A Practical Approach to Cycle Development Using Hydrogen Peroxide Vapor Decontamination

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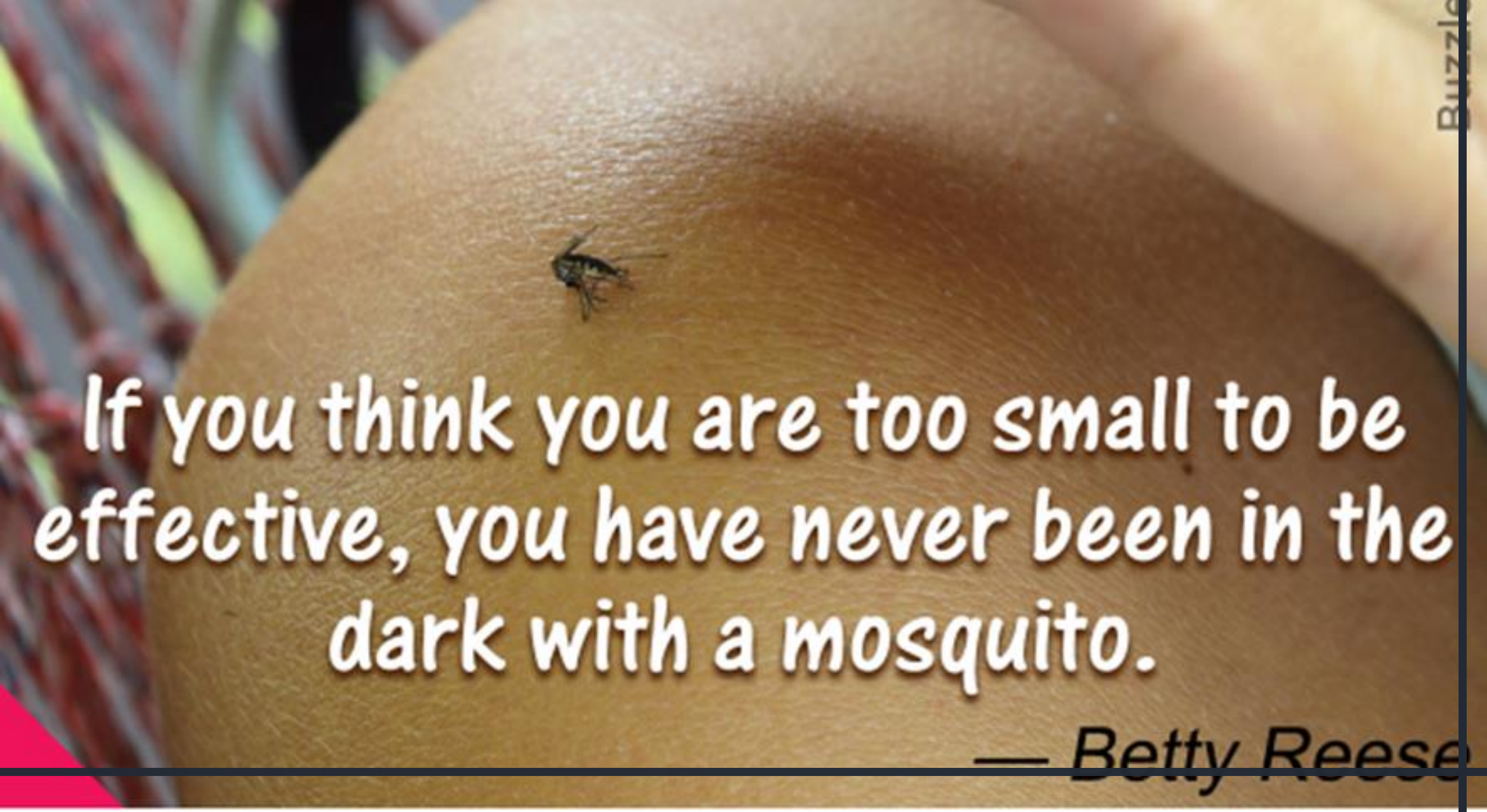

If you think you are too small to be effective, you have never been in the dark with a mosquito.
— Betty Reese

Outline

- The Basics
- Safety Considerations
- Defining a Goal
- Know Your Process!
- Chamber Loads and Loading Patterns
- A Few Notes on BI Inactivation
- Document Cycle Development Strategy
- Range Finding and Testing
- Lessons Learned

A primer on hydrogen peroxide vapor (VHP) decontamination and what we can do with it….

