



## Microbial Contamination and Control Conference

May 7<sup>th</sup> & 8<sup>th</sup>



# Future of Disinfection Efficacy Testing: Aligning Validation to Regulatory Landscapes

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May 7<sup>th</sup> & 8<sup>th</sup>



## Agenda

- Disinfectant Validation: Regulatory Requirements and Expectations
- Traditional Test Methodology
- Method Development for Cleanroom disinfectant Validation
- Study Considerations
- Beyond Laboratory Testing: In Situ Assessment





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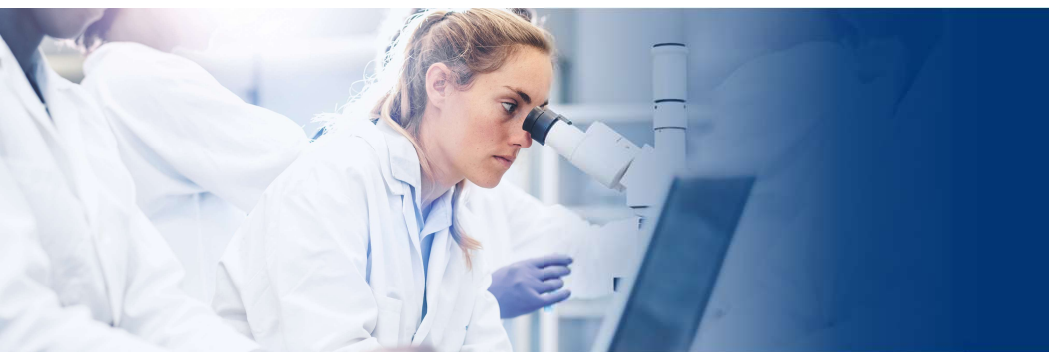
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# Regulations supporting validation

## EU GMP Annex 1 2022

“The disinfection of cleanrooms is particularly important. They should be cleaned and disinfected thoroughly in accordance with a written programme... **More than one type of disinfecting agent should be employed** to ensure that where they have different modes of action and their combined usage is effective against all bacteria and fungi. **Disinfection should include the periodic use of a sporicidal agent.** Monitoring should be undertaken regularly in order to assess the effectiveness of the disinfection program and to detect changes in types of microbial flora (e.g. organisms resistant to the disinfection regime currently in use). Cleaning programmes should effectively remove disinfectant residues.”



“The disinfection process should be validated. Validation studies should demonstrate the suitability and effectiveness of disinfectants in the specific manner in which they are used and should support the in-use expiry periods of prepared solutions.”



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# Guidance supporting validation

### FDA Guidance for Industry - Sterile drug products produced by aseptic processing

“The suitability, efficacy, and limitations of disinfecting agents and procedures should be assessed. The effectiveness of these disinfectants and procedures should be measured by their ability to ensure that potential contaminants are adequately removed from surfaces.”

### PIC/S PI 007-6 – Recommendation on the validation of aseptic processes

“The effectiveness of disinfectants and the minimum contact time on different surfaces should be validated.”





# Standards used for validation testing

Region	Method	Intended purpose of method
U.S.	USP <1072>	Guidance for disinfection in pharmaceutical manufacturing environments
U.S.	ASTM E2197	Surface-based test method to determine bactericidal, virucidal, fungicidal, mycobactericidal, and sporicidal activities of chemicals
Europe	EN 1276 & EN 1650	Suspension-based test methods for evaluating bactericidal and fungicidal activity of disinfectants, respectively
Europe	EN 13697	Surface-based test method for determining bactericidal and fungicidal activity of disinfectants
Europe	EN 13704	Suspension-based test method for evaluating sporicidal activity of disinfectants
Europe	EN 16615	Surface-based test method for determining bactericidal and fungicidal activity of disinfectants with mechanical action (wiping)



