Retrofitting VHP sanitisation an update / panel

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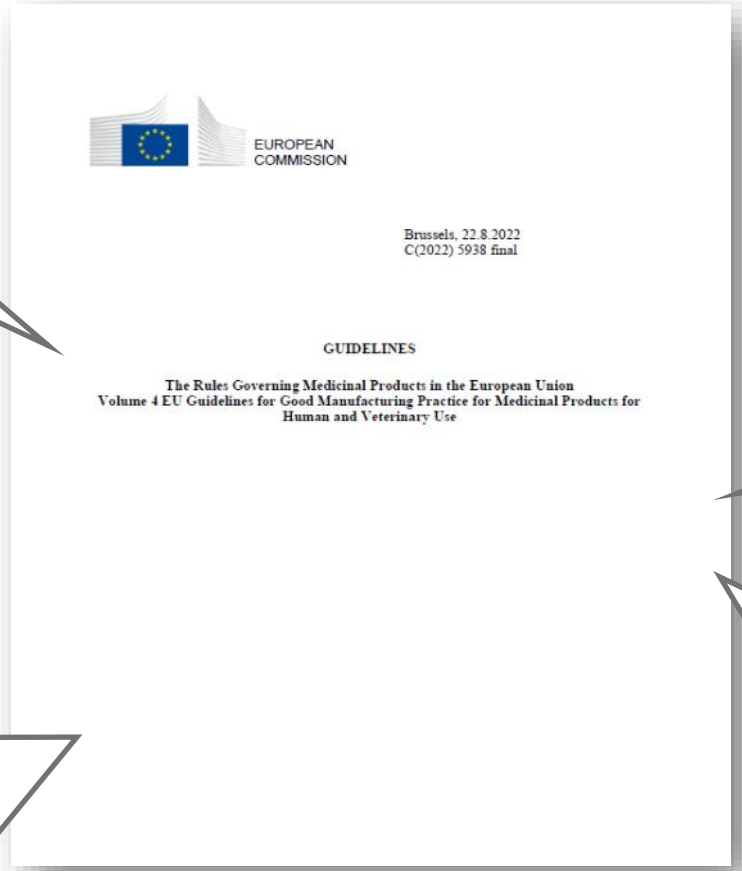
Annex 1: Updated Requirements

4.21 The materials used for glove systems (for both isolators and RABS), should be demonstrated to **have appropriate mechanical and chemical resistance**.



EUROPEAN COMMISSION

Brussels, 22.8.2022
C(2022) 5938 final

GUIDELINES

The Rules Governing Medicinal Products in the European Union
Volume 4 EU Guidelines for Good Manufacturing Practice for Medicinal Products for Human and Veterinary Use

4.22 I The bio-decontamination process of the interior should be **automated**, **validated** and **controlled** within **defined cycle parameters** and should include a sporicidal agent in a suitable form (e.g. gaseous or vaporized form). **Gloves** should be appropriately **extended** with **fingers separated** to ensure **contact** with the agent. Methods used (cleaning and sporicidal **bio-decontamination**) should **render** the **interior surfaces** and **critical zone** of the isolator **free** from **viable micro-organisms**.

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

4.36 Where fumigation or vapour disinfection (e.g. **Vapour-phase Hydrogen Peroxide**) of cleanrooms and associated surfaces are used, the **effectiveness** of any fumigation agent and **dispersion** system should be **understood** and **validated**.

User Requirement Specification (URS)

- Isolators are available in a wide range of sizes and configurations, making them extremely versatile. This versatility is reflected by the number of different applications that exist.

- Providing a classified clean or classified aseptic environment for a process or activity and protecting it from microbial and/or nonviable contamination arising from the operator and the surrounding environment.

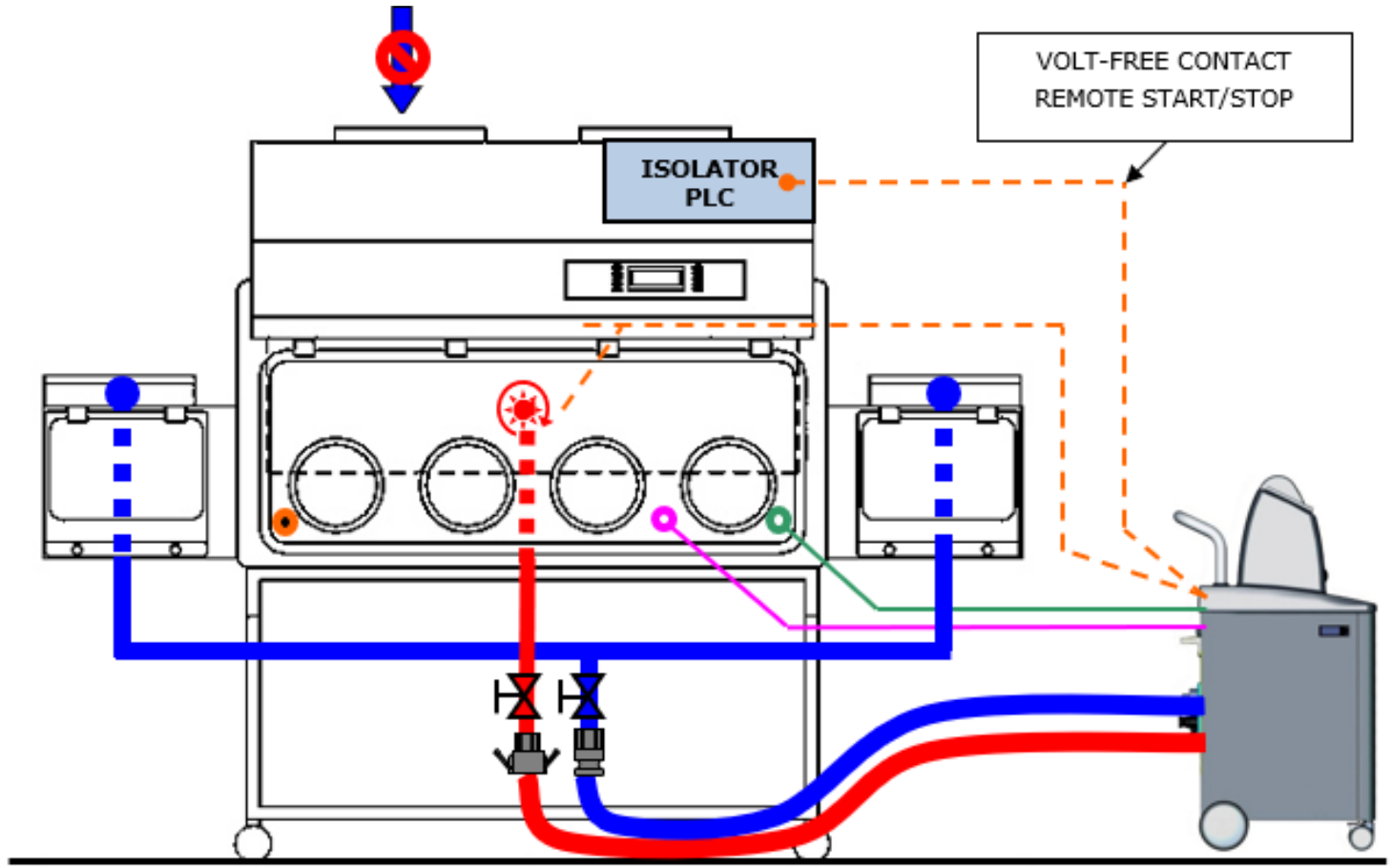
- ***The separative device – Main Chamber***