- What
  - HPV decontamination is low temperature process to decontaminate or sterilize surfaces
  - HPV is a broad spectrum and efficacious against spore formers
- How
  - Vaporization of liquid hydrogen peroxide (H2O2) solutions, distribution into enclosed spaces, dwell time, aerate
- Why
  - Reduce Risk
  - Replace Manual Processes
  - Increase Productivity
  - Maintain Microbial Control
- Where?

Safety Considerations

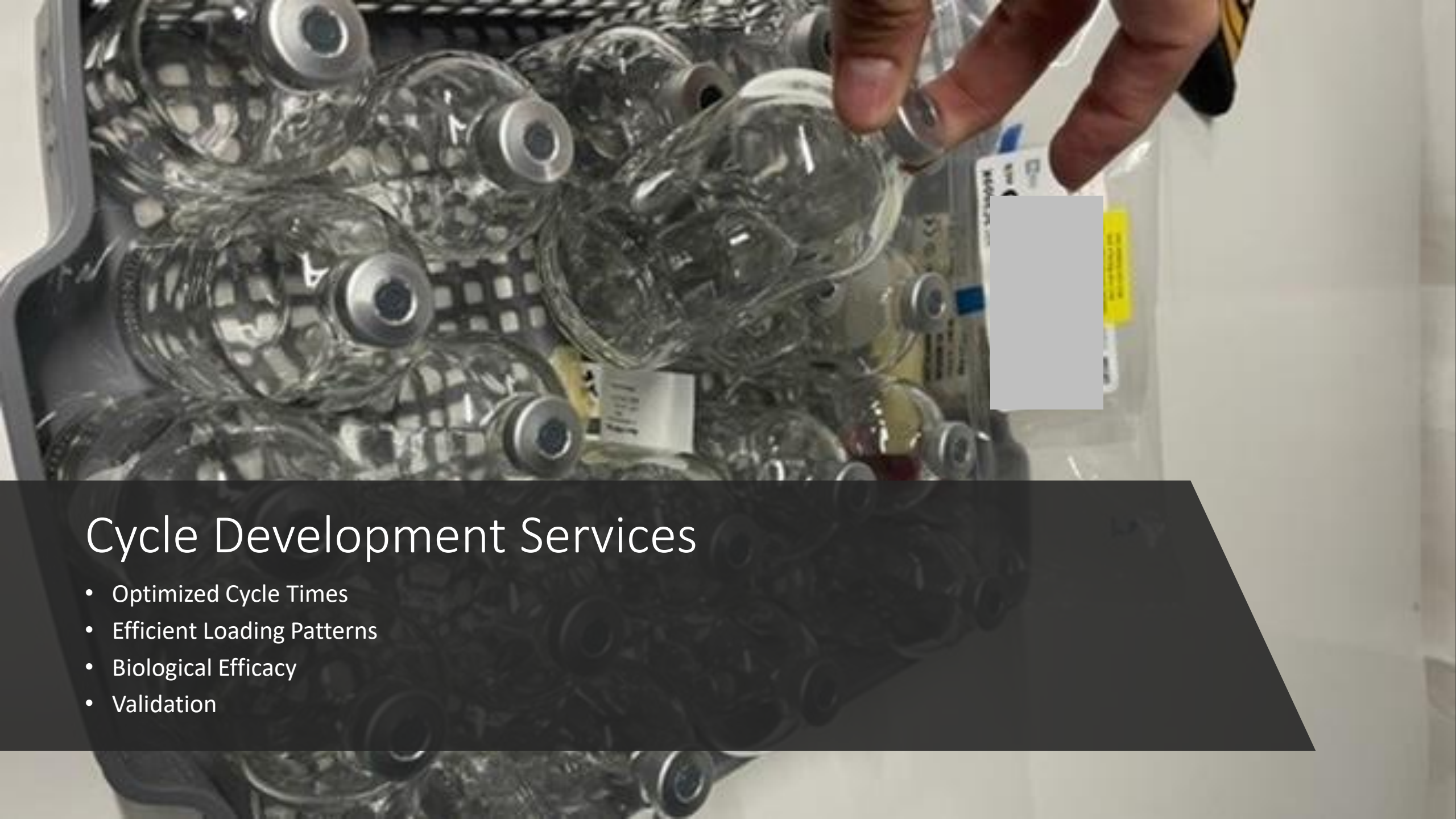
- Hydrogen peroxide is an oxidizer - consult SDS and application instructions

