Antimicrobial Pesticides
Regulatory Update

2018 EPA International Decontamination Research and Development Conference

STEPHEN TOMASINO, PH.D.
SENIOR SCIENTIST
OFFICE OF PESTICIDE PROGRAMS (OPP)
BIOLOGICAL AND ECONOMIC ANALYSIS DIVISION (BEAD)
MICROBIOLOGY LABORATORY BRANCH (MLB)
TOMASINO.STEPHEN@EPA.GOV

Disclaimer

This information is distributed solely for the purpose of pre-dissemination peer review under applicable information quality guidelines. It has not been formally disseminated by EPA. It does not represent and should not be construed to represent any Agency Determination or Policy.

Topics

- OPP Microbiology Laboratory
- Regulatory Summary/Update
- Method Development
  - OECD Quantitative Method

OPP Microbiology Laboratory

Co-located with EPA Region 3 at the EPA Environmental Science Center, Fort Meade, MD

13 Scientists (EPA, ORISE and NOWCC)

BSL-2 and BSL-3 capability - only EPA lab registered under the Federal Select Agent Program

Specialized equipment (Coy unit, confocal microscopy)

ISO 17025 accredited and GLP compliant

Expertise testing a wide range of microbes (bacteria, viruses, fungi, and spore formers)

Contract with Montana State University

OPP Microbiology Laboratory Branch

- Address public health priorities – regulatory science projects
- Reference testing lab for antimicrobial products
- Engage stakeholders, conduct and participate in collaborative studies, develop guidance and methods

MLB customers include:

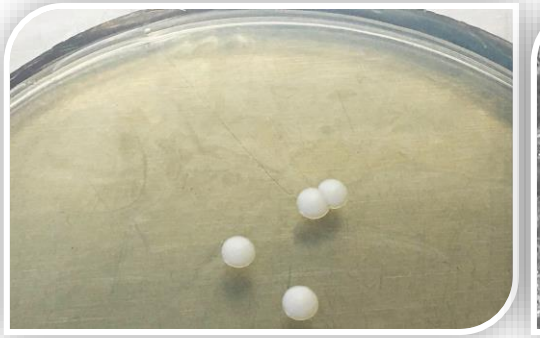
- OPP Antimicrobials Division
- Other federal agencies – CDC, DHS, USDA
- Stakeholders and trade associations
- Standard-setting organizations
- ORD – homeland security
- OECD

OPP Microbiology Laboratory

Types of Deliverables

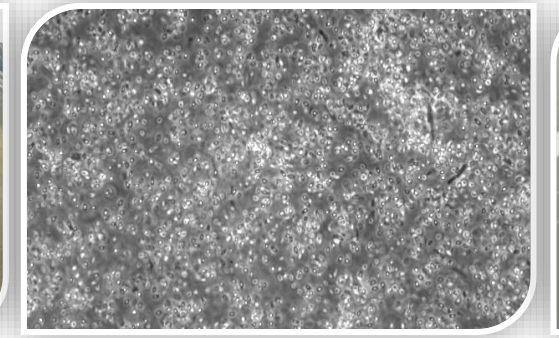
- Test procedures – SOPs and standards
- Regulatory/guidance documents
- Technical reviews
- Research on new methods and microbes
- Collaborative studies – method validation
- Regulatory data
- Peer-reviewed publications
- Outreach & workshops

Guidance and Methods
Recent examples



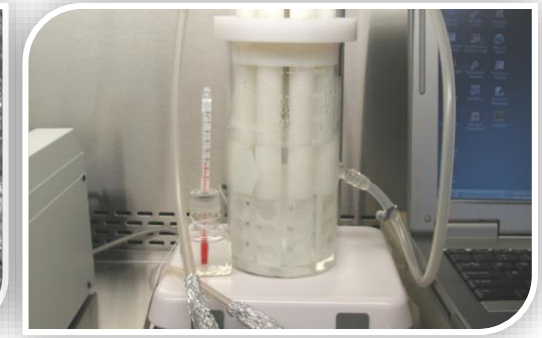
CANDIDA AURIS

- OECD Quantitative Method



CLOSTRIDIUM DIFFICILE

- OECD Quantitative Method



BIOFILM

- Single Tube Method
- CDC Reactor Method

Antimicrobial Pesticides
Brief summary

EPA's Office of Pesticide Programs oversees the regulation of pesticides under the broad authority of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA).

FIFRA requires all pesticides sold or distributed in the United States to be registered by EPA.

An *antimicrobial pesticide* is a pesticide that is intended to disinfect, sanitize, reduce, or mitigate growth or development of microbiological organisms on environmental surfaces.