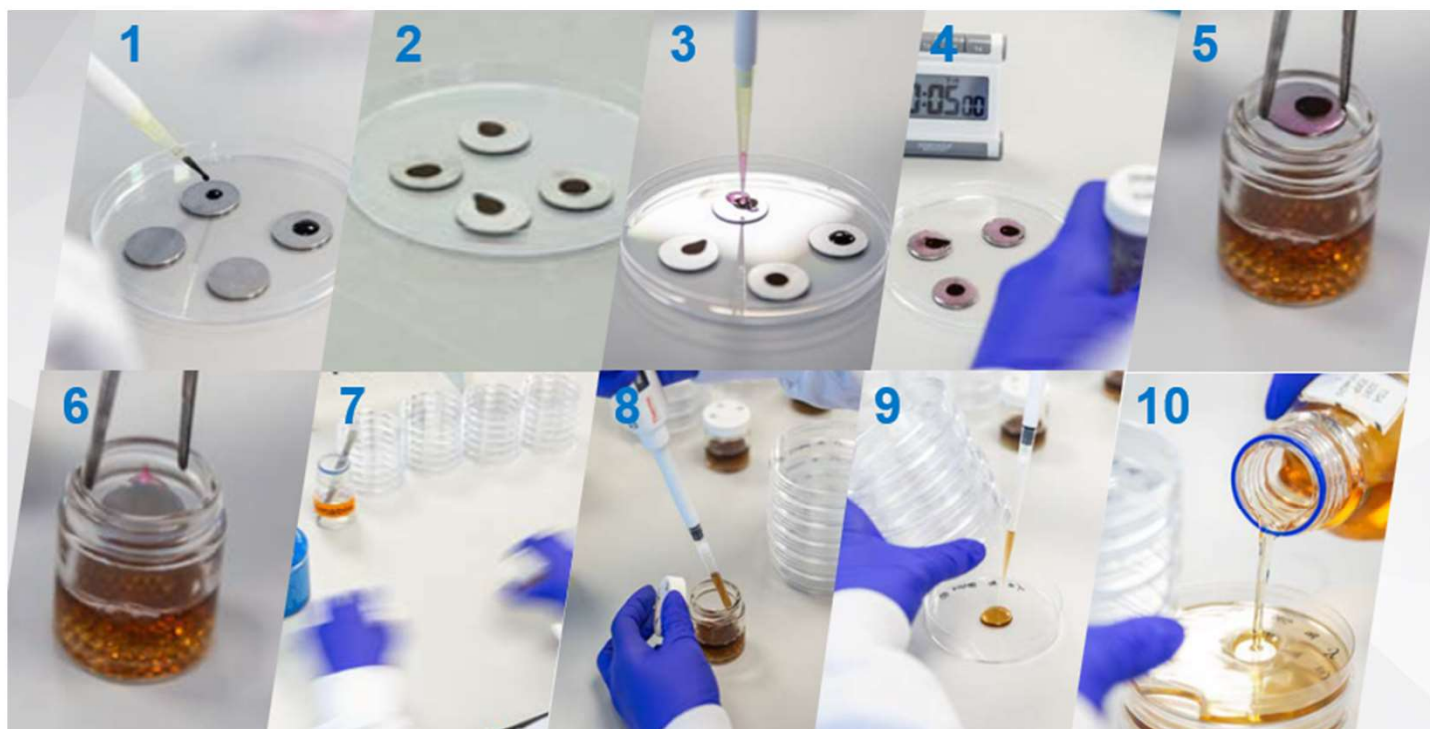
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## Disinfectant Efficacy Test Methods EN 13697

