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Good Health Can't Wait!

PANEL BRIEFING

VHP Surface Bio-Decontamination

Science, cycle development, validation and change control

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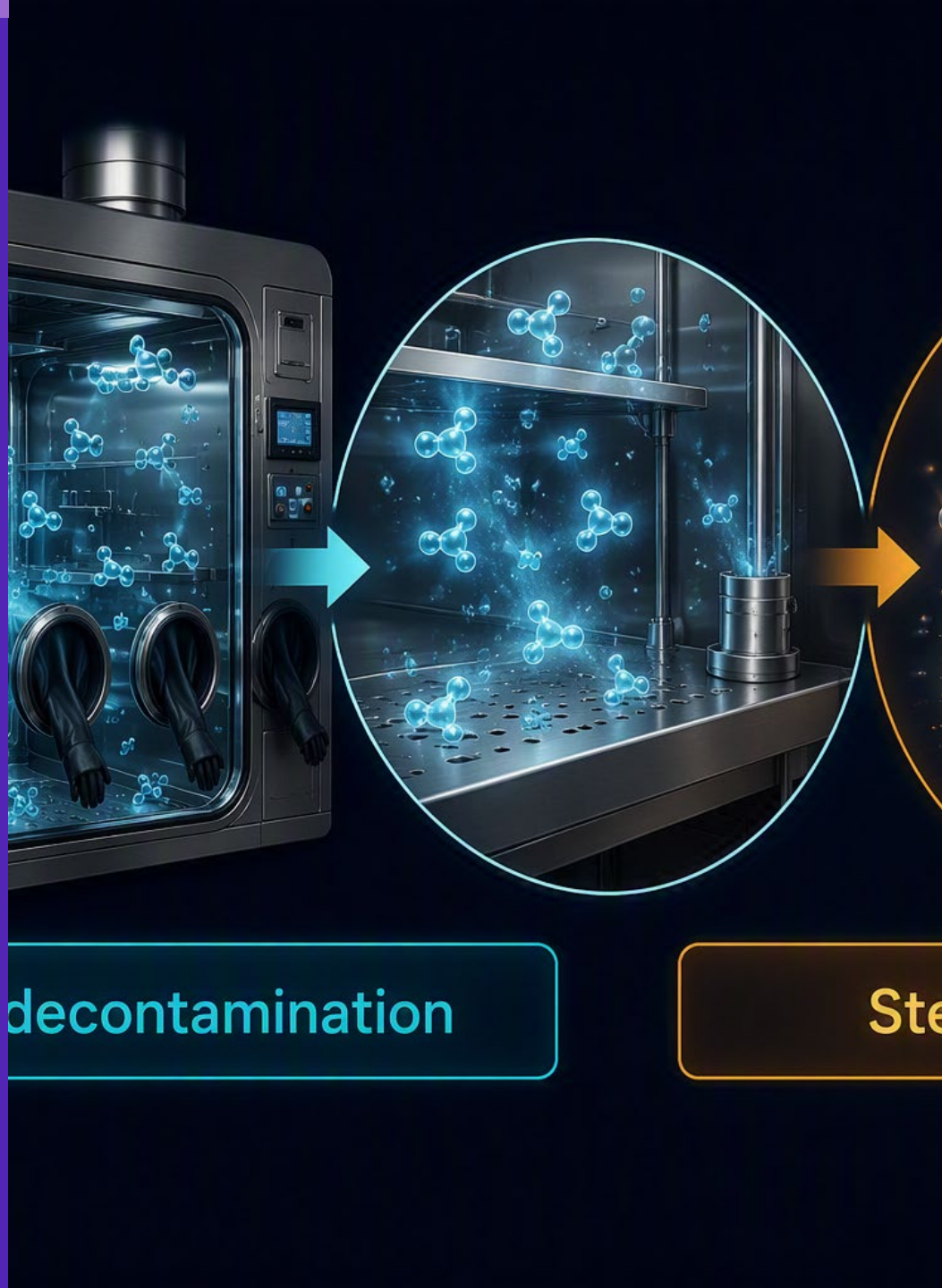


2 VHP: what it does, and what it does not claim

Surface bio-decontamination and sterilisation are related concepts, not interchangeable claims.



VHP SCIENCE

Vapour reaches exposed surfaces and oxidatively damages microorganisms. Efficacy depends on distribution and local surface conditions.