Public health disinfectants are antimicrobial products bearing claims for control of microorganisms infectious to man are considered directly related to human health.

- Registrants are required to submit product efficacy data to support the label claims.
- Test guidelines have been established.

Series 810 - Product Performance Test Guidelines

The final Product Performance Test Guidelines are generally intended to meet testing requirements for the effectiveness of pesticide products under FIFRA.

Group A — General

810.1000 - Overview, Definitions, and General Considerations (March 1998)

Group B — Antimicrobial Efficacy Test Guidelines

810.2000 - General Considerations for Testing Public Health Antimicrobial Pesticides, Guide for Efficacy Testing (February 2018)
810.2100 - Sterilants, Sporicides, and Decontaminants, Guide for Efficacy Testing (February 2018)
810.2200 - Disinfectants for Use on Environmental Surfaces, Guide for Efficacy Testing (February 2018)
810.2300 - Sanitizers for Use on Hard Surfaces--Efficacy Data Recommendations (September 2012)
810.2400 - Disinfectants and Sanitizers for Use on Fabrics and Textiles (March 2013)
810.2500 - Air Sanitizers (March 2013)
810.2600 - Disinfectants and Sanitizers for Use in Water (March 2013)
810.2700 - Products with Prion-Related Claims (December 2012)

Efficacy Testing Guidelines

Guideline Name	OCSPP Guideline Number
★ General Considerations for Uses of Antimicrobial Agents	810.2000
★ Sterilants	810.2100
★ Disinfectants for Use on Hard Surfaces	810.2200
Sanitizers for Use on Hard Surfaces	810.2300
Disinfectants and Sanitizers for Use on Fabrics and Textiles	810.2400
Air Sanitizers	810.2500
Disinfectants and Sanitizers for Use in Water	810.2600
Products with Prion-related Claims	810.2700

https://www.epa.gov/test-guidelines-pesticides-and-toxic-substances/series-810-product-performance-test-guidelines

★ Revised February 2018

OCSPP 810.2100: Sterilants, Sporicides, and Decontaminants - Guidance for Efficacy Testing

Types of Claims

Sterilant – for products with sterilant claims to inactivate spores of *Bacillus subtilis* and *Clostridium sporogenes* on both hard (testing carrier: porcelain penicylinders) and soft (testing carriers: silk suture loops) inanimate surfaces.

Sporicide – for products with surface-specific sporicide claims to inactivate spores of *Bacillus subtilis* and *Clostridium sporogenes* on that specific inanimate surface.

- **Additional Spores** – efficacy tests for all sterilant or sporicide products with claims to inactivate additional spores on inanimate surfaces.

***Bacillus anthracis* Decontaminant Claim** – addresses efficacy tests for a product with claims to inactivate *B. anthracis* spores on inanimate surfaces.

Hospital or Healthcare Disinfectant with Sporicidal Activity against *Clostridium difficile* Claim – addresses efficacy tests for a hospital or healthcare disinfectant product with claims to inactivate *C. difficile* spores on hard, nonporous, inanimate surfaces.

Method development
Overarching considerations

- As necessary, systematically review, develop and assess new efficacy methods for novel product claims and/or emergence of new clinical pathogens.
- Post methodology and testing guidance, and seek public/stakeholder comment.
- Recommend valid, practical, and cost-effective methodologies.
- Use in-house validation studies to refine methodologies and to identify technical challenges.
- Use collaborative studies to verify performance of new test methods and/or to confirm method modifications.
- Incorporate contemporary statistical analyses to support conclusions/recommendations.
- Use standard-setting organizations for further peer-review.
- Seek end-user feedback.
- Publish collaborative findings.
- Provide stewardship, training, and means to test proficiency.

Note – EPA may depart from this process to expedite methods for emerging/re-emerging pathogens.

Test Methods for Antimicrobial Pesticides

Quantitative Methods

Older qualitative methods are limited/less capable of assessing new chemistries, novel delivery systems, and emerging pathogens.

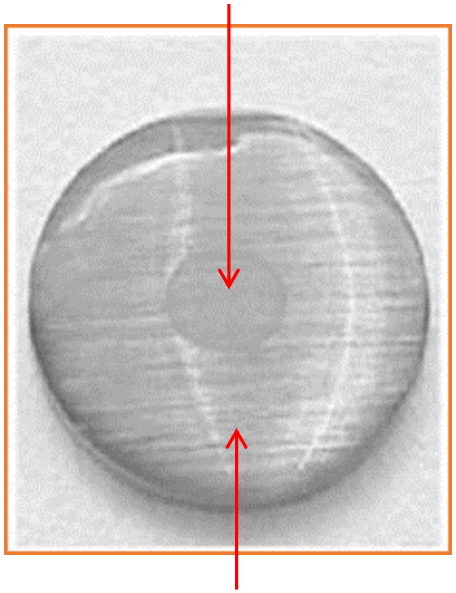
EPA's goal is to advance the science of antimicrobial product efficacy testing by adoption of new quantitative methods.