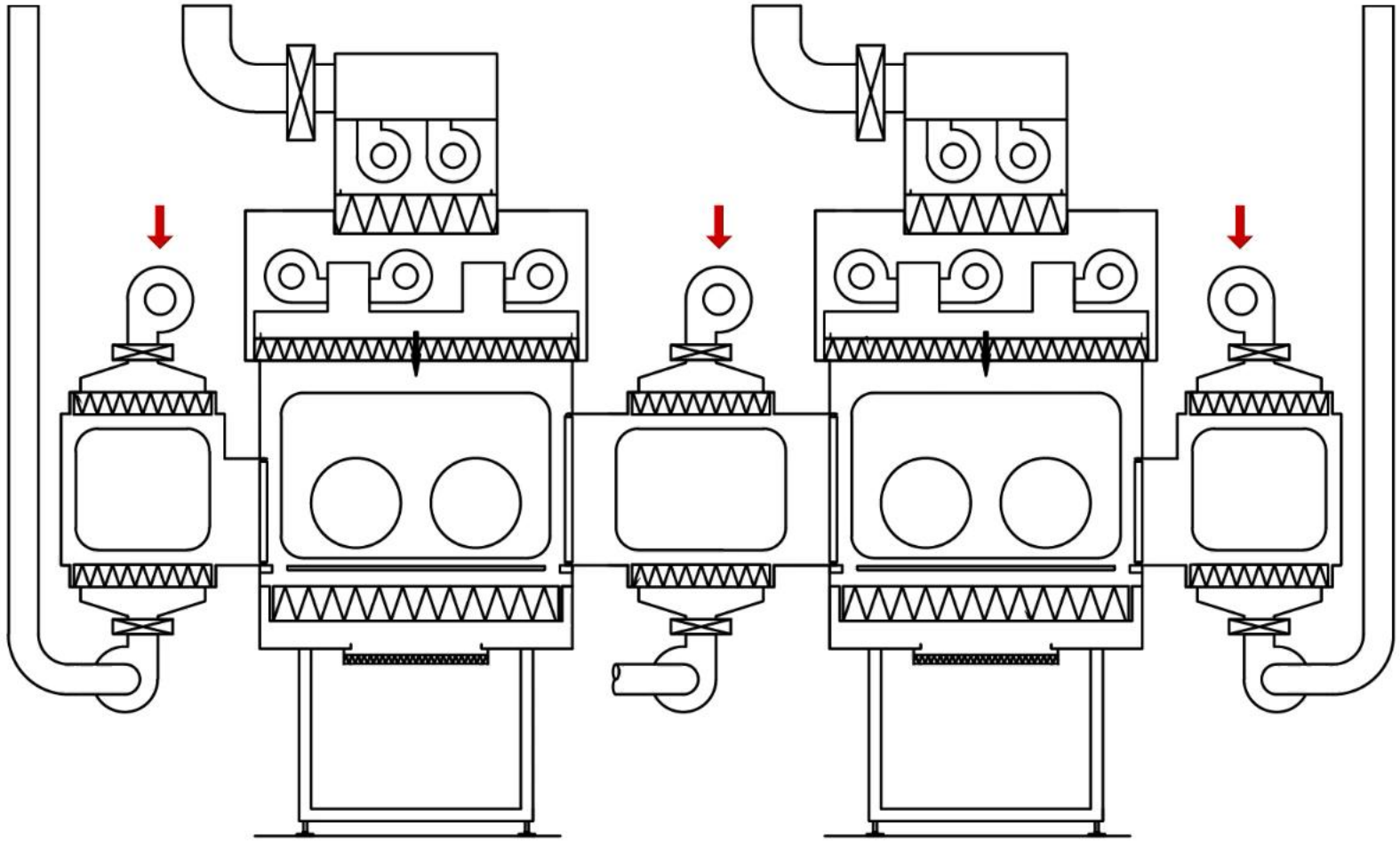
- ***The transfer device(s) – Transfer Hatches***

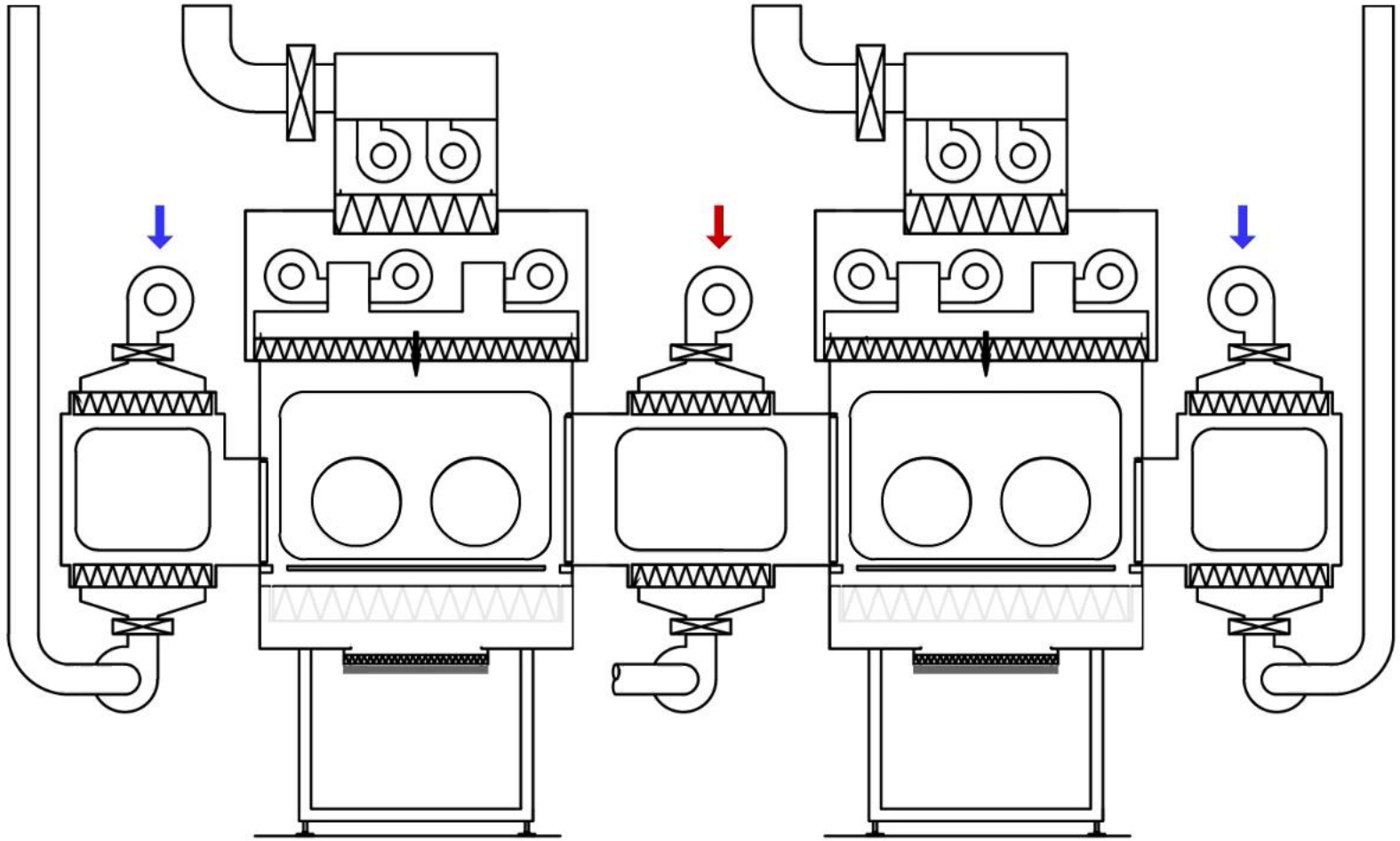
- ***The access device(s) – Ports For Operators***

- ***The automated decontamination system (Liquid, heat , gas etc).***

- ***Gassing to Log 6 reduction with VHP capability.***


VOLT-FREE CONTACT
REMOTE START/STOP
ISOLATOR
PLC





STERIS VHP® SOLUTIONS

SINGLE PASS

y (k)

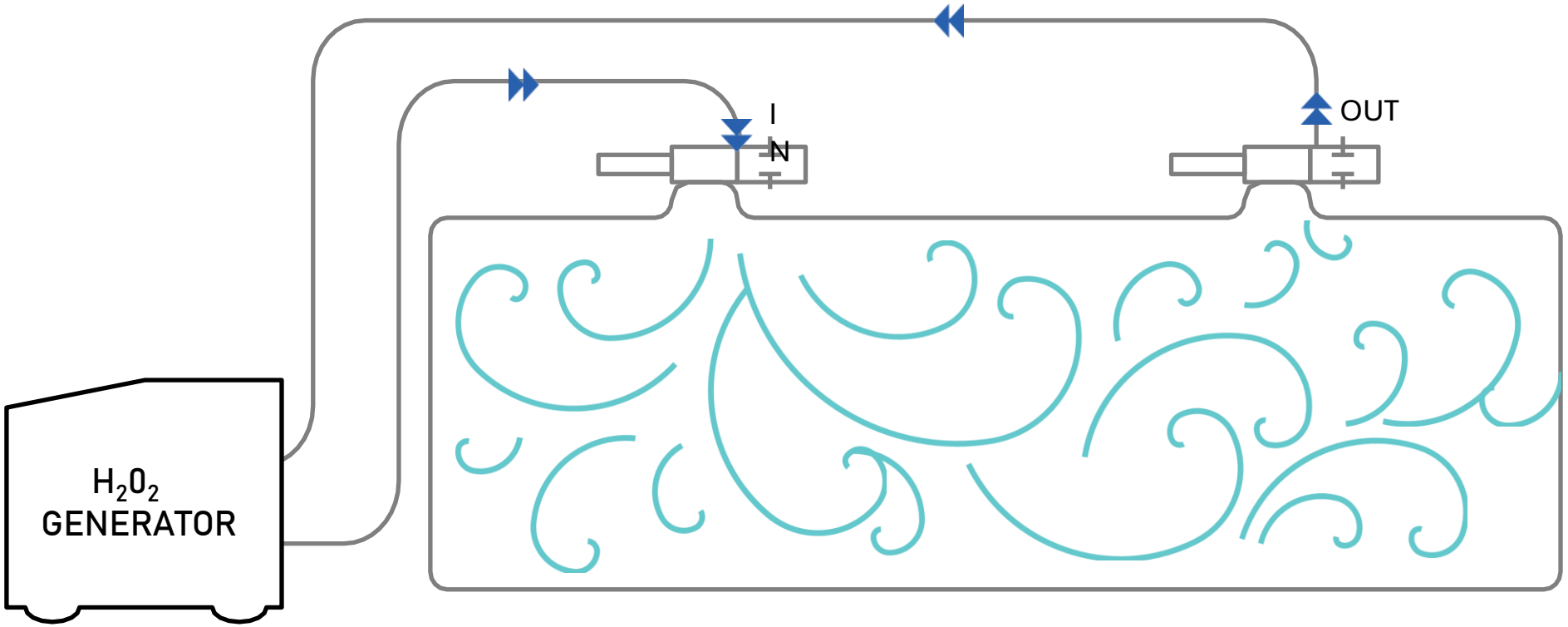
VHP Isolator technology – what to consider…