SURFACE BIO-DECONTAMINATION

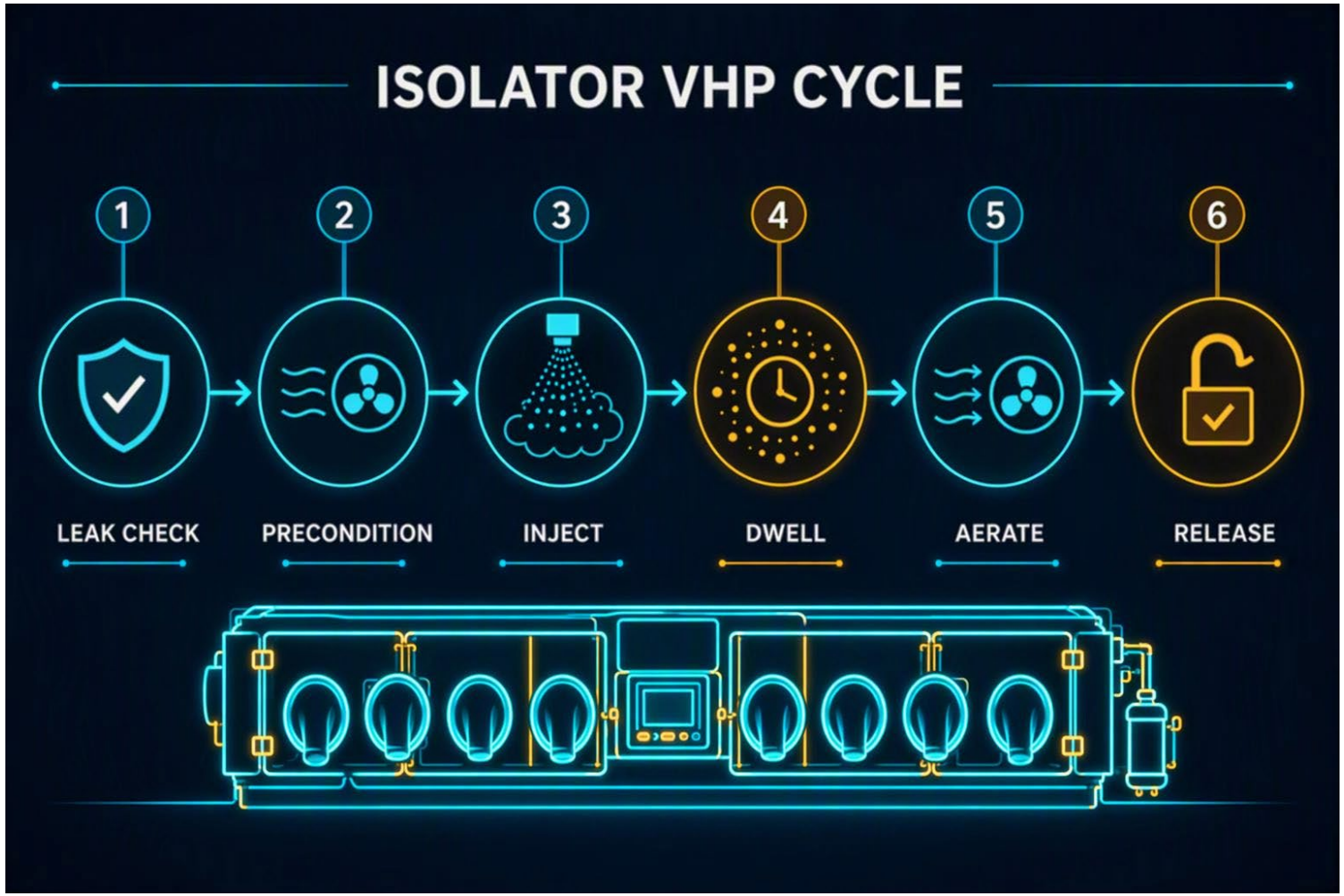
Validated reduction of viable contamination on accessible surfaces to support aseptic processing.

STERILISATION

A validated process used to render a product or article sterile within a defined sterility-assurance framework.

3 Developing the isolator VHP cycle

Build distribution and operating margin before demonstrating microbiological lethality.



DEFINE THE STATE

Clean, dry, assembled load; fixed orientation and transfer configuration.

FIND THE EDGE

Challenge cold spots, occlusions, glove folds and remote locations.

BUILD MARGIN

Set ranges for conditioning, injection, dwell and aeration.

Release only after residual clearance and cycle acceptance.

4 Validation: prove coverage, lethality and reproducibility

The evidence package must represent the actual enclosure and justified worst-case load.