For liquid products, the OECD Quantitative Method (ASTM 2197) has been under development as a candidate method for international harmonization.

Currently used for *C. difficile* and *C. auris* antimicrobial claims; considering how to apply to other regulatory applications.

1 cm brushed stainless steel disk with:

10 µL dried inoculum



50 µL disinfectant

Vial with inoculated carrier/disinfectant; following the contact time, add neutralizer and assay for survivors

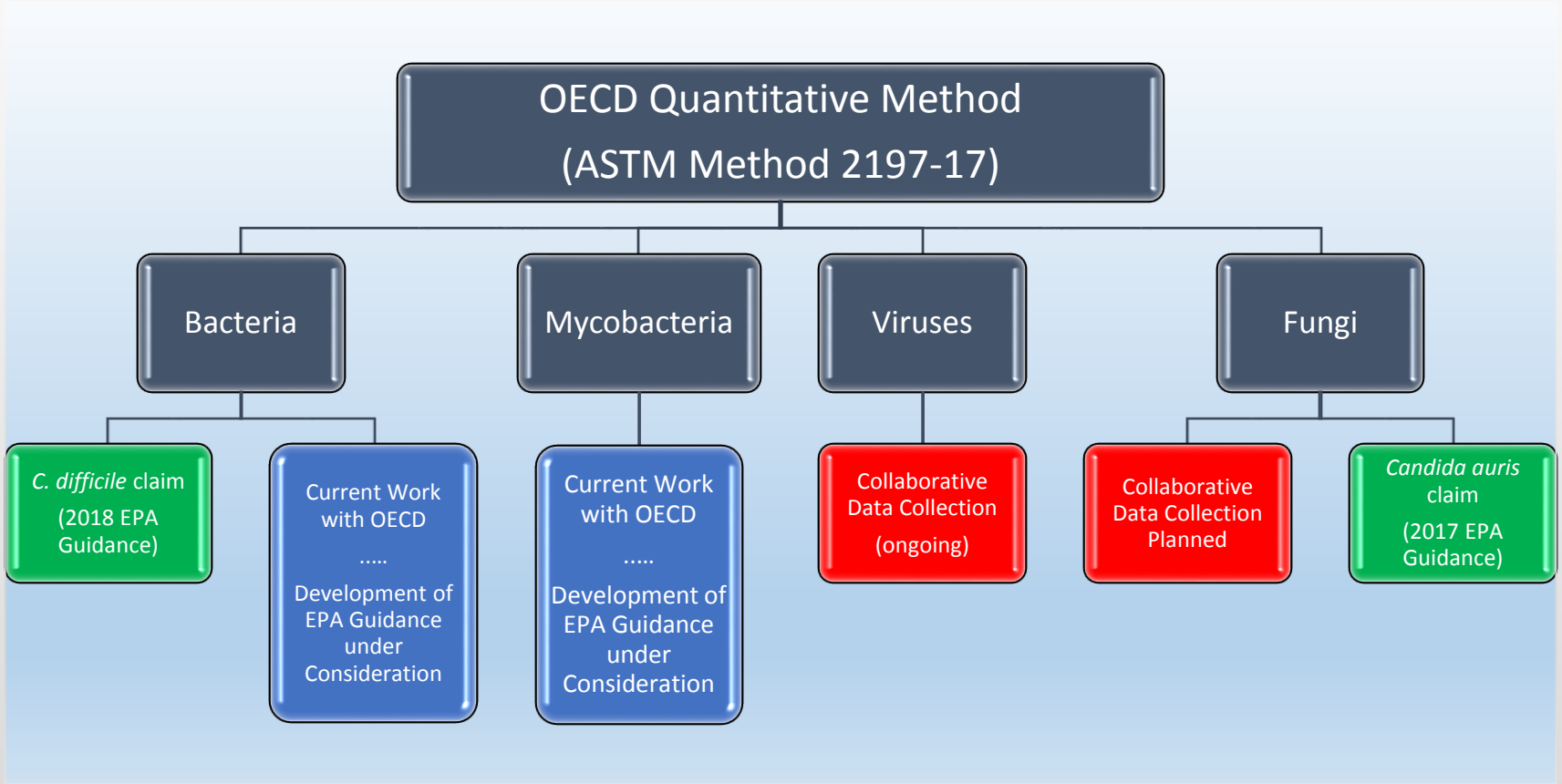
Count colonies and determine difference in log density for control and treated carriers. Results are reported as log reduction values.