- Visual and Audible indicators for monitoring H2O2

- System operator exposure – 1 ppm 8hr TWA, 2 ppm STEL

- Environmental fate of decontaminant

$$2\ H_2O_2 \rightarrow 2\ H_2O + O$$

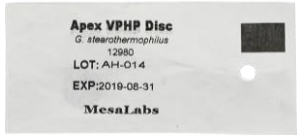


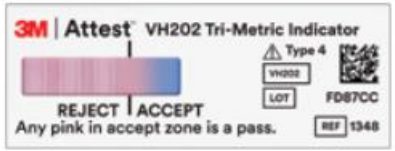
Cycle Development Services

- Optimized Cycle Times
- Efficient Loading Patterns
- Biological Efficacy
- Validation

Defining a Goal

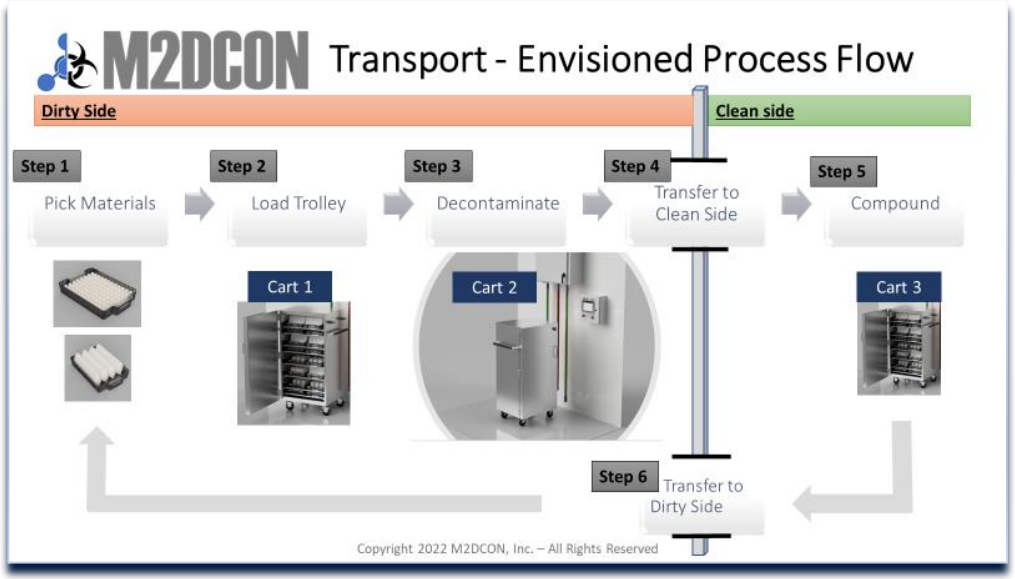
- Product Requirements
  - Rapid and effective bioburden reduction on materials before entering cleanroom spaces
  - Dry after processing, compatibility
  - Temperature range limits 4C – 25C
  - Material types: drug vials, IV bags, syringes, infusors, connectors, pipettes, tubing, hard non-porous surfaces, devices
- Cycle Requirements (desired)
  - minimum of 0.6 m3 volume of load per Hour
  - maximum 30 minutes
- Bioburden Reduction Requirements
  - 2 Log, 3 Log, 6 Log
  - Indicating Microorganism – *Geobacillus stearothermophilus*
- Cycle Efficacy Demonstration
  - Chemical Indicators
  - Biological Indicators
  - Enzyme Indicators
  - H2O2, Temp, RH Sensors

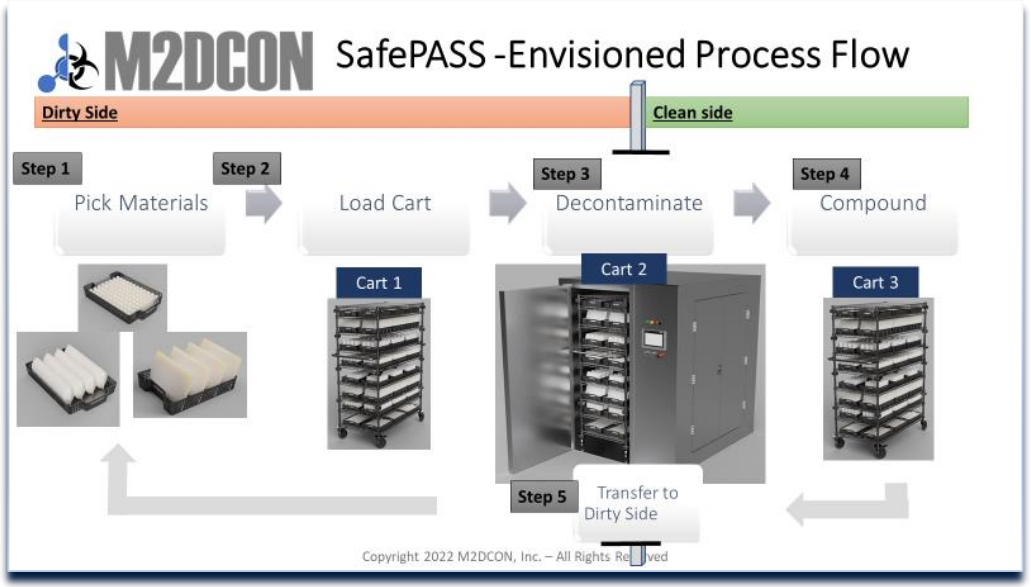




What and How Much goes into the chamber?