PHYSICAL
Recipe parameters, alarms, leak test, temperature/RH and aeration endpoint

BIOLOGICAL
Qualified BIs at justified hard-to-kill locations

CHEMICAL
CIs show exposure; they do not replace BI lethality evidence

REPEATABILITY
Successful runs using the defined worst-case load

LIFECYCLE
Trend cycle data, deviations and requalification

5 Change control: protect sterility assurance

Assess whether the change affects vapour distribution, barrier integrity or the post-cycle state.

LOAD / GEOMETRY

Orientation, density, shadowing, transfers

MATERIALS / SOILS

Compatibility, adsorption, residues, pre-cleaning

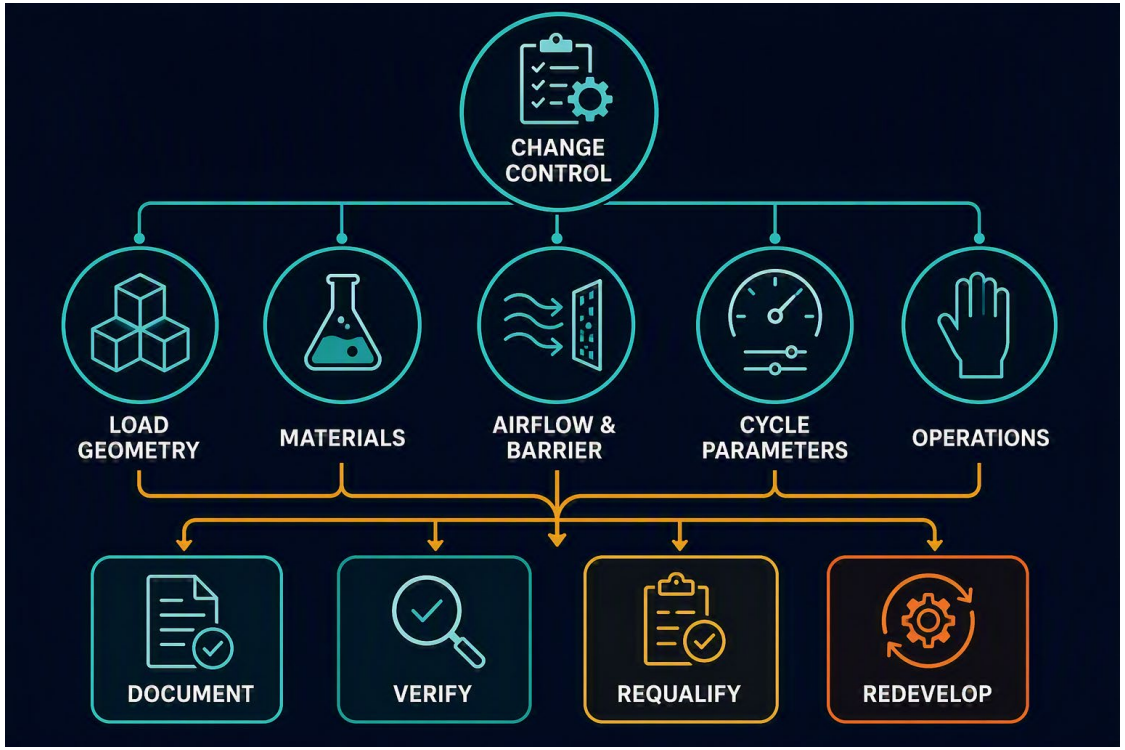
SYSTEM / AIRFLOW

Generator, HEPA, fans, seals, leak rate

CYCLE / OPERATIONS

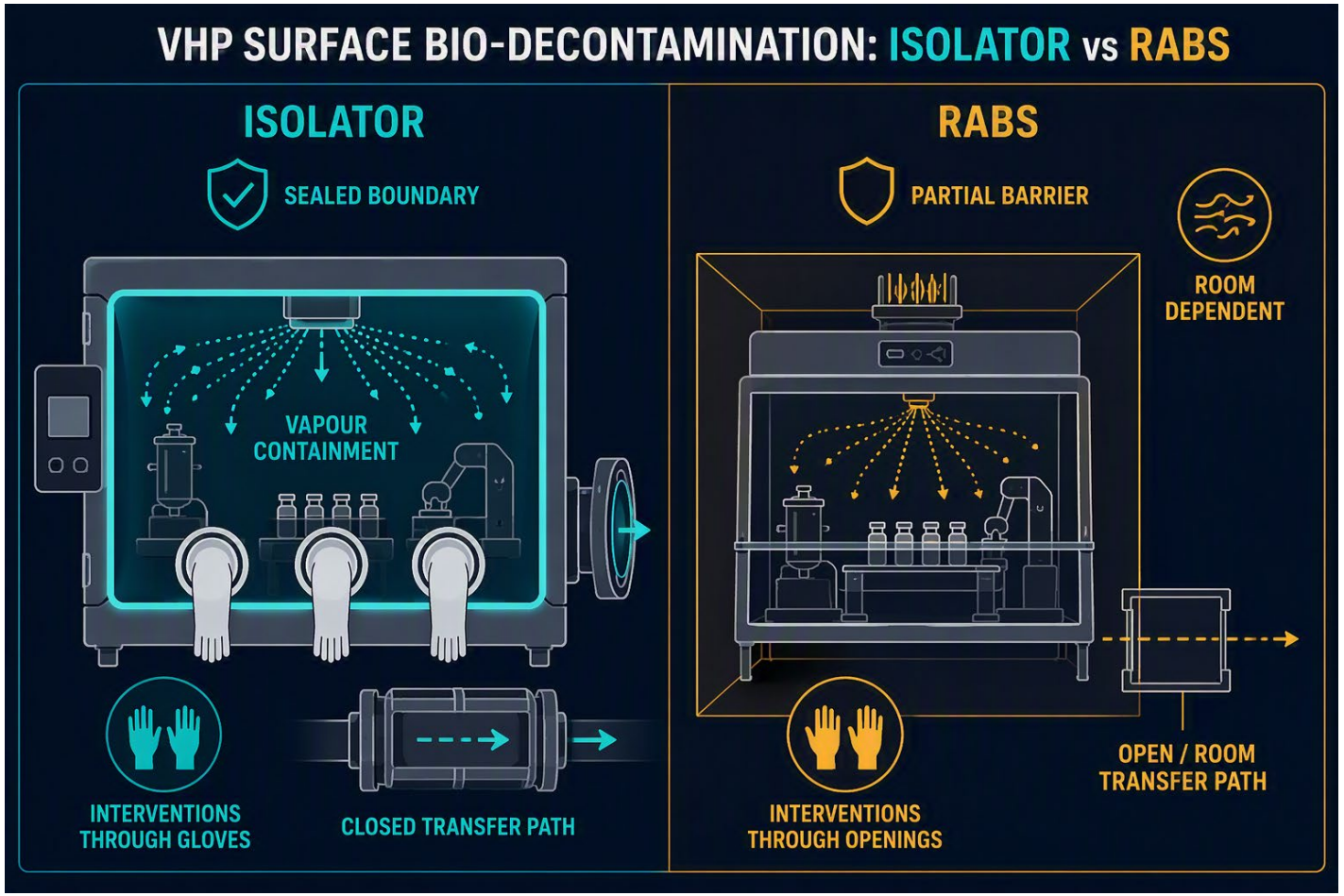
Recipe, software, RH, interventions, aeration

Response	DOCUMENT	VERIFY	REQUALIFY	REDEVELOP



6 Isolator versus RABS: the barrier is the primary difference

VHP capability cannot be separated from boundary integrity, room dependence and interventions.



ISOLATOR – Grade A over Grade C possible

Closed, leak-testable boundary; contained cycle; interventions through gloves; closed transfer strategy.

RABS – Grade A over Grade B required

Partial barrier. Open and closed RABS differ; protection retains greater dependence on room and intervention discipline.

DESIGN CONSEQUENCE

Select containment, transfer and intervention philosophy before defining the VHP control strategy.

7 How VHP use differs: isolator versus RABS

The same agent operates within two different contamination-control architectures.

ISOLATOR

BOUNDARY	Sealed and leak-tested
VHP APPLICATION	Contained, automated enclosure cycle
AFTER THE CYCLE	Protected state maintained by closed boundary
AERATION	Engineered removal within the sealed system
DEPENDENCE	Lower room and operator dependence

RABS

BOUNDARY	Partial barrier; open/closed design matters
VHP APPLICATION	Surface treatment capability is design-specific
AFTER THE CYCLE	Greater reliance on room and operating discipline
AERATION	Must account for room interface and leakage paths
DEPENDENCE	Higher room and intervention dependence

8 Air quality requirements: ISO 14644-1 vs EU GMP Annex 1 vs FDA

Maximum airborne particles per m^3 (≥ stated size) and viable air action limits, by cleanroom grade and occupancy state.