What is H_2O_2 Bio-decontamination used for?

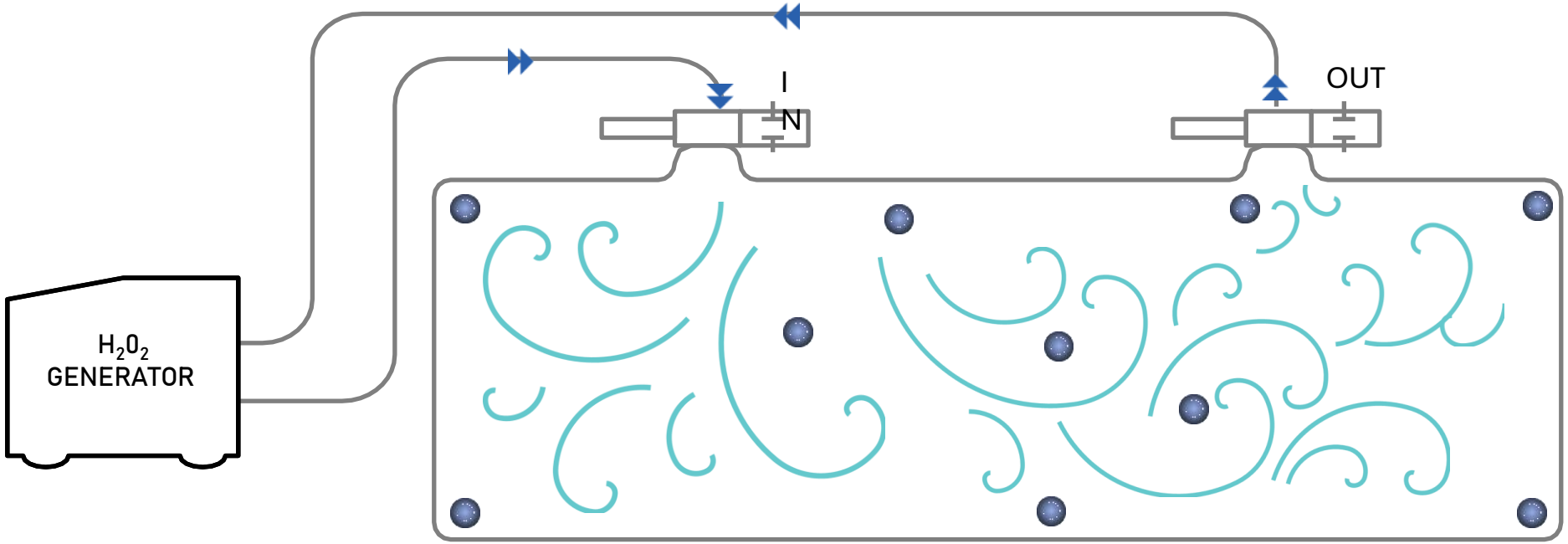
"A substance that destroys or eliminates all forms of microbial life in the inanimate environment, including all forms of vegetative bacteria, bacterial spores, fungi, fungal spores, and viruses"

Source: "EPA: Pesticides - Vaporized Hydrogen Peroxide". US Environmental Protection Agency. Archived from the original on October 10, 2006.

What is H_2O_2 Bio-decontamination?

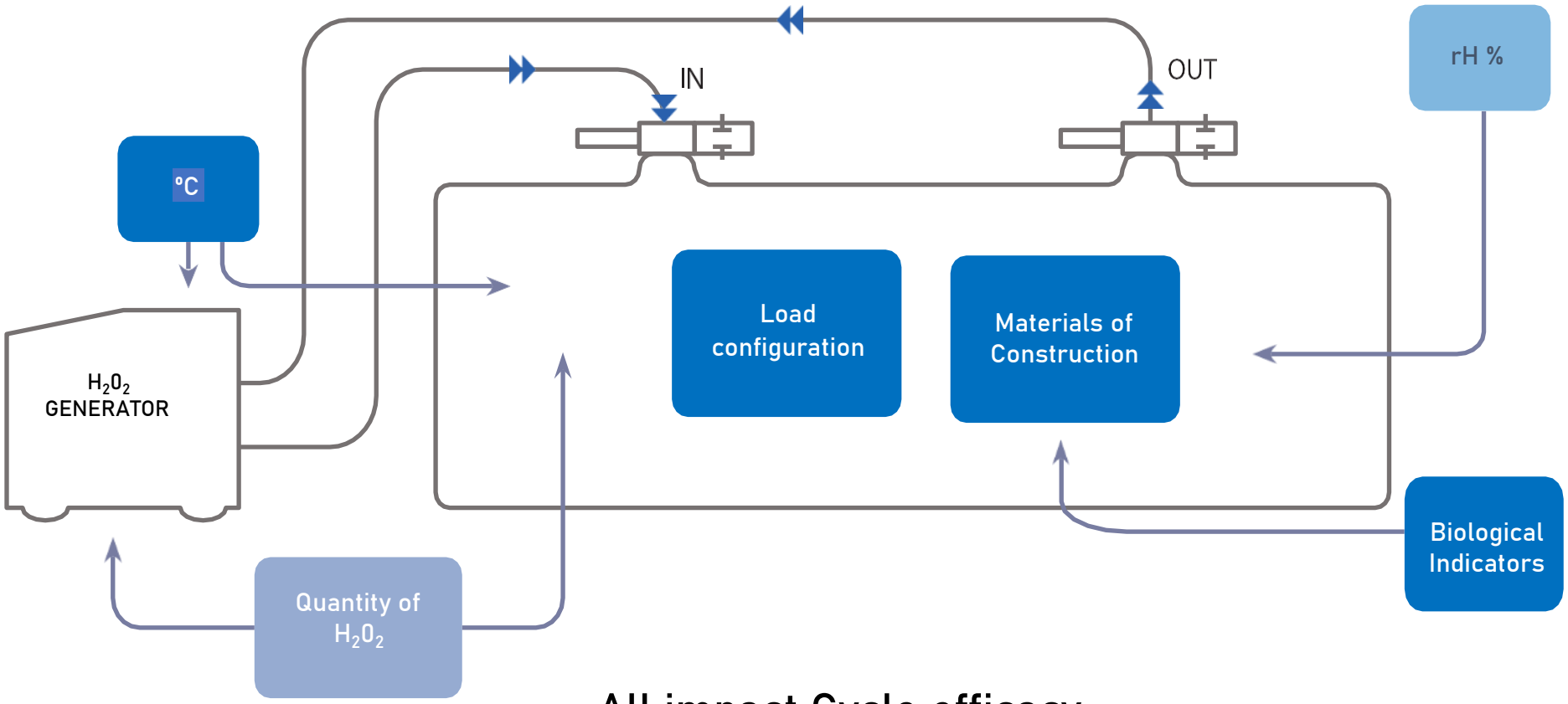


How is H_2O_2 Bio-decontamination validated?



Simple?

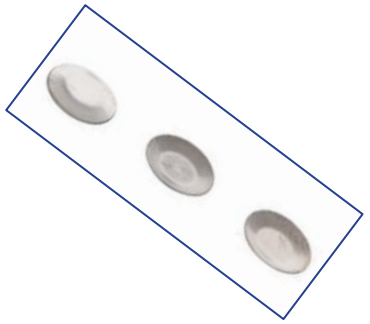
What impacts H_2O_2 Efficacy?