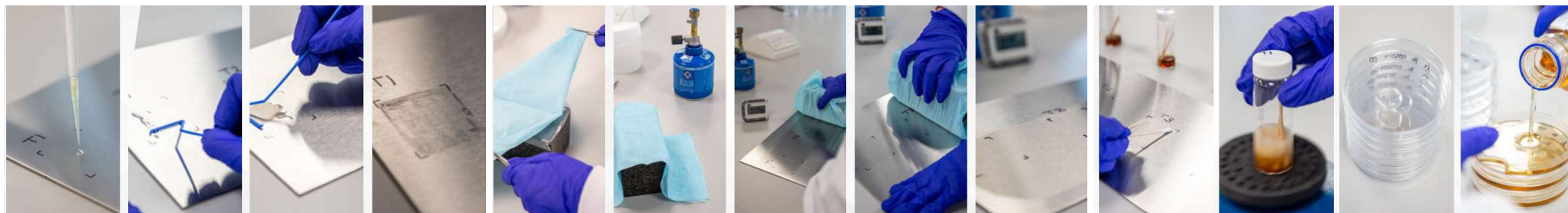
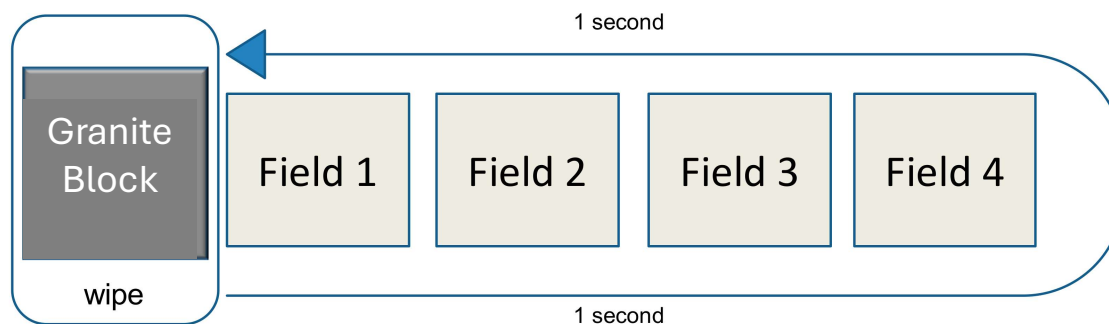
AOAC 961.02





# Disinfectant Efficacy Test Methods

## EN 16615





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# Study Considerations and Development



- Compare differences in regional test standards
- Organism and surface selection
- Test surface size
- Volume of inoculum and disinfectant
- Strength, preparation and application of test inoculation
- Drying process of organism on test surface
- Method repeatability

Specific to  
**disinfectant wipe  
assessment**

- Wipe substrate
- Saturation
- Wiping motion
- Weight application
- Number of wipe folds/layers
- Organism recovery method



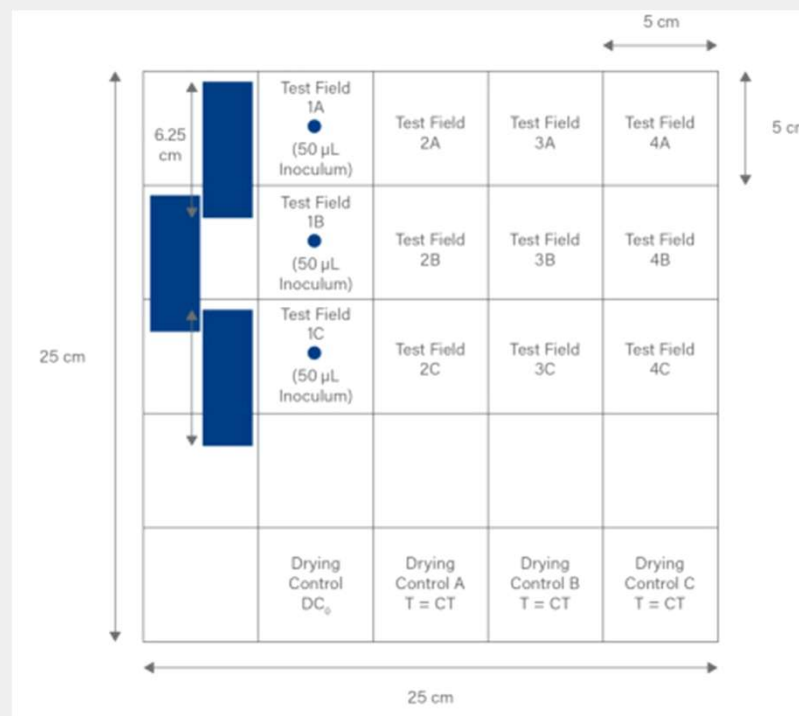
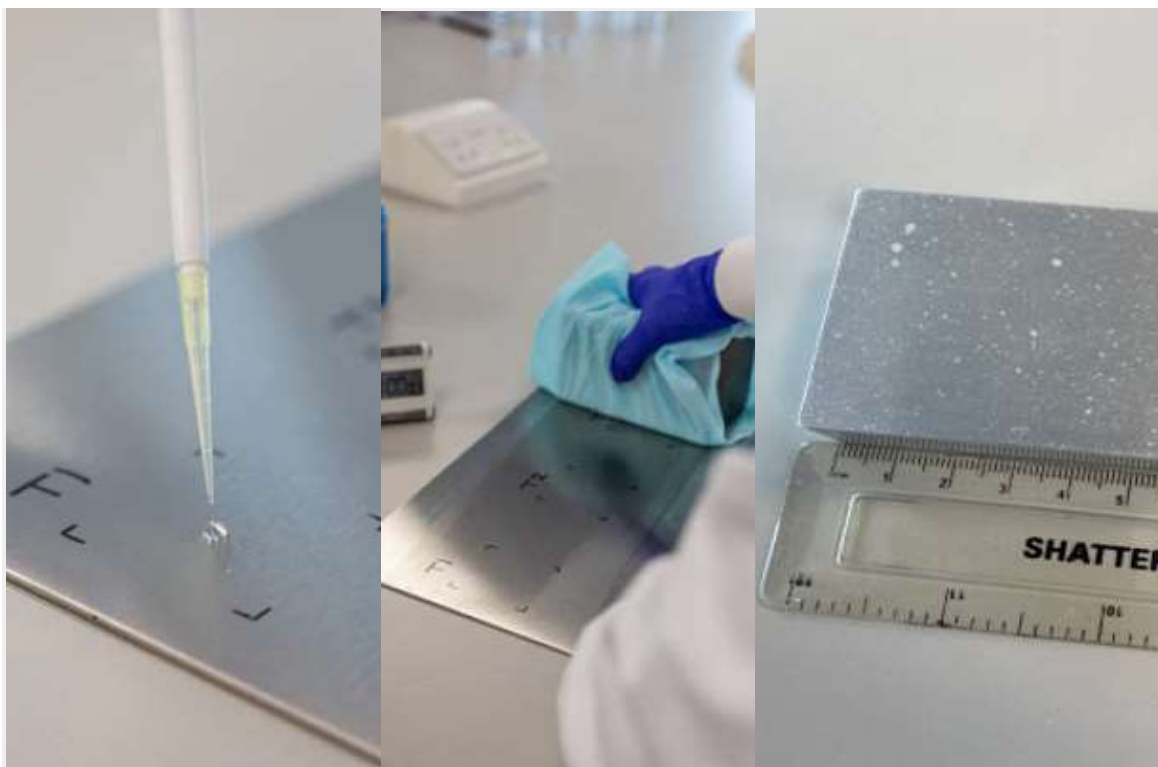