Cleanroom grade (EU)	ISO 14644-1 class (at rest / in op.)	EU Annex 1 — at rest		EU Annex 1 — in operation		FDA 2004 — in operation	Viable air action limit (CFU/m^3)	
		≥0.5 µm	≥5.0 µm*	≥0.5 µm	≥5.0 µm*	≥0.5 µm (ISO class)	EU Annex 1	FDA 2004
Grade A	ISO 5 / ISO 5	3,520	29	3,520	29	3,520 (ISO 5)	No growth	1
Grade B	ISO 5 / ISO 7	3,520	29	352,000	2,930	352,000 (ISO 7)	10	10
Grade C	ISO 7 / ISO 8	352,000	2,930	3,520,000	29,300	3,520,000 (ISO 8)	100	100
Grade D	ISO 8 / —	3,520,000	29,300	Not predetermined	Not predetermined	Not defined	200	Not defined

** ≥5.0 µm: Annex 1 monitoring limit (Table 5); not specified for Grade A/B classification (Table 1). ISO 14644-1 classes ISO 5 at ≥0.5 µm only. FDA states no ≥5.0 µm limit and uses no grades — closest ISO class shown (ISO 5 = Class 100, ISO 7 = Class 10,000, ISO 8 = Class 100,000; FDA also lists ISO 6 at 35,200 particles/m^3, 7 CFU/m^3). Sources: ISO 14644-1:2015 Table 1; EU GMP Annex 1 (2022) Tables 1, 5, 6; FDA Guidance (2004) Table 1.*

ISO 14644-1:2015

Classification only: one limit per class, the same in every occupancy state (state must be declared).

No ≥5.0 µm limit at ISO 5 (sampling losses); no microbial limits — monitoring sits in ISO 14644-2.

EU GMP ANNEX 1 (2022)

Grades A–D with separate at-rest and in-operation limits.

≥5.0 µm removed from A/B classification but kept for monitoring (29/m^3); continuous Grade A monitoring and “no growth” viable limit.

FDA ASEPTIC GUIDANCE (2004)

In-operation (dynamic) limits only, at ≥0.5 µm only — no ≥5.0 µm limit.

Sampled within 1 ft of the work site; ISO 5 action level 1 CFU/m^3 with ISO 7 background.

9 Panel questions (1/2): science, cycle development and validation

Short prompts for the panel — source documents shown beneath each question.

1 **VHP in an isolator is bio-decontamination, not sterilisation. What does that mean in practice for how we justify and document the claim?**

EU GMP Annex 1 – Barrier technologies, decontamination methods | FDA Aseptic Processing Guidance – Isolators

2 **FDA accepts a 4–6 log reduction depending on the application. How do you set the target, and when is 6-log really needed?**

FDA Aseptic Processing Guidance – Appendix on aseptic processing isolators (decontamination)

3 **Gloves must be extended with fingers separated. Which other hard-to-reach spots catch teams out during cycle development?**

EU GMP Annex 1 – Barrier technologies, decontamination methods

4 **Load pattern, materials and condensation all affect efficacy. How much should be fixed in cycle design versus handled by procedure?**

EU GMP Annex 1 – Premises, fumigation and vapour disinfection

5 **How do you justify the worst-case locations and the number of biological and chemical indicators?**

EU GMP Annex 1 – Barrier technologies | FDA Aseptic Processing Guidance – Isolators

10 Panel questions (2/2): residuals, change control and barrier choice

Short prompts for the panel — source documents shown beneath each question.

6 How do you prove residual peroxide after aeration does not affect product quality or sterility-test sensitivity?

EU GMP Annex 1 – Quality control, sterility testing | FDA Aseptic Processing Guidance – Isolators

7 Which changes trigger full requalification rather than a risk-assessed check, and how should the CCS record that decision?

EU GMP Annex 1 – Pharmaceutical Quality System and Contamination Control Strategy

8 Can VHP in a RABS ever give the same assurance as in an isolator, and where is the gap?

EU GMP Annex 1 – Barrier technologies, RABS sporicidal disinfection

9 After an open-RABS intervention, how do room classification and recovery become part of the decontamination argument?

ISO 14644-1 / 14644-2 – Cleanroom classification and monitoring | EU GMP Annex 1 – Barrier technologies

10 How do leak testing, glove integrity and pressure control link back to whether the VHP cycle stays valid?

ISO 14644-7 – Separative devices | EU GMP Annex 1 – Barrier technologies