All impact Cycle efficacy

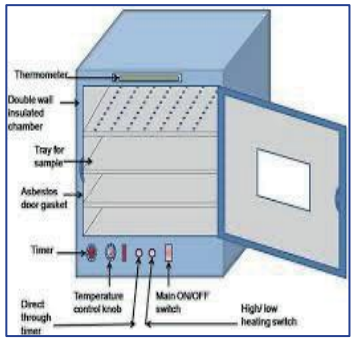
Traditional technology and methodology
Biological Indicators

0 → 7days



Biological Indicator

Growth Media



Incubation

The Result

- Monolayer ~ clumping
- USP 55: MT: viable spores per carrier -50% & +300%
- Triplicate use (MPN approach) ~ large amount used in CD & validation

Enzyme Indicator technology

0

Enzyme Indicator

Bioluminescence

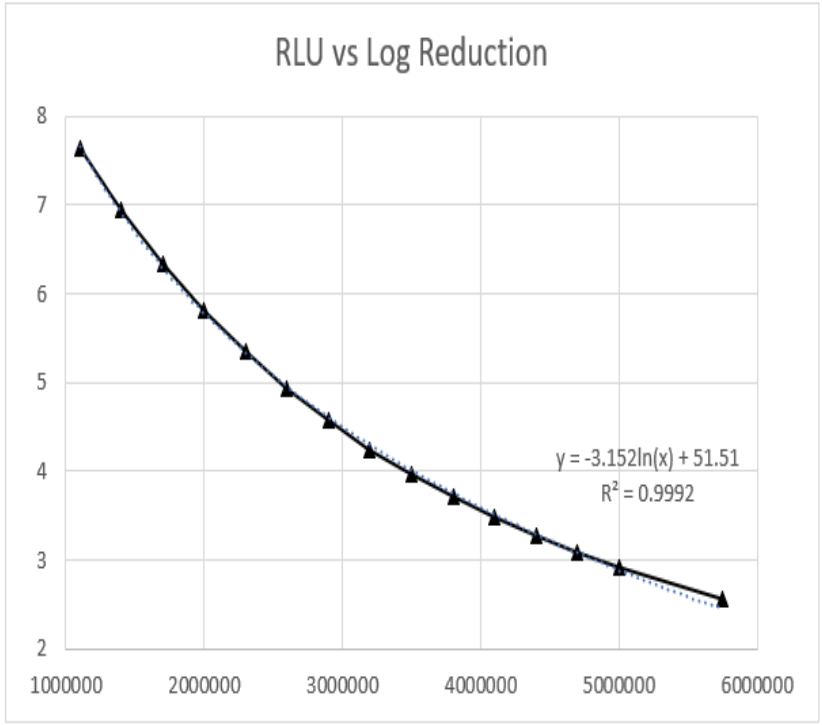
Protak Reader

The Result

60 seconds

Enzyme Indicator technology - EI/BI Correlation

Log Kill	RLU
2.56	5750000
2.92	5000000
3.09	4700000
3.28	4400000
3.48	4100000
3.71	3800000
3.97	3500000
4.25	3200000
4.57	2900000
4.94	2600000
5.35	2300000
5.81	2000000
6.34	1700000
6.95	1400000
7.65	1100000



EI/BI correlation curve generation

d	Log Reduction	Comment
3		
7	< 2.5	1 minute
7	< 2.5	2 minutes
7	< 2.5	3 minutes
5	2.6	4 minutes
5	3.0	5 minutes
5	3.4	6 minutes
5	3.7	7 minutes
5	4.3	8 minutes
5	4.9	9 minutes
5	6.1	10 minutes
5	7.5	11 minutes
5	8.0	12 minutes
5	8.8	13 minutes
5	> 9.0	14 minutes
5	> 9.0	15 minutes
5	> 9.0	

Representation during testing

Source: Parenteral *drug association (PDA) technical report 2017 - Evaluation of novel process indicators for rapid monitoring of hydrogen peroxide decontamination process, J.M Sutton et al).*

Limit testing

Liverpool University Hospitals
NHS Foundation Trust

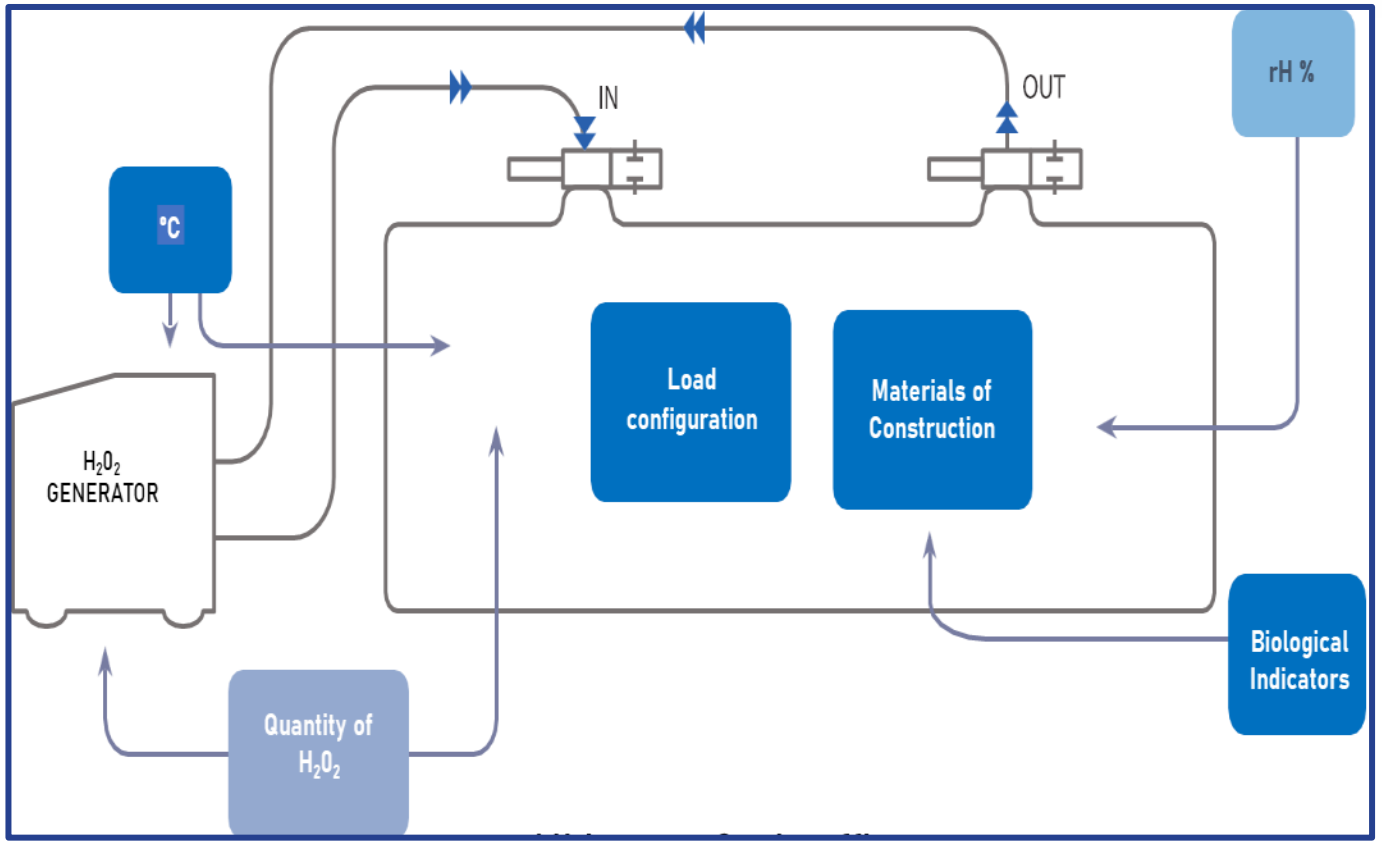
Limit testing: These tests stressed the cycle parameter limits to prove the developed cycle robustness with Els and Bls

Conditioning
- Isolator integrity
- Humidity
- Temperature
- Load configuration/ Room Set up
- Airflow

Gassing Phase
- Temperature of H2O2 generation dosing rate
- Volume of H2O2 used
- Duration of gassing phase
- Airflow

