

# FDA Panel Meeting

June 10, 2008

John M. Lally, PhD  
**Advanced Medical Optics**



# Outline

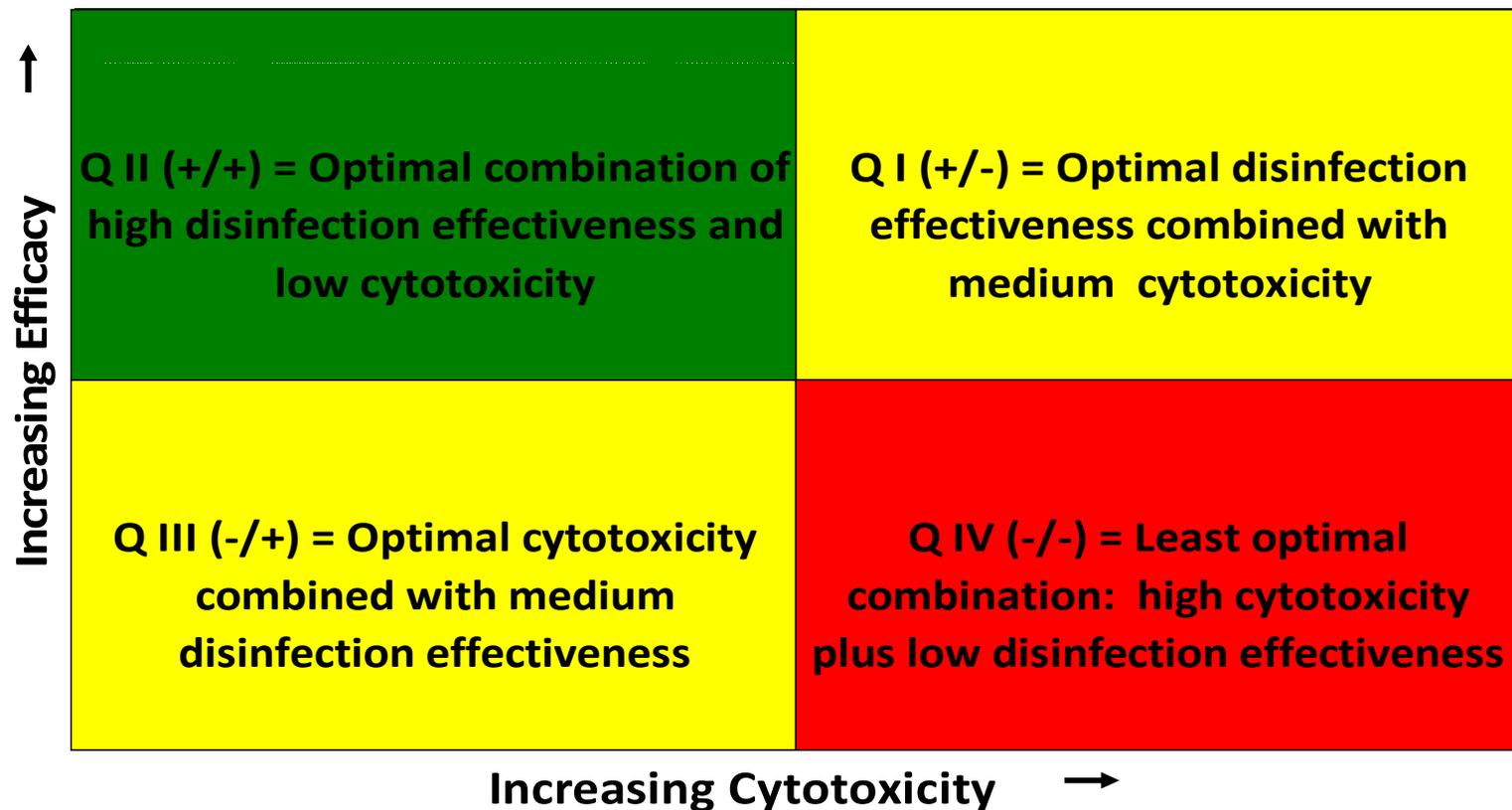
- Contact lens care products must provide effective disinfection yet maintain corneal integrity
- 2Hr Short-term staining does not correlate with clinical cytotoxicity
- Disinfection effectiveness testing must address real-life patient use, lack of standardized *Acanthamoeba* testing, and non-compliance.
- Scientific data supports a rub and rinse regimen in reducing microbial load and enhancing effectiveness of all lens care solutions