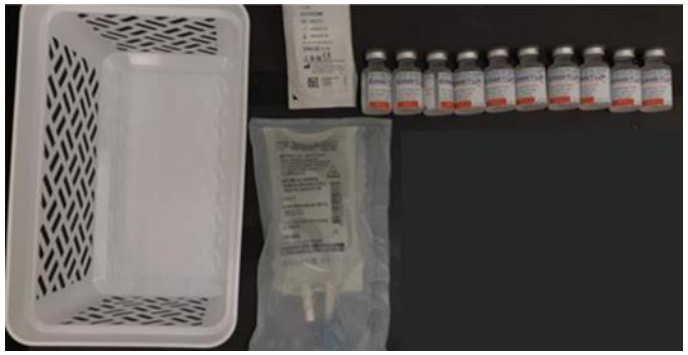
End User should have a Clear understanding of process flow





Example of Client Batch Configurations

Materials	Batch A	Batch B	Batch C	Batch D
Vials (size and qty)	22x50mm 110	45x110mm 40	25x55mm 54	25x55mm 69
IV Bags (size and qty)	500mL x 1 1000mL x 2	500mL x 1 1000mL x 3	500mL x 2 1000mL x 2	1000mL x 3
Pipettes (size and qty)	5mL x 20	None	5mL x 10	None
Syringes (size and qty)	20mL x 40	1mL x 40	None	1mL x 69
Sterile containers	100mL x 1	None	100mL x 1	None



Worst Case Load and Chamber Loading Patterns

Considerations:

- What is the maximum loading scenario?
- What is the minimum loading scenario?
- Are there differences in the materials that may impact HPV distribution or concentration?
- Operator challenges?
- Identify key factors up front and then Test!

Biological Inactivation (BI)

- BI inactivation variability
- Inactivation rate is a function of HPV concentration, water vapor concentration, and temperature
  - As the humidity increases the inactivation rate increases, however condensation should be avoided
  - Controlling RH in the enclosure is essential to ensure reproducible log reduction

Measuring Microorganism Recovery

Most Probably Number

- Estimates the surviving population
- Grow/no grow evaluation
- Experimentally simple
- Only valid in the fraction negative range (low recovery)
- Cost due to number of BI's used

Dilution and Enumeration

- Quantitative assessment of surviving population
- Plate count method
- Experimentally more complex
- Time consuming
- Requires skilled technique
- Low number of BI's used

Cycle Development Strategy

BI Characterization

- Population enumeration, media growth promotion
- CofA

Range Finding/Feasibility Testing

- Chamber concentrations @25C (temp, time, max conc)
- Load Configurations –
  - Application loads – mix of 1L saline bags and vials, 3 load configurations (Full, ½, ¼ Chamber)
  - Wort case prediction – all 1L saline bags and vials, max density of absorptive materials
- BI Challenge locations – throughout chamber, interspaced within load
  - Grow/No-Grow and/or enumeration of surviving population

Final Protocol

- 3 Consecutive Runs – based on identified worst case
- TBD# BI per chamber
- Acceptance criteria – all pass (no growth)

