 sizes, integrity may be verified based on other criteria, such as the beginning and end of each
360 manufacturing session. RABS gloves used in Grade A zone should be sterilized before installation
361 and sterilized (or effectively decontaminated by a validated method which achieves the same
362 objective) prior to each manufacturing campaign. The frequency of glove replacement should be
363 defined within the CCS.

SKAN Version 2 coming up soon:

- Enhanced DI function
- Even more hygienic design
- Latest battery management

Solutions for Toxic Products



Developments in Isolator Technology for Toxic Application

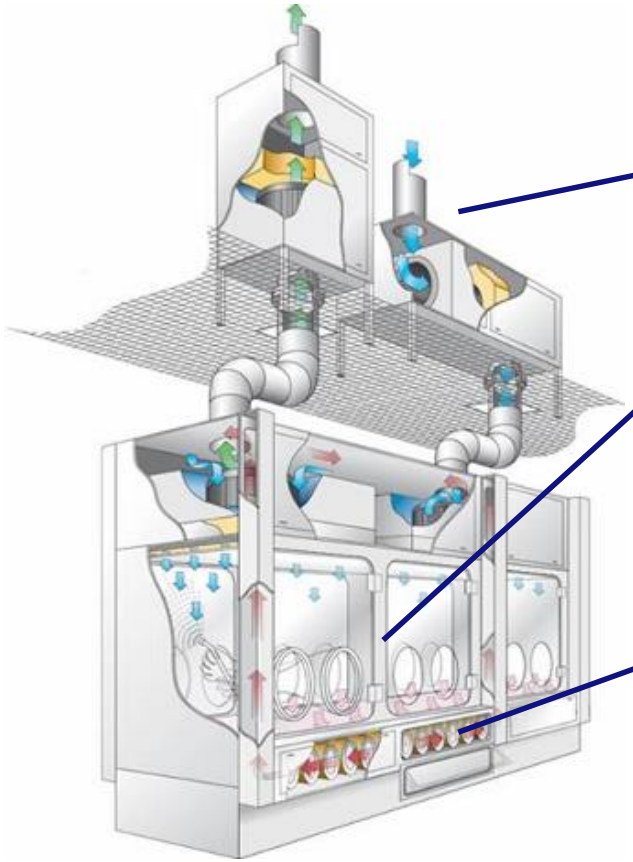
2000 - today

2015 - today

2020

Safe Change Filter System (FIPA) for Toxic Application

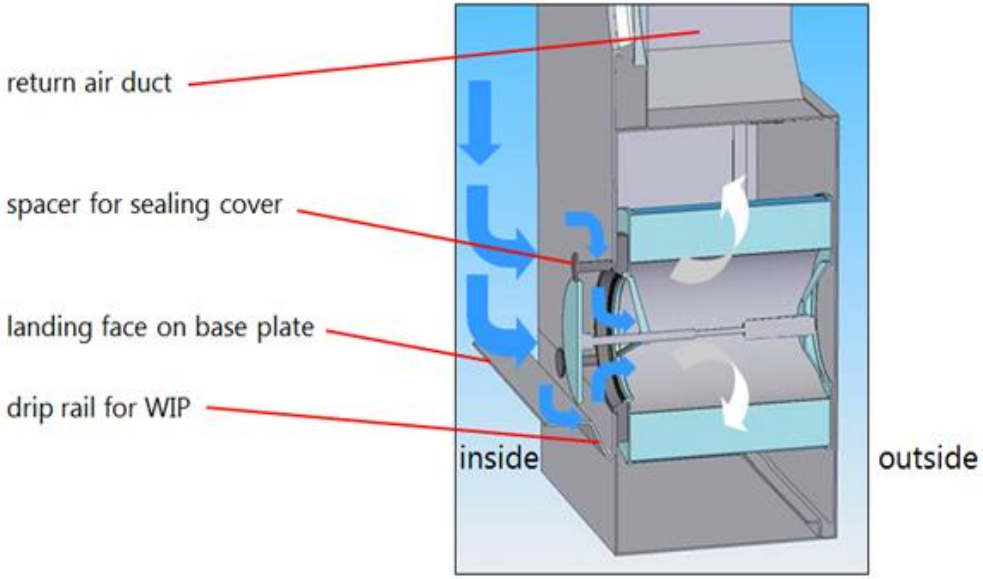
Cartridge HEPA - Safe Change filter system FIPA:



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



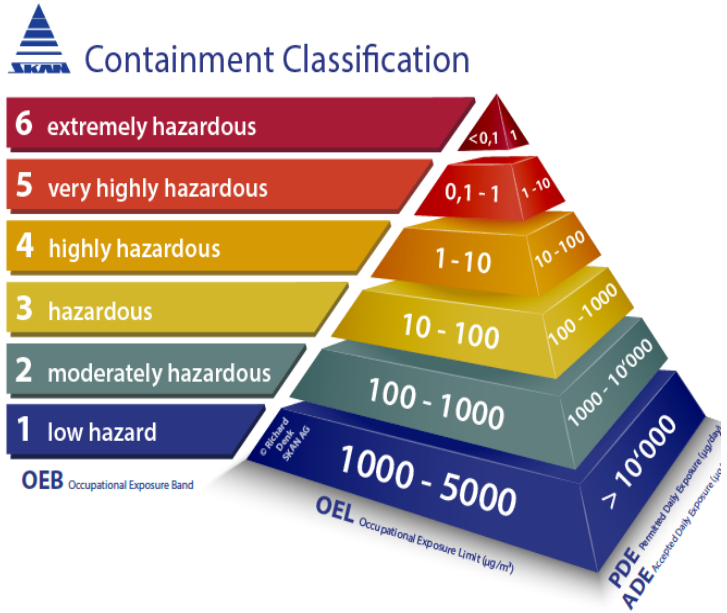
FIPA cartridge filter

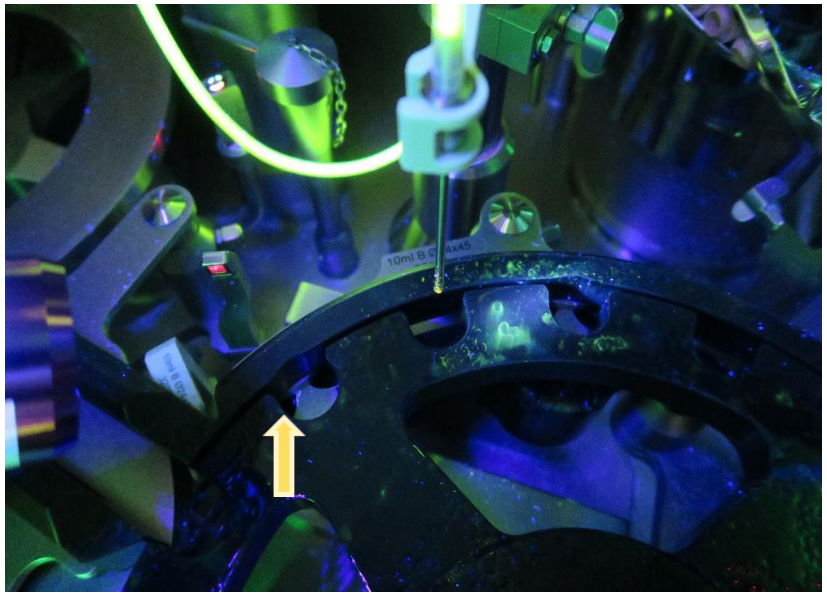
Aseptic Toxic Isolators

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

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Thank you!

Questions?

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