Dwell Phase
- Injection rate
- Duration of dwell phase
- Airflow

De-gassing Phase (aeration)
- Airflow (target no. of air changes



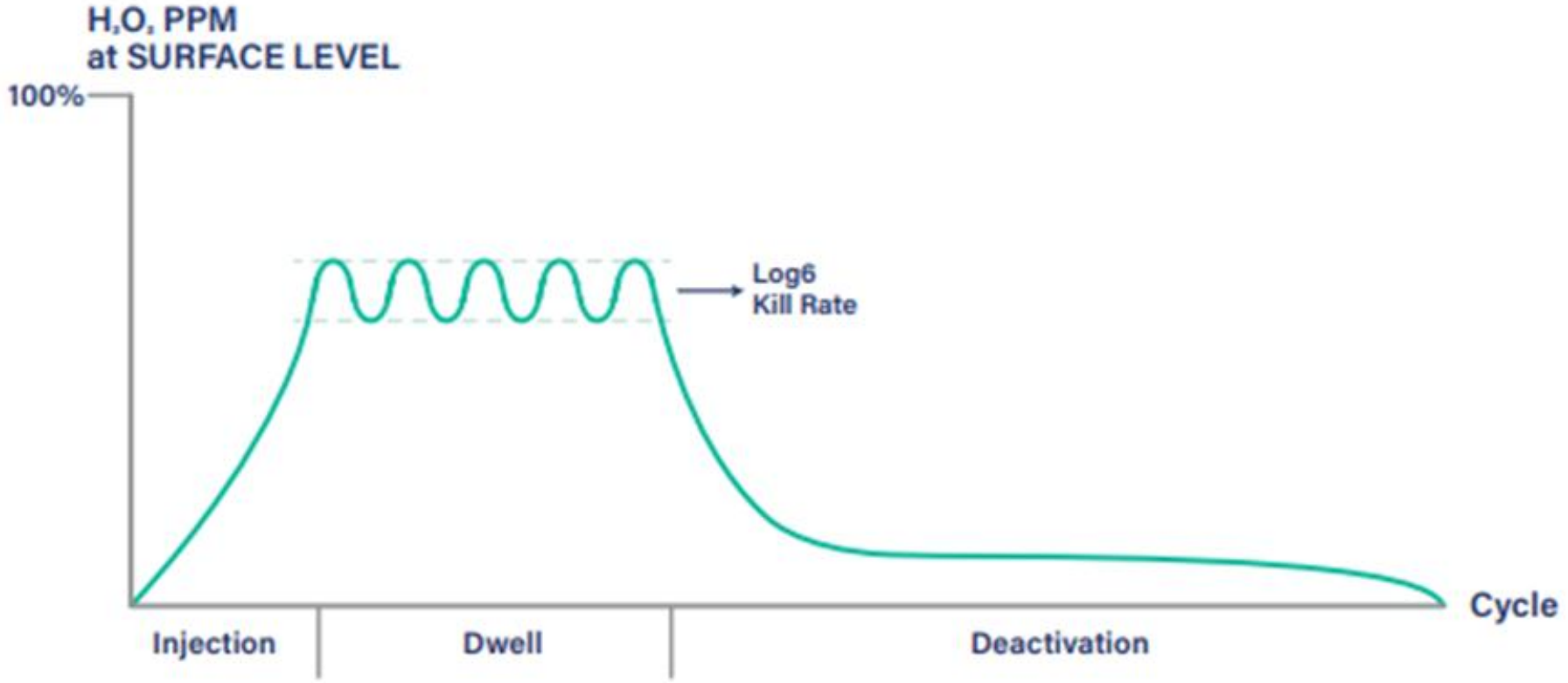

Mount for hanging of the device from the ceiling or fence
Status LED indicates the operating mode of the unit
Dräger
Robust housing, withstands even harsh environmental conditions
D-1777-2021
Proven DrägerSensor® meets industrial standards

ProXcide Mini


Cartridge
Filter
Power Button
Touch Screen
Filter Tray
Injection
Cassette
Rechargeable Battery