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## Validex™ Mechanical action (wiping)





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## VALIDEX™ PROGRAM

**1** Select customer specific surfaces

- Stainless steel 304 & 316
- PVC
- Glass
- Trespa
- Polycarbonate
- Plastic vinyl
- Polymeric (Dycem)
- PVC Decoclean chalk
- Plexiglass
- Polyurethane
- Epoxy
- Vinyl
- Nitrile/neoprene gloves
- HDPE plastic bags
- Polyethylene
- Butyl isolator glove

**2** Select customer relevant organisms

- *S. aureus*
- *P. aeruginosa*
- *C. jeikeium*
- *C. albicans*
- *E. coli*
- *M. luteus*
- *B. cepacia*
- *B. cereus*
- *B. subtilis*
- *P. chrysogenum*
- *S. epidermidis*
- *A. baumannii*
- *M. bovis*
- *A. brasiliensis*

**3** Validate method repeatability & robustness

- No statistical difference between NA and EU methods (i.e., organism strains, coupon sizes and method soils)
- Inter-lab and intra-lab repeatability



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# Study Considerations – Bracketing Plastics

Cleanroom surfaces are commonly comprised of polymers (plastics) as these are often durable, smooth and easier to clean and disinfect. These polymers are also common coatings of metal substrates.

Common cleanroom surfaces can include:

- Polycarbonate
- Poly Vinyl Chloride (PVC)
- Polyethylene Terephthalate (PET)
- Polystyrene
- Polypropylene
- Polyamide (Nylon)
- Polysiloxanes (Silicone)



Sources:



# Study Considerations – Bracketing Plastics

- To achieve optimum conditions for surface disinfection, the liquid biocide should be able to effectively wet the surface of the material.
- Wettability, which is the “ability of a liquid to maintain contact with a solid surface” depends on this **surface free energy** of the solid and the **surface tension** of the liquid
- Surface energy directly affects how well a liquid wets the surface and is measured by millinewtons per meter (mJ/m<sup>2</sup>).
- The higher the surface energy of the solid substrate, along with the surface tension of the liquid, the better it’s wettability and the smaller the contact angle of the applied liquid.
- Therefore, the lower the surface free energy, the greater challenge a surface is to wet with disinfectant