OECD Quantitative Method

OECD Quantitative Method

Potential benefits

- Accommodates testing of multiple microbes, including emerging pathogens
- Allows for rigorous statistical analyses
- Clear interpretation of the quantitative results
- Useful to risk-based strategies
- Potential for international harmonization
- Reduced laboratory biosafety hazards
- Ease of use and training
- Accommodates multiple carrier types including porous materials
- Method more relevant to real-world applications and use-sites
- Reduction in repeat testing



OECD Quantitative Method Overview of the initiative

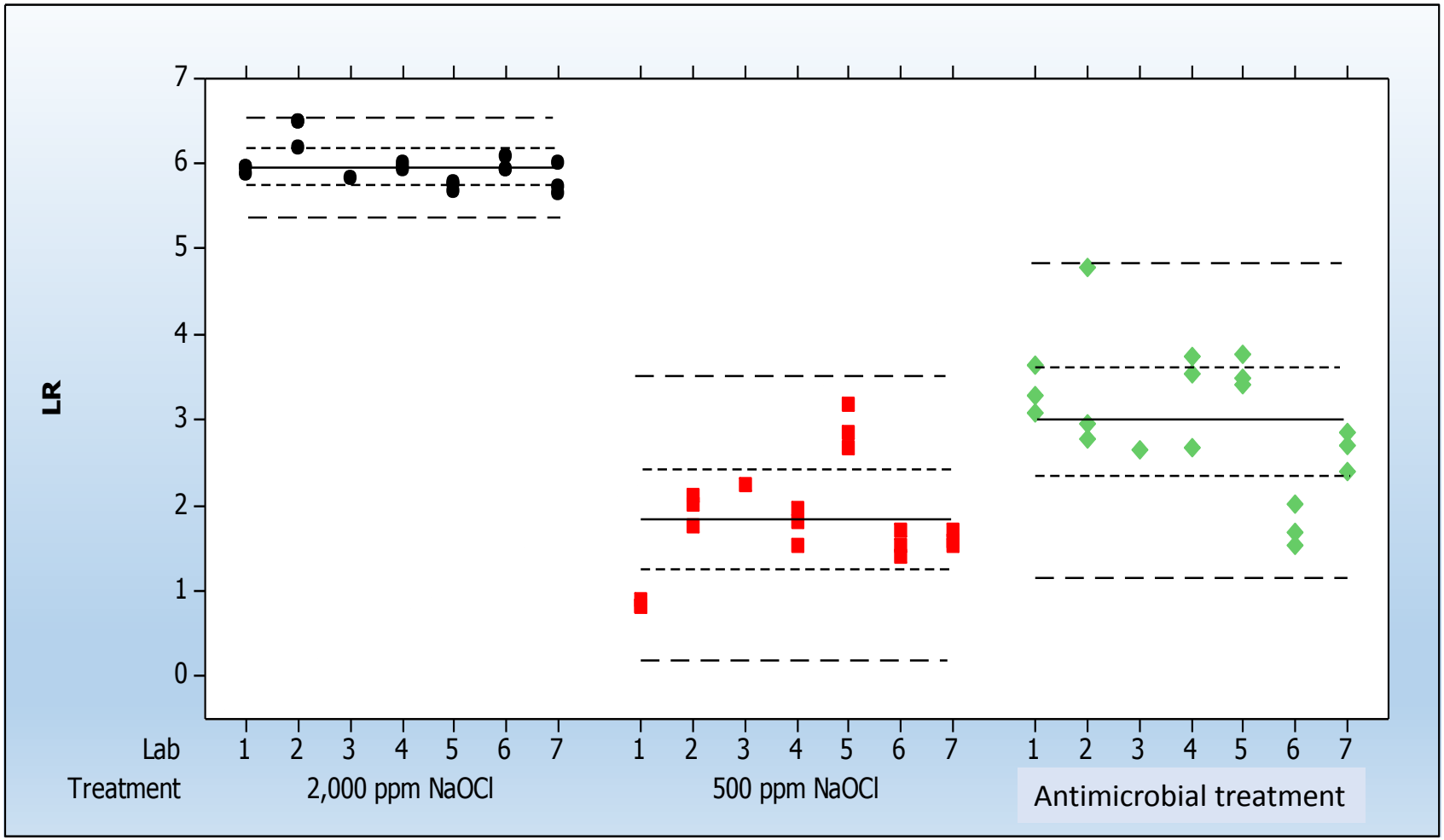
OECD Quantitative Method

Collaborative data collection

Test Organism	Collaborative Study Period
Staphylococcus aureus *Pseudomonas aeruginosa*	2012/2013 (method performance)
Mycobacterium terrae	2013/2014 (method performance)
✓ *Clostridium difficile*	2015 (spore storage and method performance)
Feline Calicivirus & Influenza Virus	2016-2017 (method performance) Planned for 2018 (method performance)