Inivos
Inivos

Gas Cycles

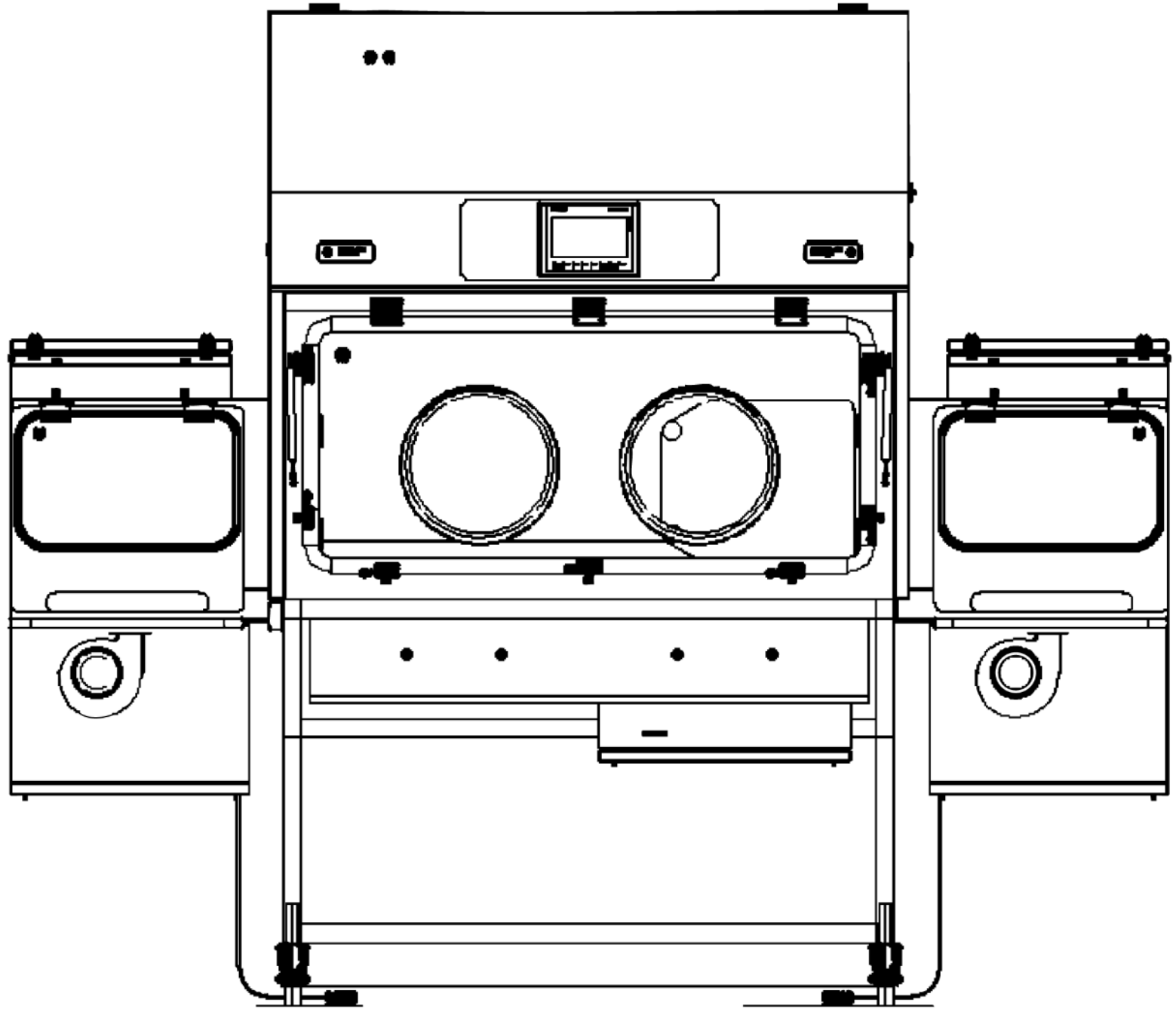


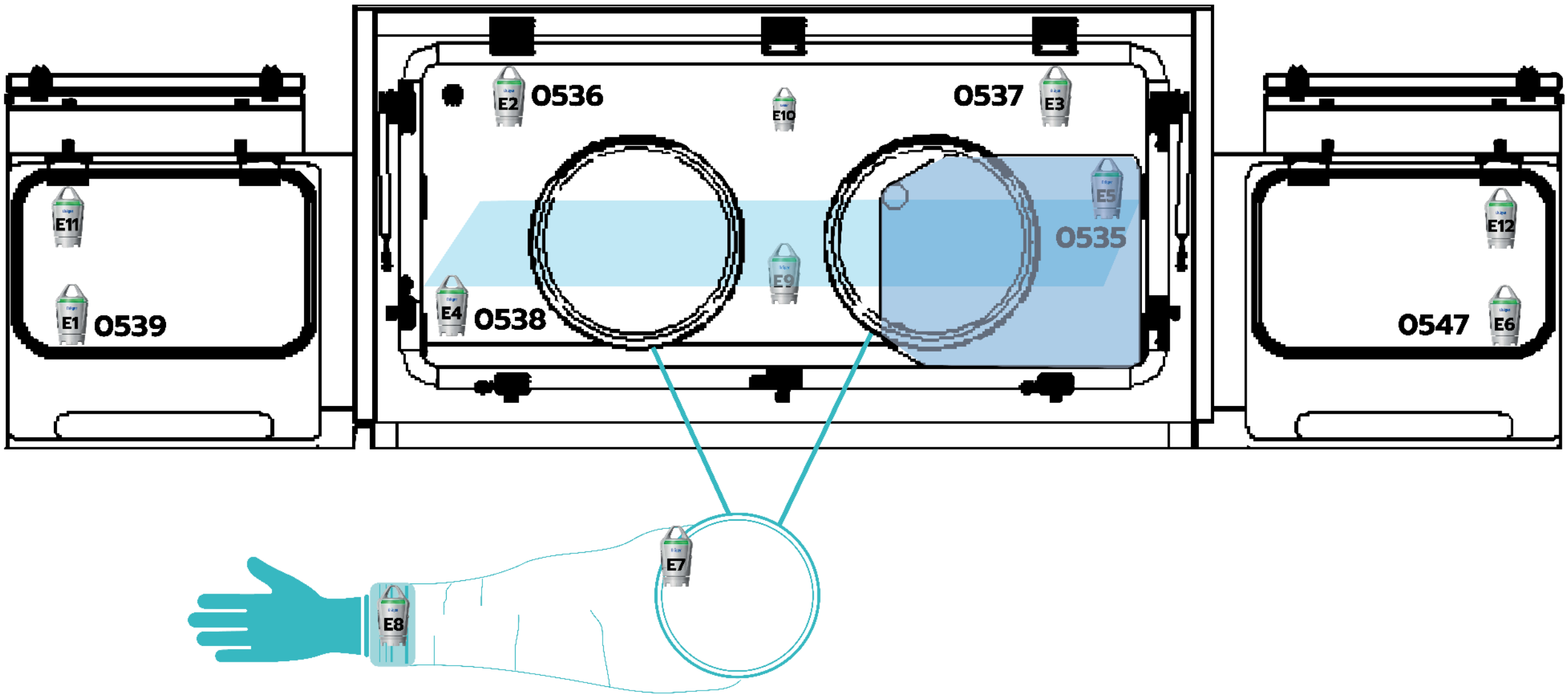
ProXcide® Mini

Injection Phase

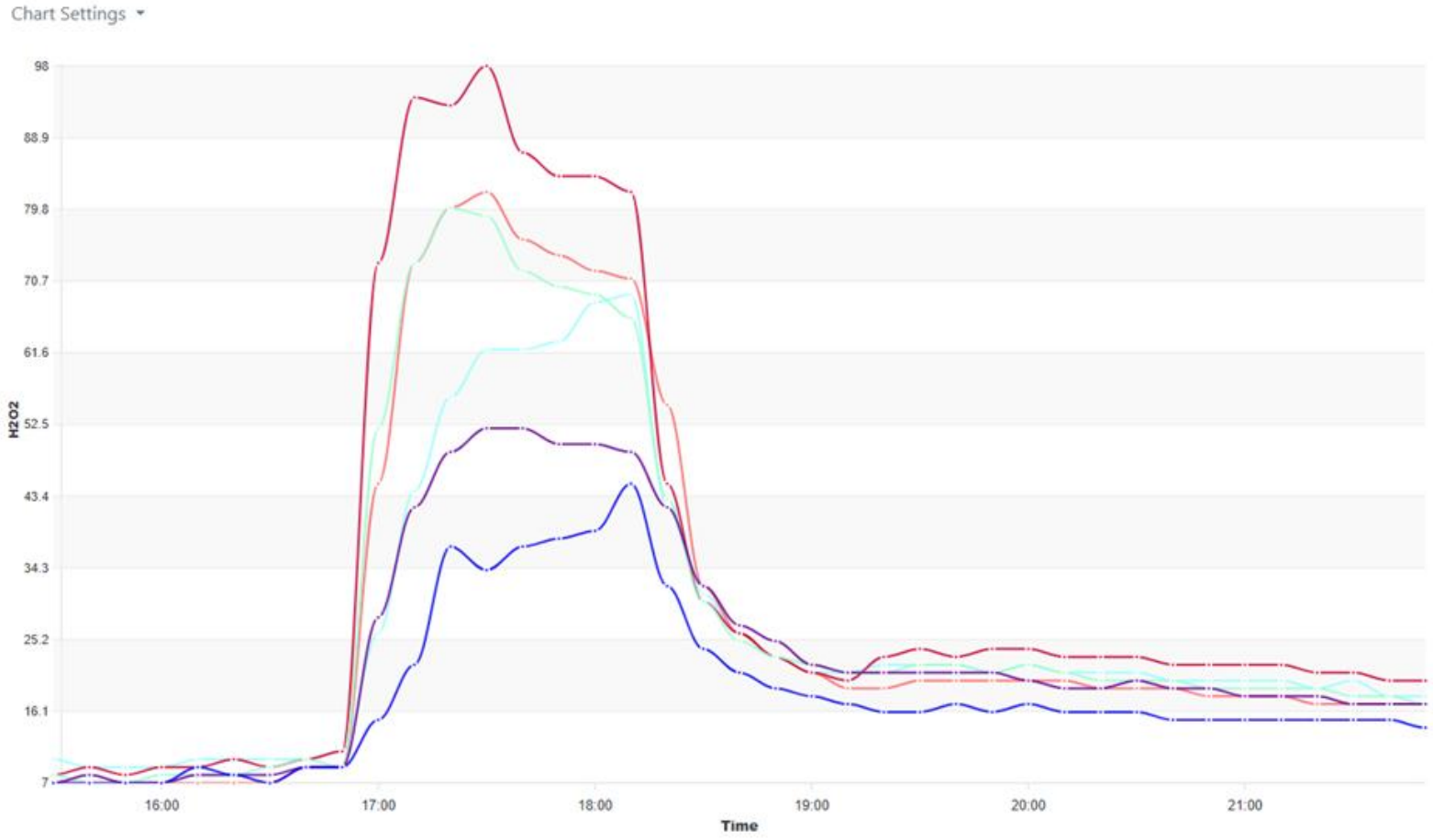
Dwell Phase

Deactivation Phase



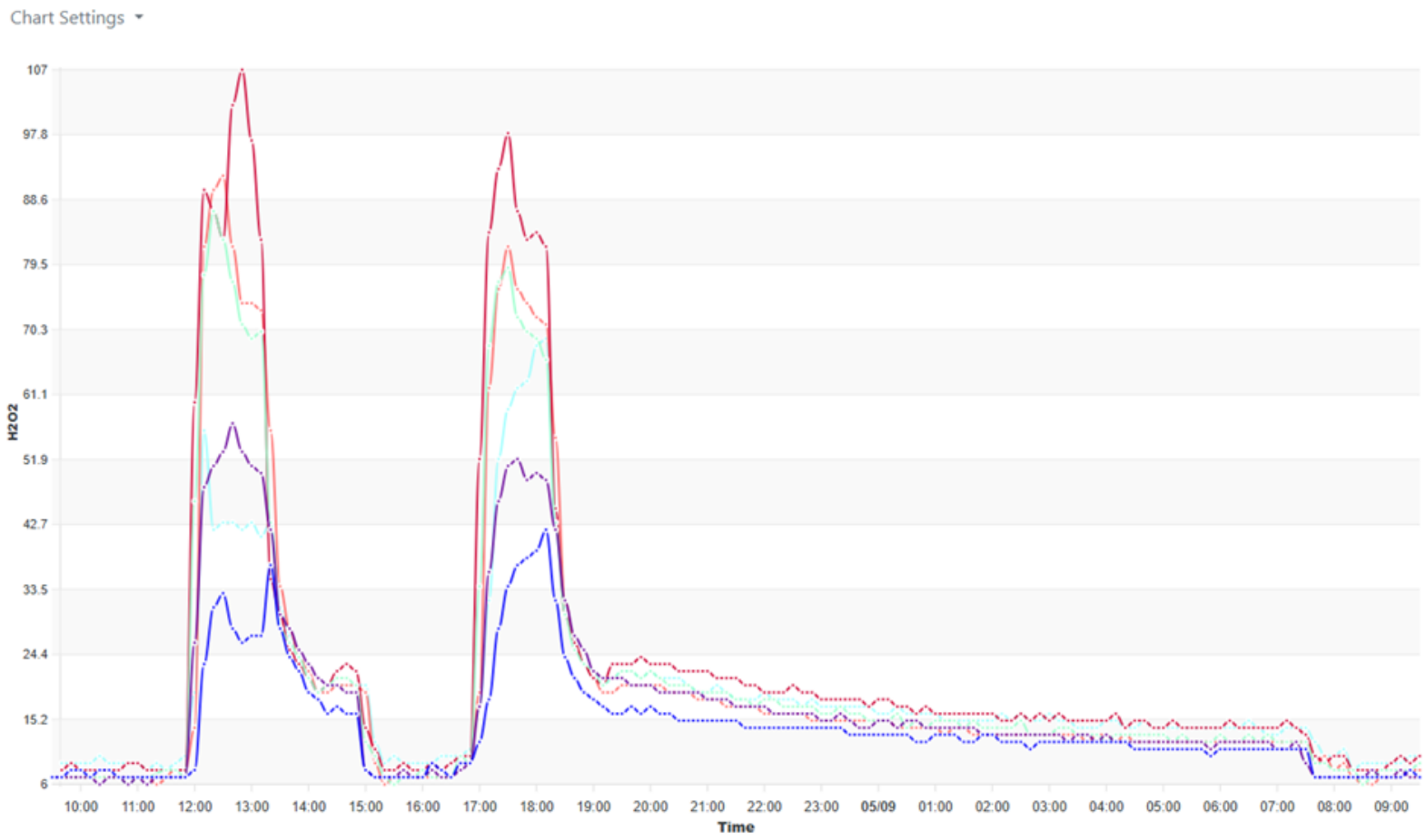

E11
E1
0539
E2
0536
E10
0537
E3
E5
0535
E4
0538
E9
E12
E6
0547
E7
E8

H2O2 Concentration Curves



Device	Gas	Show	A1/A2	Color
KSRH-0535	H2O2	☑	○	
KSRH-0537	H2O2	☑	○	
KSRH-0538	H2O2	☑	○	
KSRH-0536	H2O2	☑	○	
KSRH-0547	H2O2	☑	○	
KSRH-0539	H2O2	☑	○	

Sequential Cycles - H2O2 Concentration Curves



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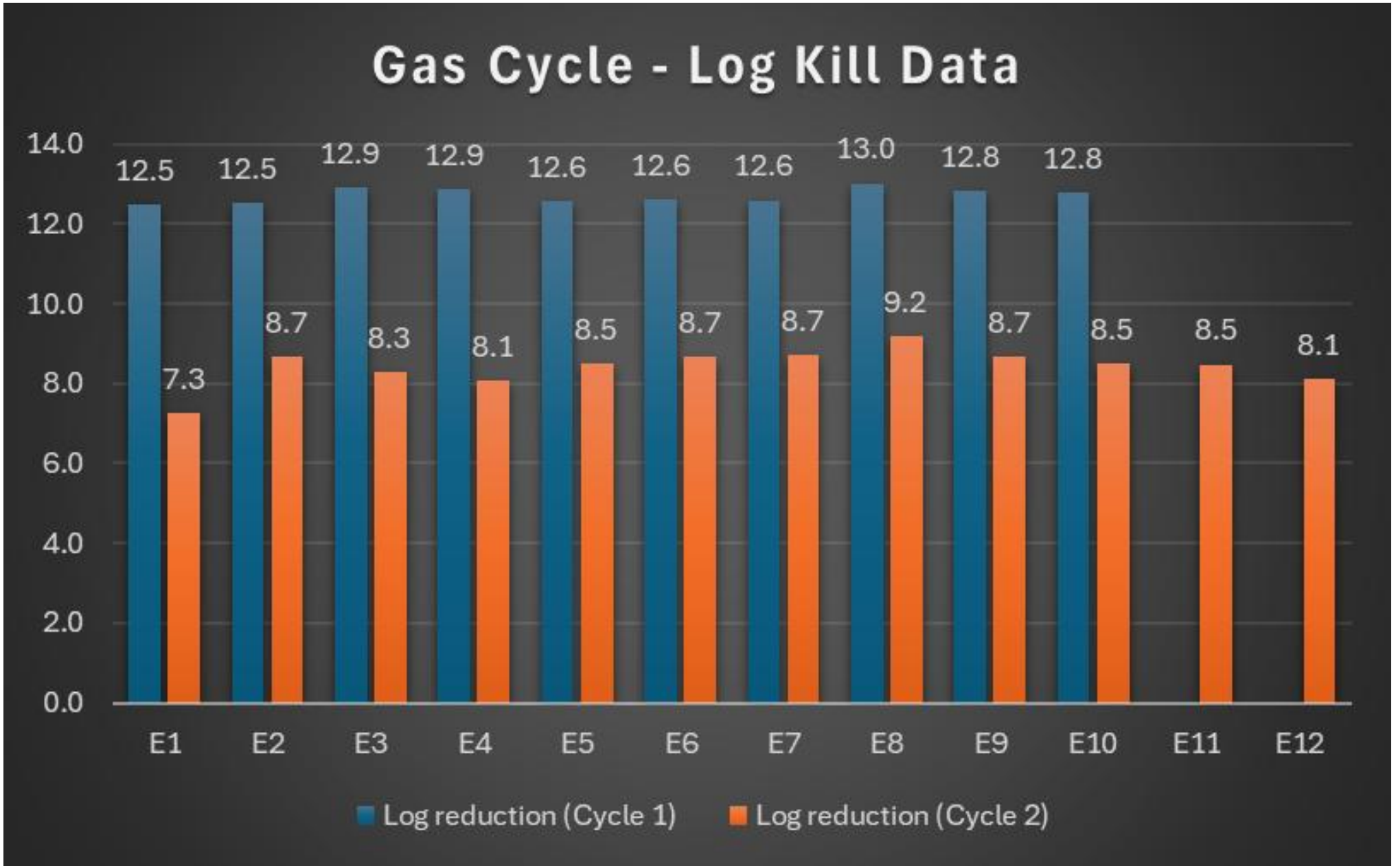
KSRH-0535	H2O2	☑	○	
KSRH-0537	H2O2	☑	○	
KSRH-0538	H2O2	☑	○	
KSRH-0536	H2O2	☑	○	
KSRH-0547	H2O2	☑	○	
KSRH-0539	H2O2	☑	○	


Gas Cycle - Log Kill Data
14.0
12.0
10.0
8.0
6.0
4.0
2.0
0.0
12.5
7.3
12.5
8.7
12.9
8.3
12.9
8.1
12.6
8.5
12.6
8.7
12.6
8.7
13.0
9.2
12.8
8.7
12.8
8.5
8.5
8.1
E1
E2
E3
E4
E5
E6
E7
E8
E9
E10
E11
E12
Log reduction (Cycle 1)
Log reduction (Cycle 2)

EI and BI results