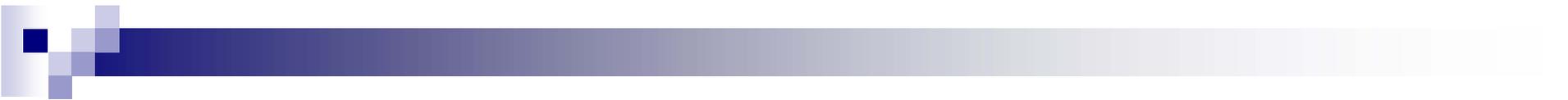


# Formulation Development

- Test beyond the current ISO standards and the FDA guidelines – additional testing for real-life use
  - Correlations of preservative uptake and release data from contact lens/care solution interactions to microbiology and cytotoxicity test data (each lens / lens care combination has a unique uptake/release kinetic profile)
  
- Tests for robustness against potential non-compliance
  - Effects of evaporation on antimicrobial effectiveness
  - Impact on product effectiveness from topping off and reusing solutions
  - Effects of shorter rub and rinse times than recommended in labeling

# MPS Product Development Challenge: Disinfection Without Clinical Cytotoxicity





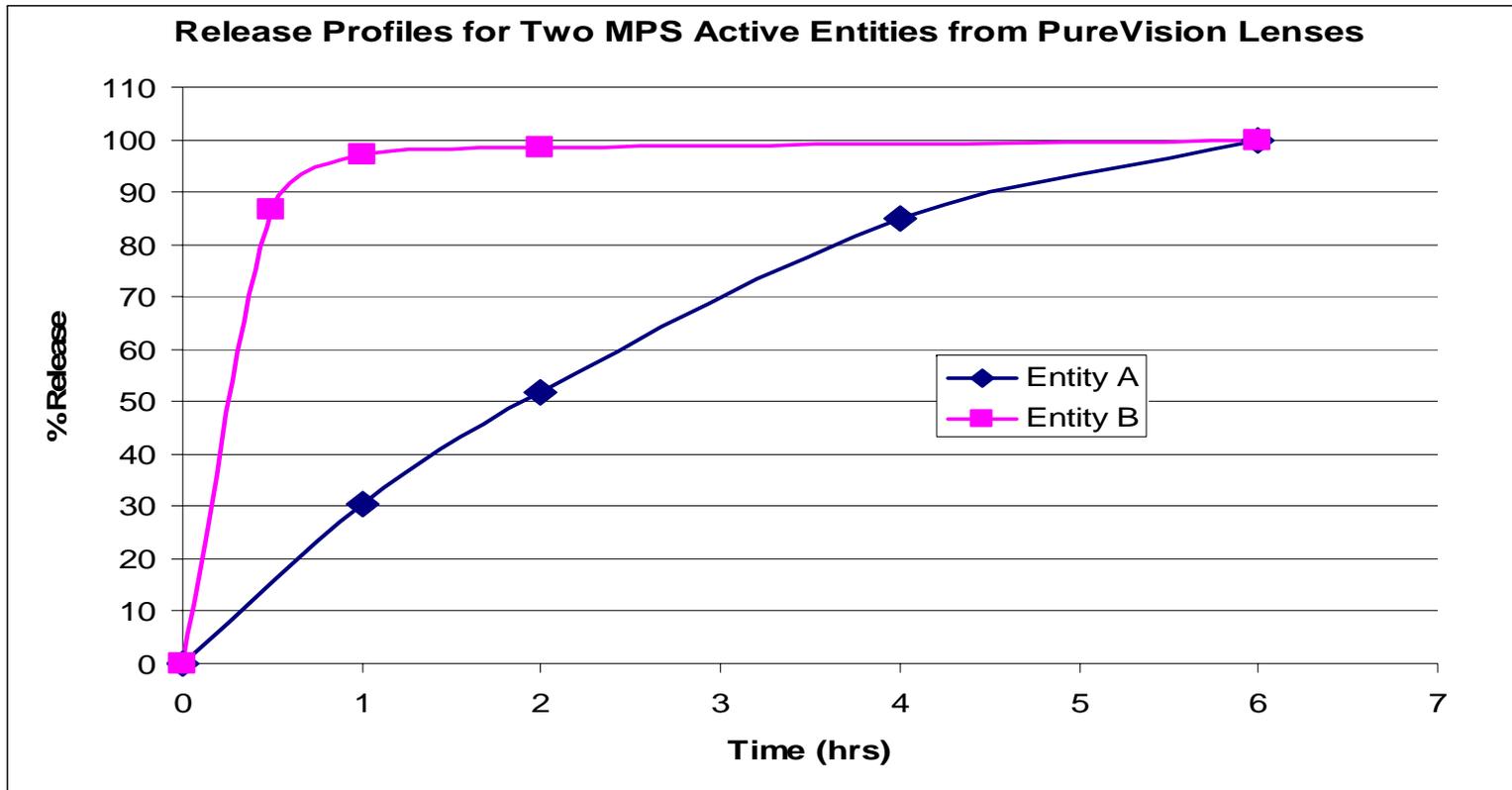
# 2Hr Short-term Staining Does Not correlate with clinical cytotoxicity