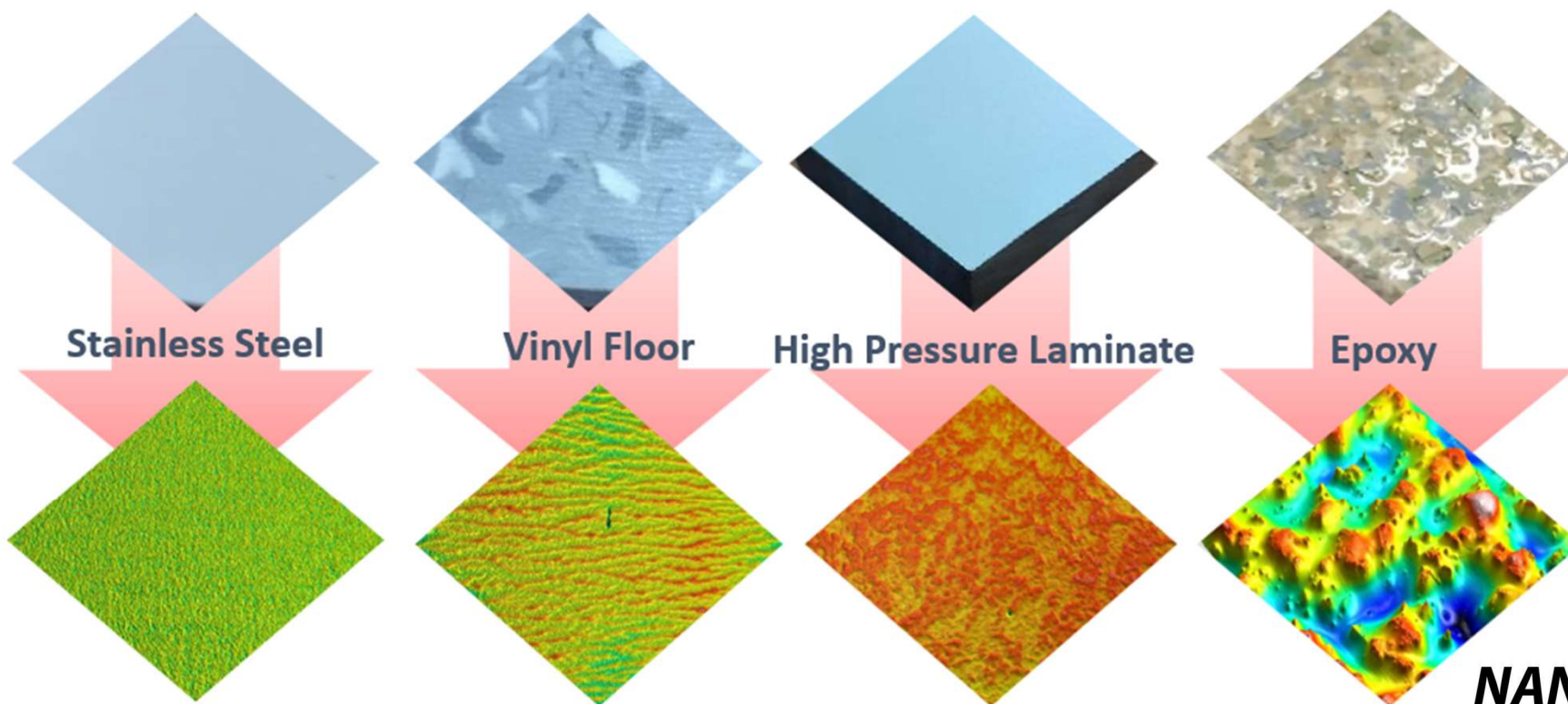
# Study Considerations – Bracketing Plastics

Surface Material	Surface Free Energy (mJ/m <sup>2</sup> )
Polycarbonate	42.3
Poly Vinyl Chloride (PVC)	40.1
Polyethylene (PET)	33.5
Polystyrene	38.3
<b>Polypropylene</b>	<b>30.2</b>
Polyamide (Nylon)	34.0
Polysiloxane (Silicone)	35.0