✓ *Candida auris*	2017 (*single lab validation*)
Trichophyton mentagrophytes (*T. interdigitale*)	2017 (pre-collaborative)

Example of Collaborative Data

Log reduction (LR) of *Staphylococcus aureus*



Data Analysis

	Microbe	Treatment	Mean LR	S_r	S_R
2012	*P. aeruginosa*	NaOCl 250 ppm	3.17	0.34	0.88
		NaOCl 2000 ppm	5.29	0.19	0.28
		Phenol	5.33	0.33	0.49
		Peroxide	5.40	0.32	0.39
		Citric Acid	5.39	0.25	0.36
		Quaternary Ammonium	3.26	0.84	1.22
	S. aureus	NaOCl 500 ppm	1.51	0.23	0.47
		NaOCl 2000 ppm	5.34	0.16	0.23
		Phenol	4.50	0.43	0.56
		Peroxide	5.28	0.16	0.33
		Citric Acid	5.23	0.27	0.36
		Quaternary ammonium	3.68	0.41	0.85
2014	*P. aeruginosa*	NaOCl 200 ppm	2.69	0.40	1.14
		NaOCl 2000 ppm	5.71	0.26	0.43
		Quaternary ammonium	1.36	0.59	0.72
	S. aureus	NaOCl 500 ppm	1.84	0.18	0.66
		NaOCl 2000 ppm	5.95	0.12	0.23
		Quaternary ammonium	2.98	0.54	0.80

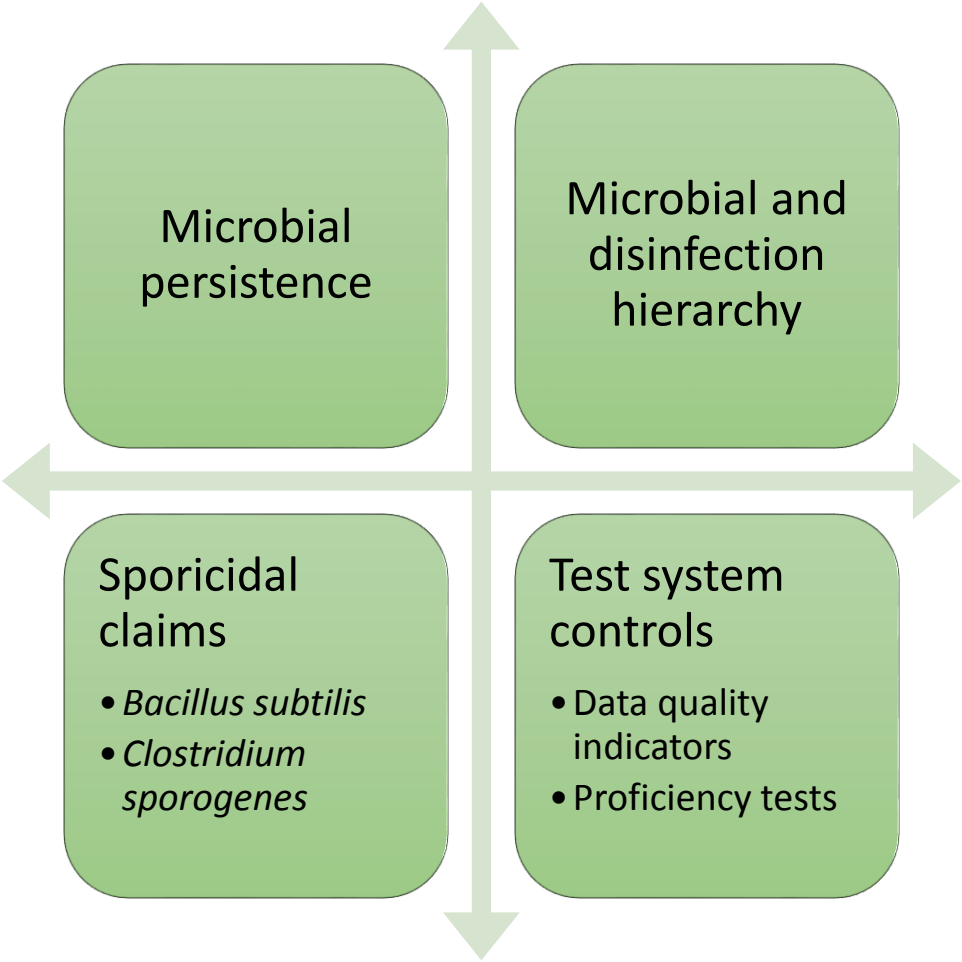
Data generated for EPA as part of collaborative studies