- **Staining Methodology:**

- **2-Hour**

- 2Hr staining does not correlate with clinical cytotoxicity information
    - Depends on the time of observation
    - Two hour exposure to SiHy lens/solution combinations does not reliably predict three-month clinical findings (CL Spectrum March 2008)

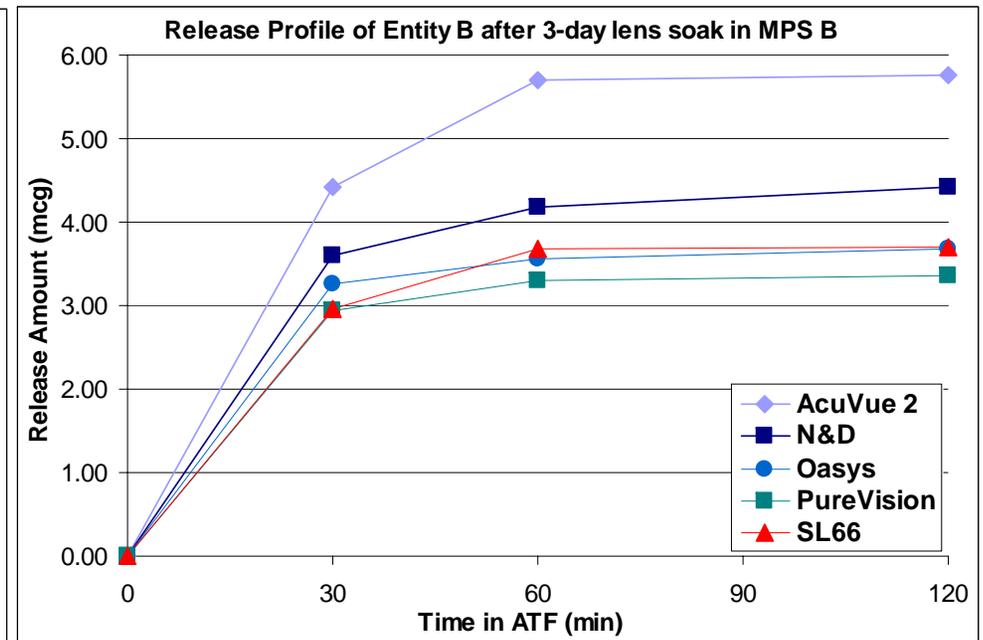
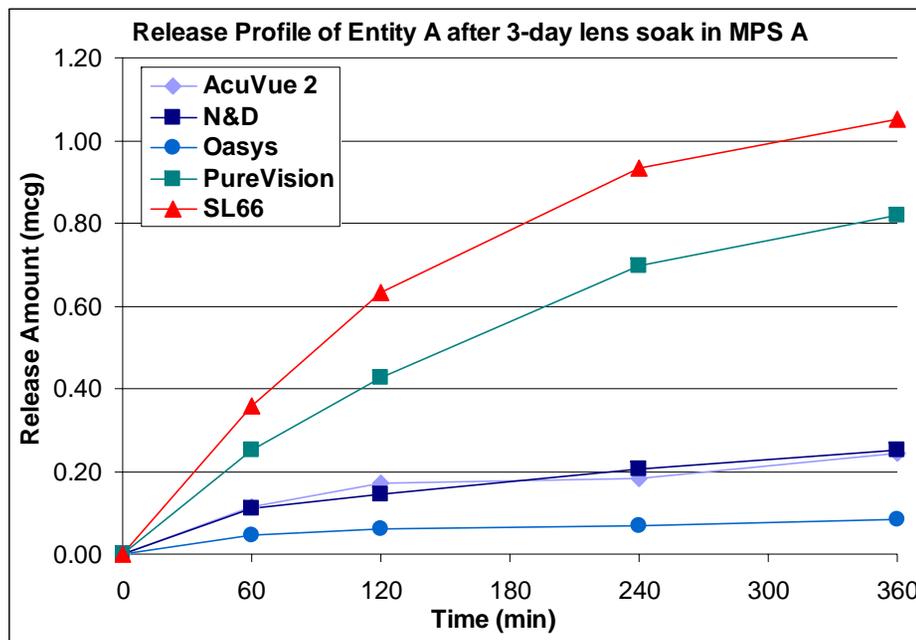
# Release Kinetics May Influence the Degree of Staining at Various Time Points



MPS A may exhibit highest staining at 2-4 hrs, while MPS B may exhibit highest staining at 30-60 min.