[www.accudynetest.com/polytable](http://www.accudynetest.com/polytable)



# Study Considerations – Surface Topography



**NANOVEA**<sup>®</sup>



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## Screening Tests / Phase I

- Laboratory suspension tests
- Establish the basic activity of the product or active substance
- For disinfectant manufacturers to screen / perform R&D
- **These tests are not accepted for product authorisation**

## Challenge Tests / Phase II

- Phase 2, step 1
  - Laboratory suspension tests to establish at what concentrations the product is effective under “in-use” conditions. (e.g. temperature, contact time, interfering substances)
- Surface Challenge / Phase 2, step 2
  - Laboratory surface tests applying disinfectants to surfaces at the selected use concentration with a specified contact time, and determining the log reduction of the challenge microorganisms (reference and environmental isolates)

## Field Tests / Phase III

- **Statistical comparison** of the frequency of isolation and numbers of microorganisms isolated prior to and after the implementation of a new disinfectant
- Evaluation of the product under actual conditions of use on specified surfaces or materials in a specified environment
- No validated test methods currently available



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# Beyond Lab Testing: In-situ Field Trial (Phase III)

## EN 14885 Application of European Standards for chemical disinfectants and antiseptics (Annex C Phase III Tests)

### Guidance

*“This annex sets out guidance in the form of factors to be considered in the design of field trials and when determining the acceptability of data derived from field trials in support of the claims made for a disinfectant or antiseptic”*

Note – Annex is applicable to any field which uses disinfectants (catering, laundry etc.)

### Scope

*“...establish directly the performance of a product under actual conditions of use”*

*“...a phase 3 test consists of a set of measurements so that the overall performance can be evaluated from a series of individual treatments”*

### Design

*“The key feature of a phase 3 test is that it is **carried out under typical operational conditions** in a process in which a product is or may be used routinely, but that a **series of measurements is taken according to a pre-determined plan** to provide data that can be **analysed statistically** against defined criteria to demonstrate whether a product has the required antimicrobial performance”*



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## Beyond Lab Testing: In-situ Field Trial (Phase III)

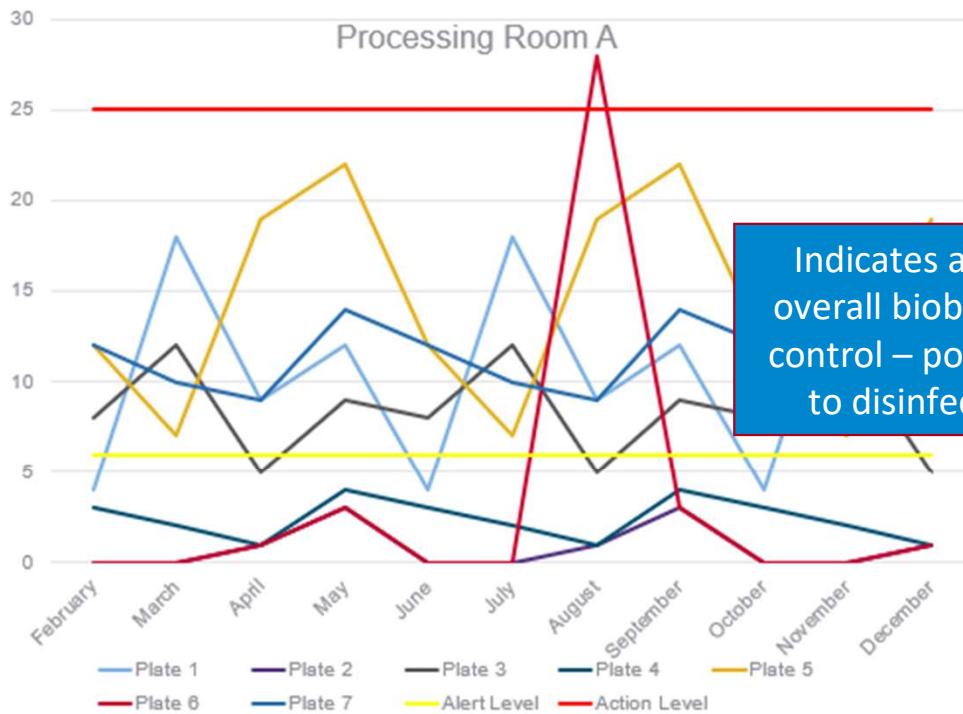
- Disinfection is of surfaces
  - Surface monitoring techniques are most appropriate
  - Contact plates for flat surfaces
  - Swabs for difficult to access locations
- Expanded monitoring programme to cover all surface types being disinfected
- Consider the value of performing Phase III in Grades A and B
  - Less likelihood of contamination therefore difficult to show effectiveness of the regime
- Timeliness of sampling (Pre and Post Disinfection)
  - Post disinfection needs to be within hours of the application
  - Purpose of the study is measuring success of the disinfection not activities within the room
- Which species are present pre disinfection and which are present post disinfection (if any!)
- Any remaining species, can be reviewed if present when the rotational sporicide is used
- Seasonal variation in cleanroom flora can be demonstrated as controlled depending on length of study