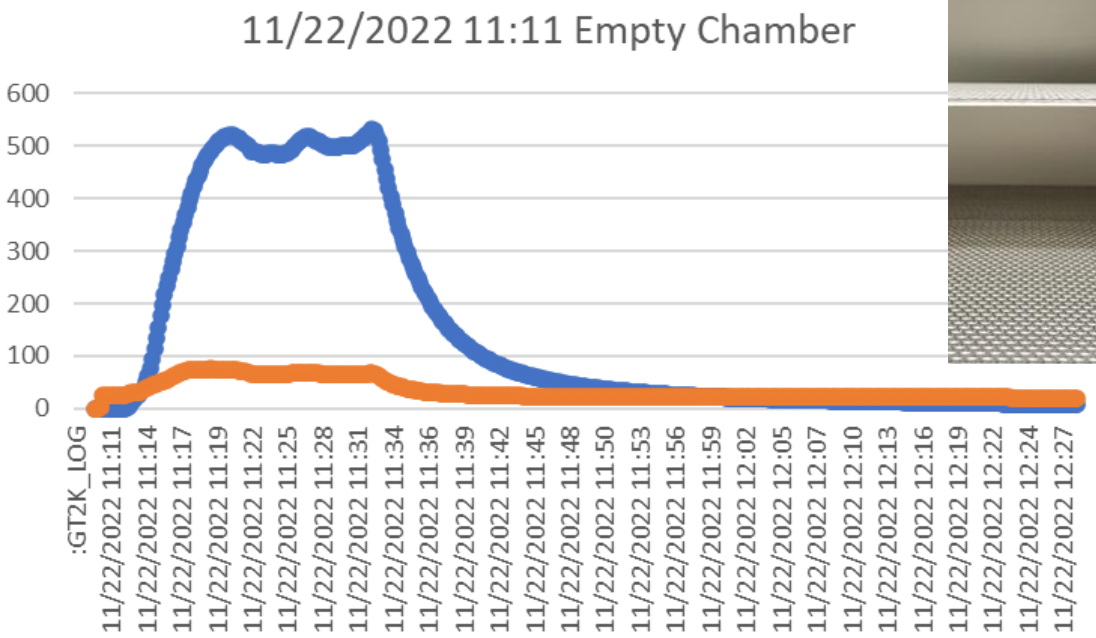
Questions

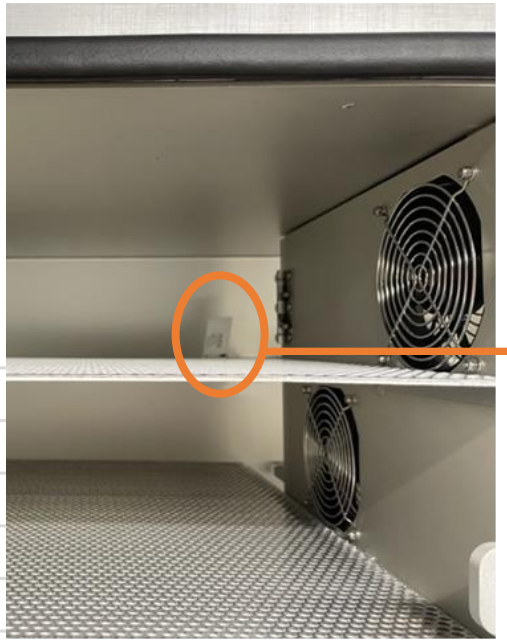
- Any visual report out for materials?

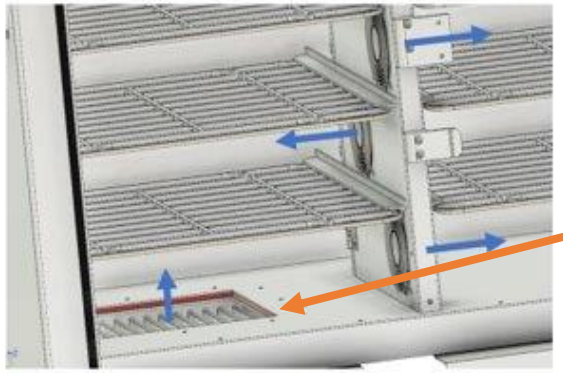
Range Finding/Chamber Mapping

- Identify range of conditions that provide desired log reduction
  - Empty Chamber – Distribution
  - Loaded Chamber – ¼, ½, Full Chamber
  - Worst Case Load and Loading Pattern
- Vary HPV concentration, water saturation, exposure time
- Use of chemical, biological and/or enzyme indicators, and H2O2, temp, RH sensors

Empty Chamber







Keeping Track of Testing Components

HPV Out

	Left Side			Right Side	
Shelf	Front	Back		Front	Back
1	② V	V		EMPTY	
2	V③	V		I4④	I4
3	V	V		I4	I4
4	V	V⑤		I4	I4
5	V⑥	V		① I4	I4⑦
6	V	V		I4	I4
7	V⑧	V		I4	I4
8	I4	I4		I4⑨	I4
9	EMPTY			I4	I4 ⑩