Locations	Log reduction (Cycle 1)	Log reduction (Cycle 2)	Biological Indicator (BI)	Result (Day 7)
E1	12.5	7.3	B1	No Growth
E2	12.5	8.7	B2	No Growth
E3	12.9	8.3	B3	No Growth
E4	12.9	8.1	B4	No Growth
E5	12.6	8.5	B5	No Growth
E6	12.6	8.7	B6	No Growth
E7	12.6	8.7	B7	No Growth
E8	13.0	9.2	B8	No Growth
E9	12.8	8.7	B9	No Growth
E10	12.8	8.5	B10	No Growth
E11		8.5	B11	No Growth
E12		8.1	B12	No Growth
			Control	Growth

Phileas Genius

With thanks to Quality teams at IP5 (NWSSP) & and Wrexham (BCUHB)

Phileas Genius

- Portable
- Remote connectivity
- Programmable
- Decontamination 0.5-5m^3

Microdrop Technology

- centrifugal force projects calibrated micro (5 to 10 µm) liquid
- creates a fine non-wetting mist ➡ evaporation on contact with surface ➡ biocide penetrates cell ➡ log_6 to log_4 reduction

Diffusion

Contact Time

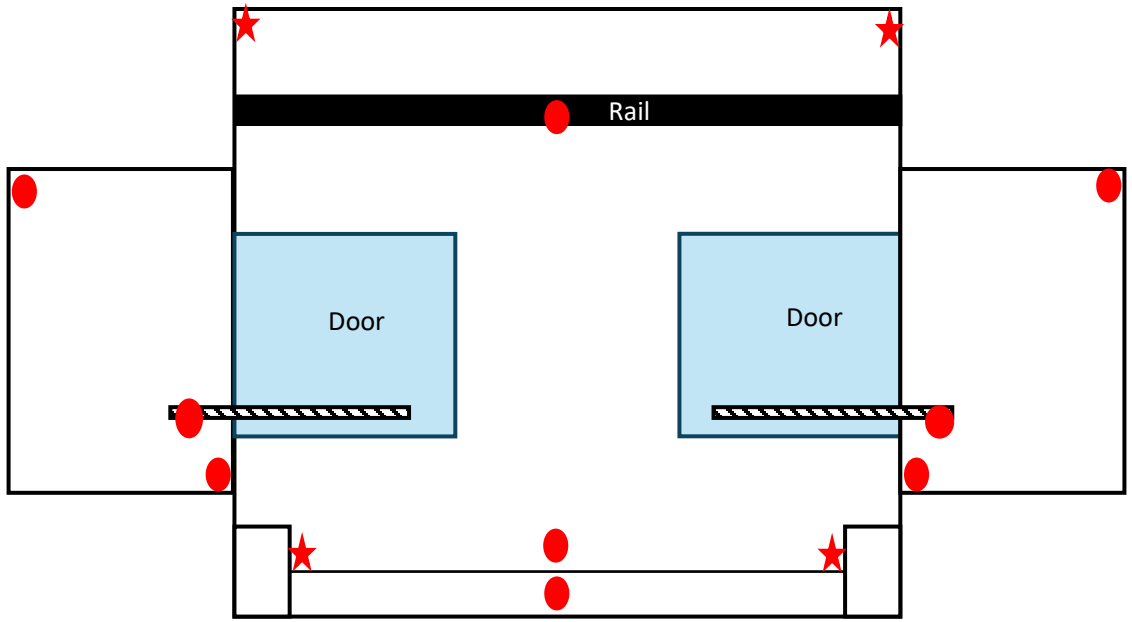
Aeration

Work to Date

- Three +ve pressure isolators at two sites (North and South Wales)
- *Envair (scoping),* Atlas and Amercare (2 and 4 glove)
- Protocol
  - Critical zone and hatches
  - Triplicate BIs (& EIs)