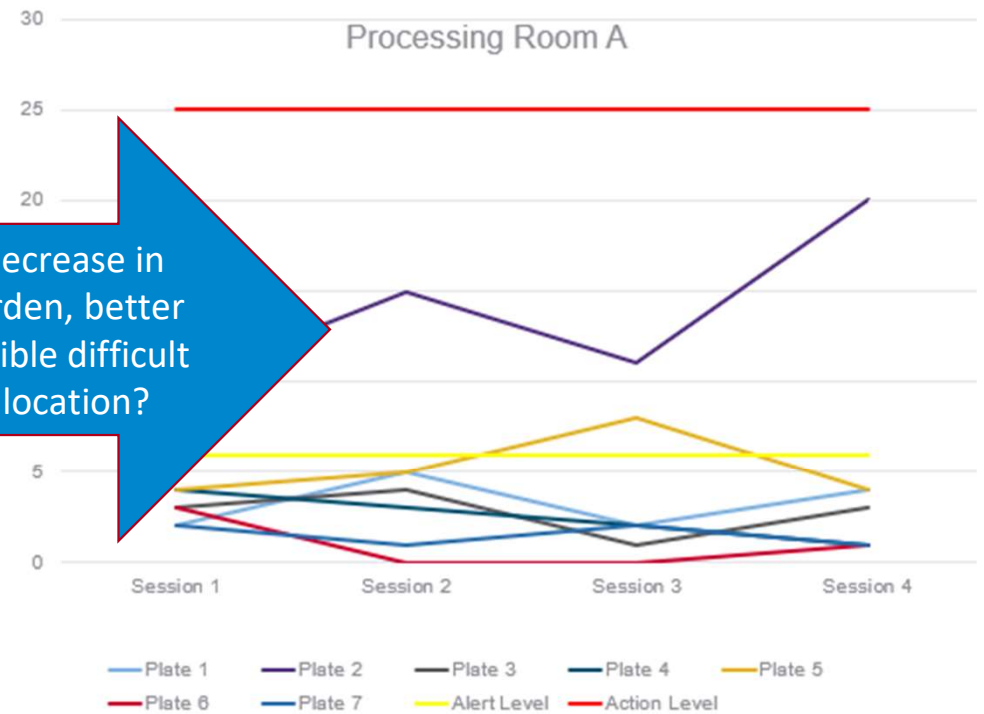


# Beyond Lab Testing: In-situ Field Trial (Phase III)

## Historical Data



## Phase III Data





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## Summary

- A Validation Plan should be documented to capture:
  - Assessment of Test Materials (Surfaces and Organisms)
  - Test Methodology – Modified Standard Methods?
  - Appropriate Test Parameters (Contact Time, Inoculum Levels, Wiping?)
- Laboratory Assessment of Disinfectant Efficacy
  - Test Protocol Review and Approved
  - Documented Efficacy Reports
  - Third Party Supplier? Accreditation and Supplier Approval Assessment
- Phase III / In-situ Validation
  - Disinfectant Performance for Real World Conditions

Partner with the Experts  
for your Contamination  
Control Strategy

Support for compliant cleaning,  
disinfection & bio-decontamination

The graphic features a collage of approximately 15 professional headshots of individuals, arranged in a grid-like pattern with blue and white geometric shapes. The text is positioned to the left of the collage.

**The Validation Package  
can contribute to your  
CCS**