HPV In

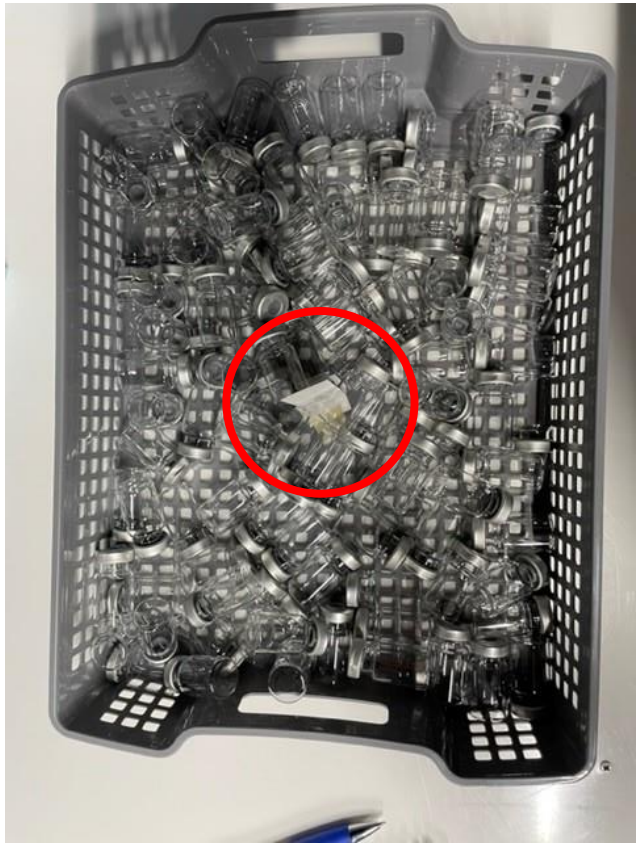
BI Number	Location in Chamber
1	Taped to fan panel in center of chamber, Right side shelf row 5
2	Taped to Left uppermost chamber wall, Left side shelf row 1
3	Inside Vial tray, BI taped to center bottom of tray between large vials. Tray placed on shelf row 2, left side, front position
4	Inside wrapped Infuser tray, BI taped to center bottom of tray between 2 infusers. Tray placed on shelf row 2, right side, front position
5	Inside Vial tray, BI taped to center bottom of tray between large vials. Tray placed on shelf row 4, left side, back position
6	Inside wrapped vial tray, BI taped to center bottom of tray between large vials. Tray placed on row 5 shelf, left side, front position
7	Inside wrapped Infuser tray, BI taped to center bottom of tray between 2 infusers. Tray placed on shelf row 5, right side, back position
8	Inside wrapped vial tray, BI taped to center bottom of tray between large vials. Tray placed on row 7 shelf, left side, front position
9	Inside wrapped Infuser tray, BI taped to center bottom of tray between 2 infusers. Tray placed on shelf row 8, right side, front position
10	Inside wrapped Infuser tray, BI taped to center bottom of tray between two infusers. Tray placed on shelf row 9, right side, back position

Legend:

V = tray with vials as main component

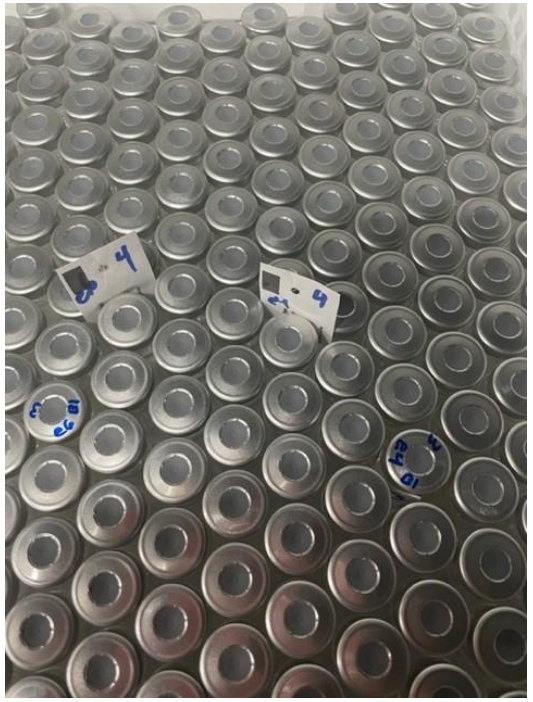
B = tray with IV bags as main component

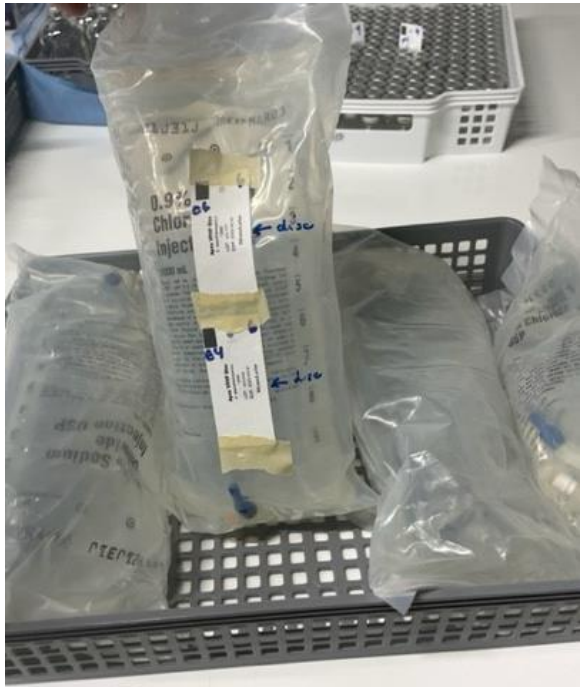
I = tray with infusors with main component (# indicates how many)



BI Placement

Locations will be selected based on perceived worst-case mixing or occlusion scenarios (amongst multiple vials in the bottom of a tray, trapped between IV bag and bottom/wall of tray etc.).





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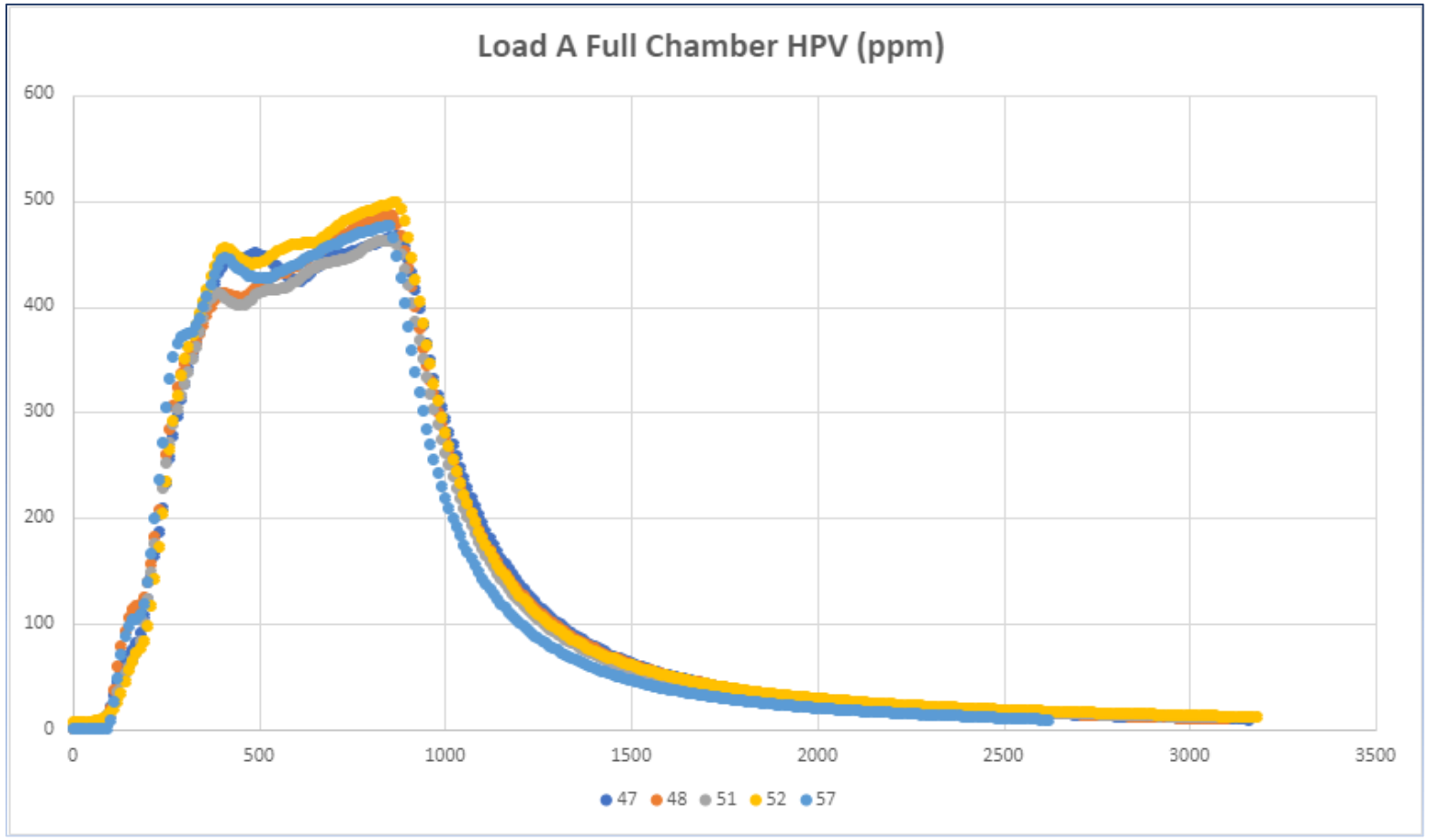
Lots and Lots of Testing…



Lessons Learned…

Client:

“We had a discussion with our Regulatory Authority …

they would like us to use a dust cover….”