Key method performance indicators:

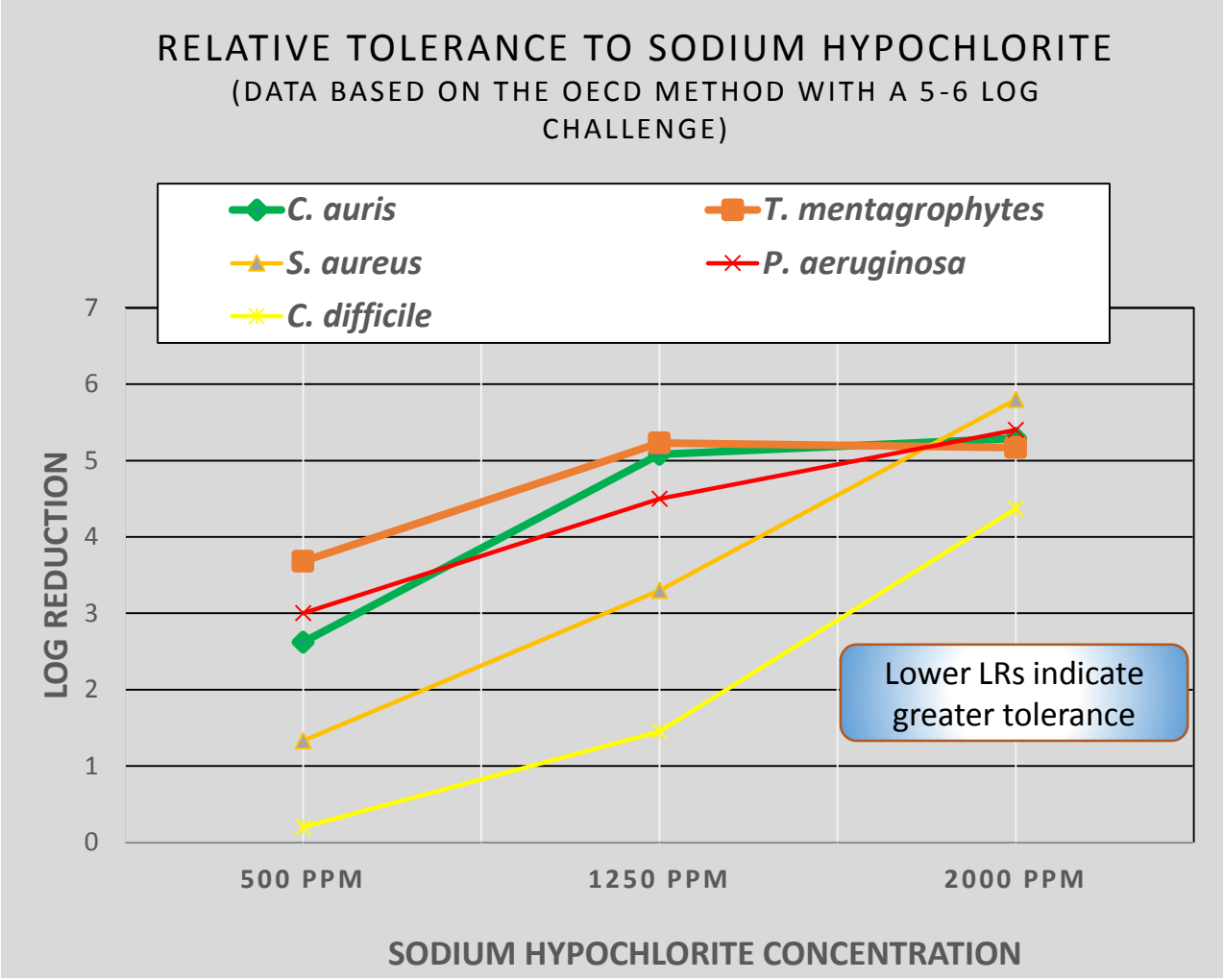
- S_r = repeatability standard deviation (within-lab)
- S_R = reproducibility standard deviation (between-lab)