Test Protocols

- Atlas (North Wales)
  - 17 BI locations
  - +ve and –ve controls



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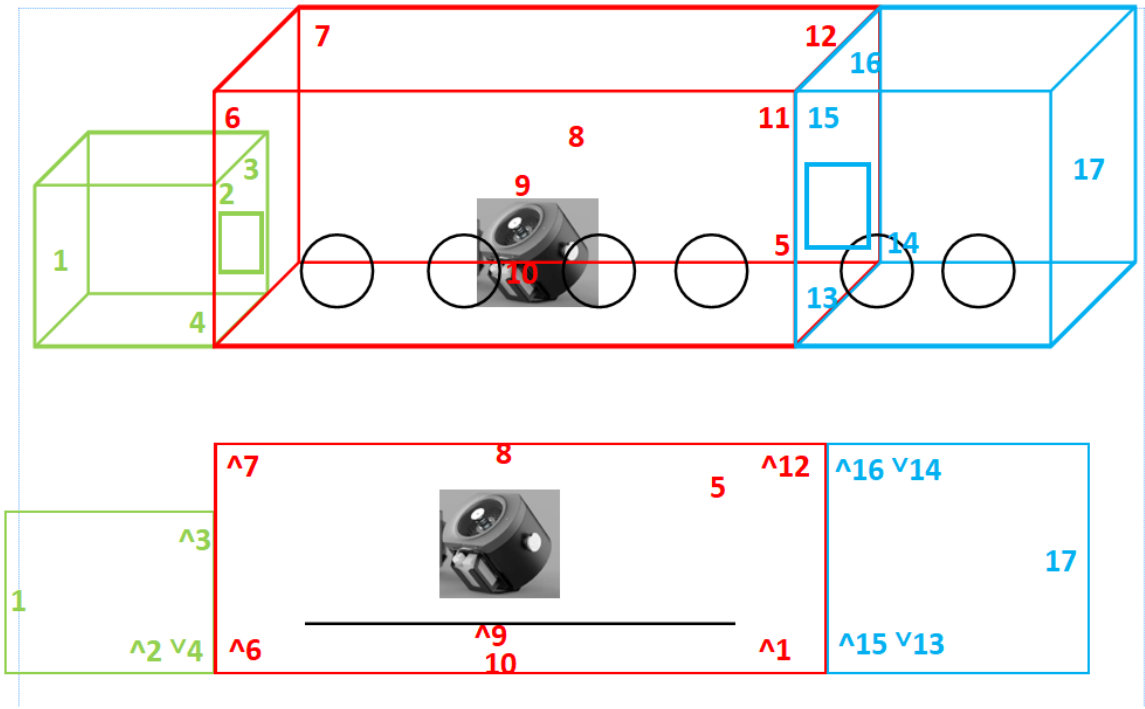
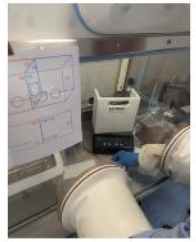
  - 17 BI locations
  - +ve and –ve controls

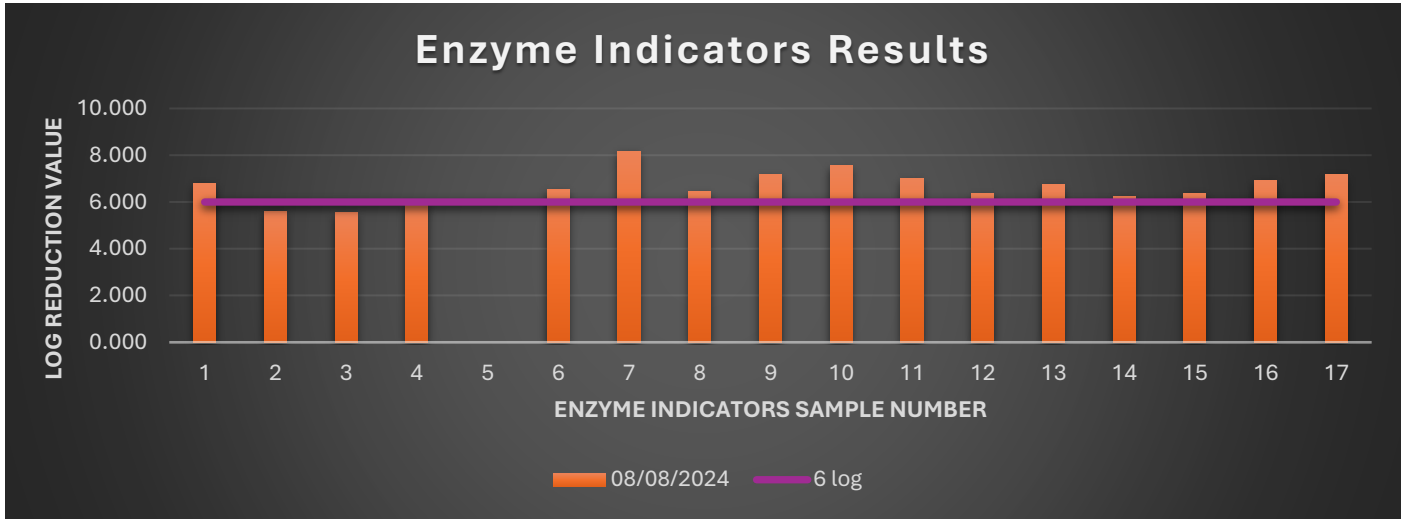


Results – SW (Amercare)

- Overnight dwell
- Total number of cycles run = 1

1A	PASS
2A	PASS
3A	PASS
4A	PASS
5A	PASS
6A	PASS
7A	PASS
8A	PASS
9A	PASS
10A	PASS
11A	PASS
12A	PASS
13A	PASS
14A	PASS
15A	PASS
16A	PASS
17A	PASS

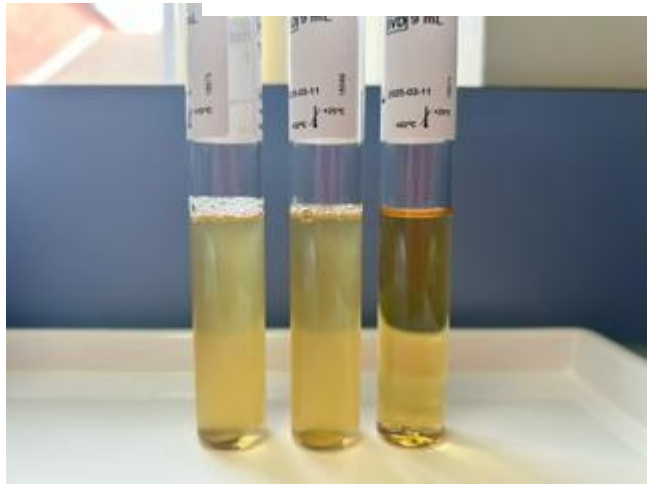




Results – NW (Atlas)

- Overnight dwell
- Total number of cycles run = 3

Location	Cycle 1	Cycle 2	Cycle 3
1			
2			
3			
4			
5			
6			
7			
8			
9			
10			
11			
12			
13			
14			
15			
16			
17			
Positive	+	+	+
Negative	–	–	–



Log_4

Summary

Success

- Simple to use and set up
- BI runs largely successful
- Hatches successfully decontaminated on a single run
- 0ppm H2O2 recorded in cleanrooms
- Promising as a retrofit solution

Issues

- Some cycles recorded higher than permitted levels of H2O2 in working zone (pooling)
- Isolator design impact (log_6 vs $log_{4)}$
- EI results variable
- Overnight cycles/dwell only

Summary

- Work needed on cycle times
- Optimal isolator parameter for gassing
- Repeatability
- -ve pressure isolators
- Acceptable log kill values in ‘non-critical/active’ workspaces

Thank you