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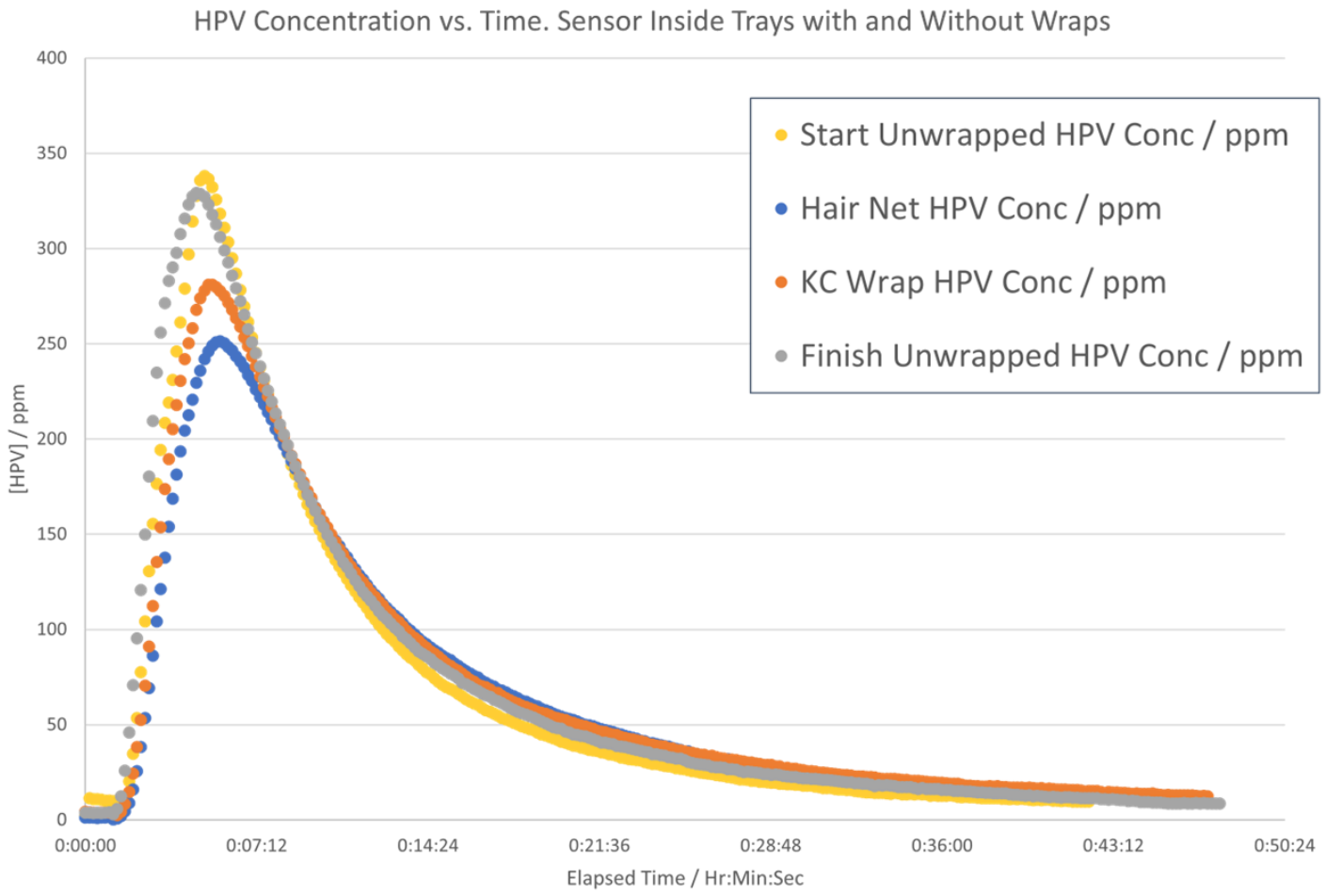

Repeat Testing

<u>Barrier may impact:</u>

- HPV concentration
- HPV Distribution
- Aeration
- Cycle Time

More Lessons Learned …

- Final Verification Cycle Testing Resulted in Positive BI's at same location…

- Investigation Ensues…
  - Visual Inspection of Chamber, Materials, Cycle Data
  - Confirmatory Testing

- Culprit …

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