OECD Quantitative Method

Other areas of application



Hierarchy/relative tolerance



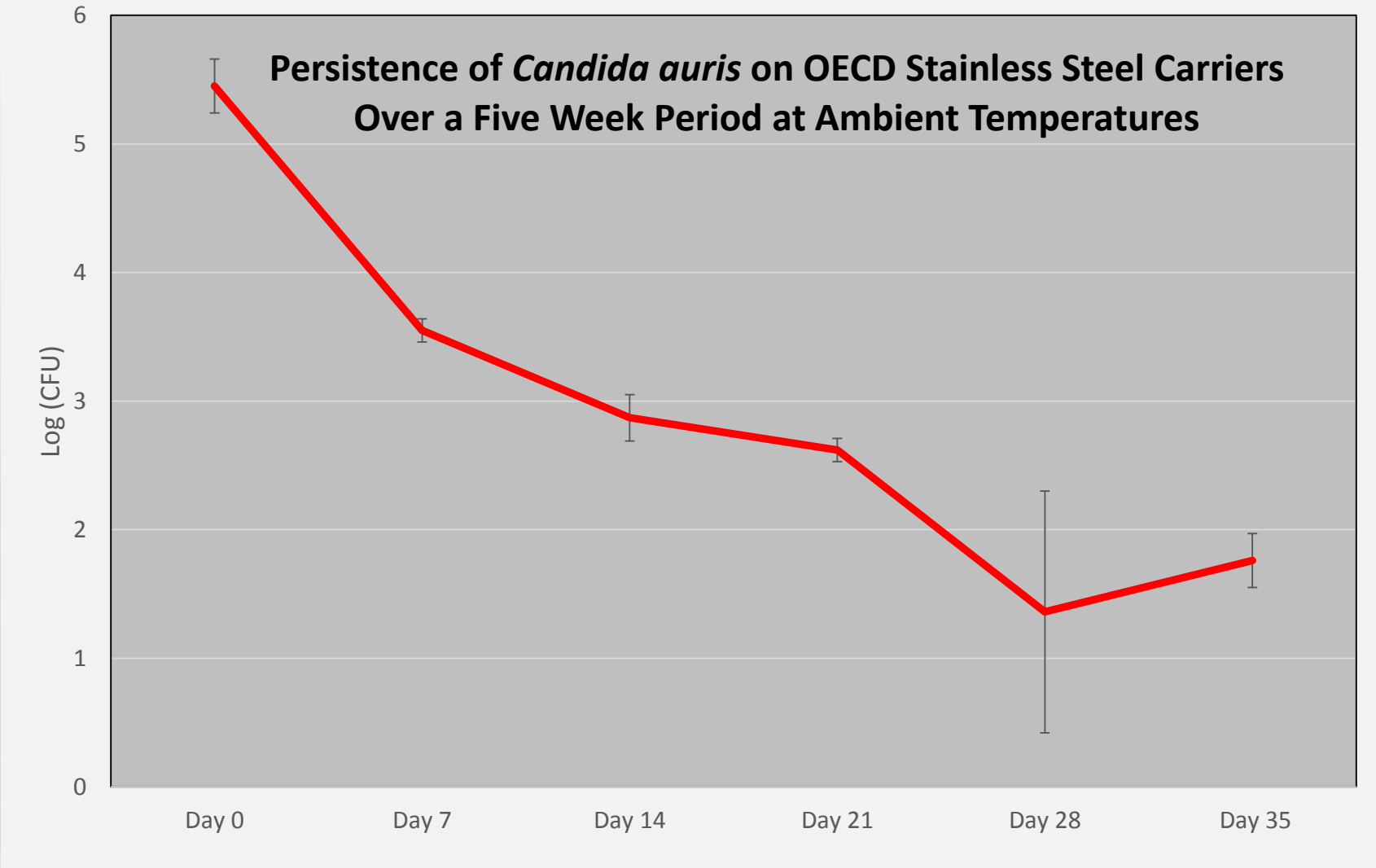
Most Tolerant

- Bacterial spores
- Mycobacteria
- Non-enveloped viruses
- Fungi
- Vegetative bacteria
- Enveloped viruses

Least Tolerant

Data generated by EPA

Example of persistence evaluation

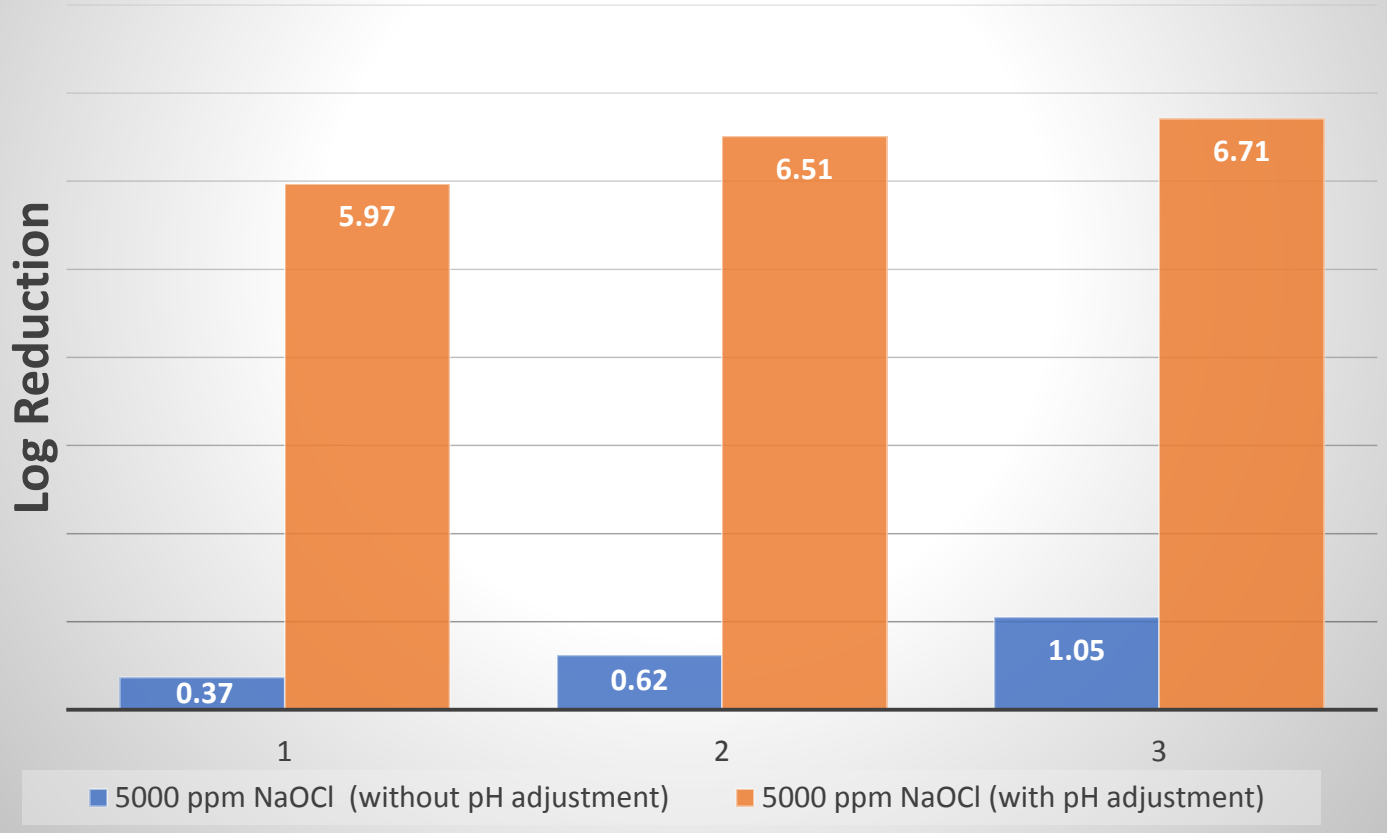


Data generated by EPA

Recent Demonstration Study

OECD Quantitative Method

Mean Log Reduction of spores of *Bacillus subtilis*



Data generated by EPA

Key References

OCSPP 810 Series Guidelines (Group B): https://www.epa.gov/test-guidelines-pesticides-and-toxic-substances/series-810-product-performance-test-guidelines

Antimicrobial Policy and Guidance: https://www.epa.gov/pesticide-registration/antimicrobial-policy-and-guidance-documents

Antimicrobial Pesticide Registration: https://www.epa.gov/pesticide-registration/antimicrobial-pesticide-registration

BEAD/MLB SOPs: https://www.epa.gov/pesticide-analytical-methods/antimicrobial-testing-methods-procedures-developed-epas-microbiology

MLB SOP MB-25-04 (OECD Quantitative Method for Evaluating Bactericidal and Mycobactericidal Activity of Microbicides Used on Hard, Non-Porous): https://www.epa.gov/pesticide-analytical-methods/antimicrobial-testing-methods-procedures-mb-25-04

Questions ?