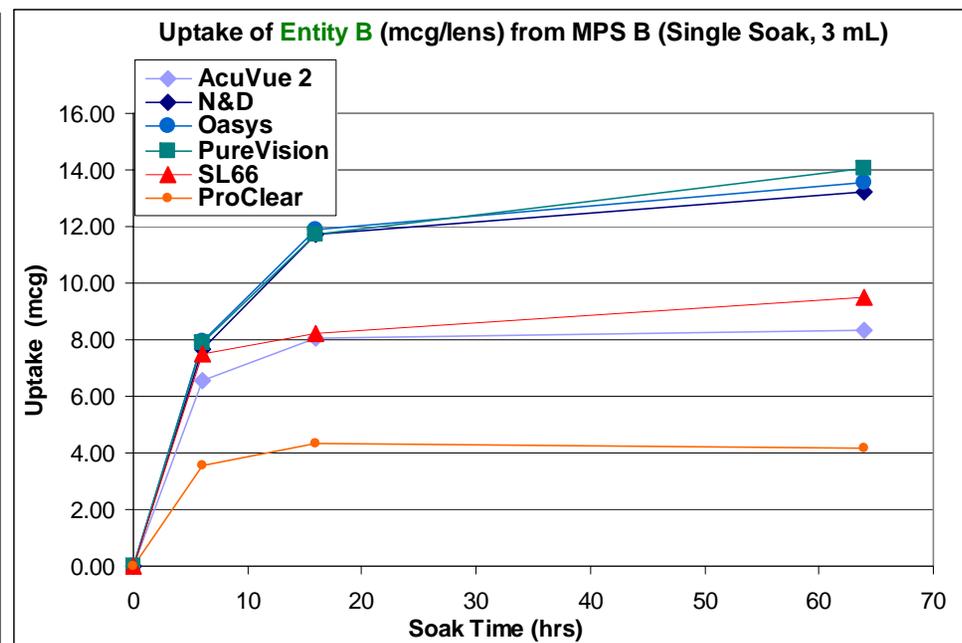
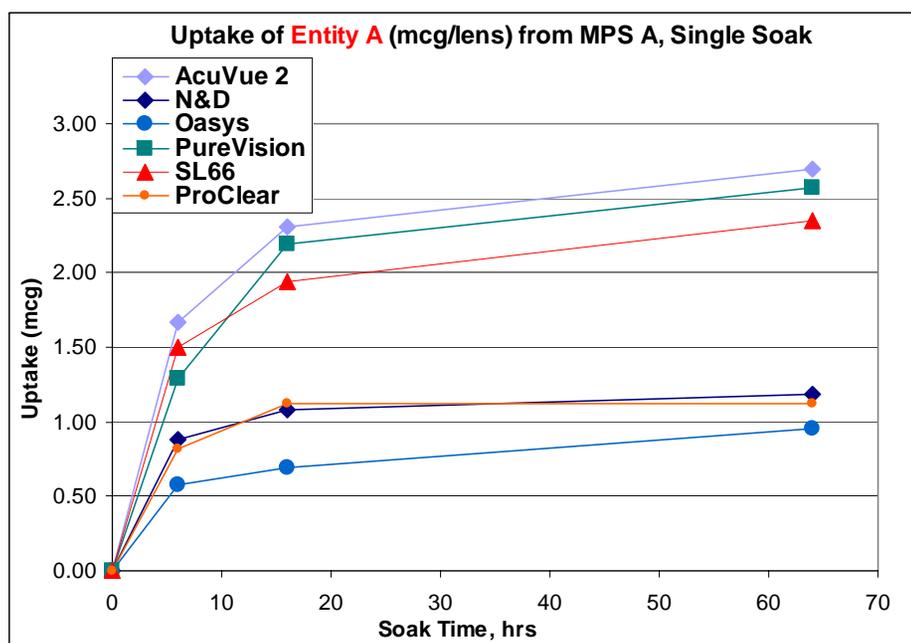
**Assessing Effective Hydrophobic and Ionic Content of Contact Lenses Based on Uptake/Release of Two Chemically Diverse Active Entities Found in MPS products** C.H. Powell, S.W. Huth, J. Lally and L.D. Hoong (BCLA Poster 2008).

# Clinical Testing Should Include Worst Case Lenses for Release of the Primary Active Entity



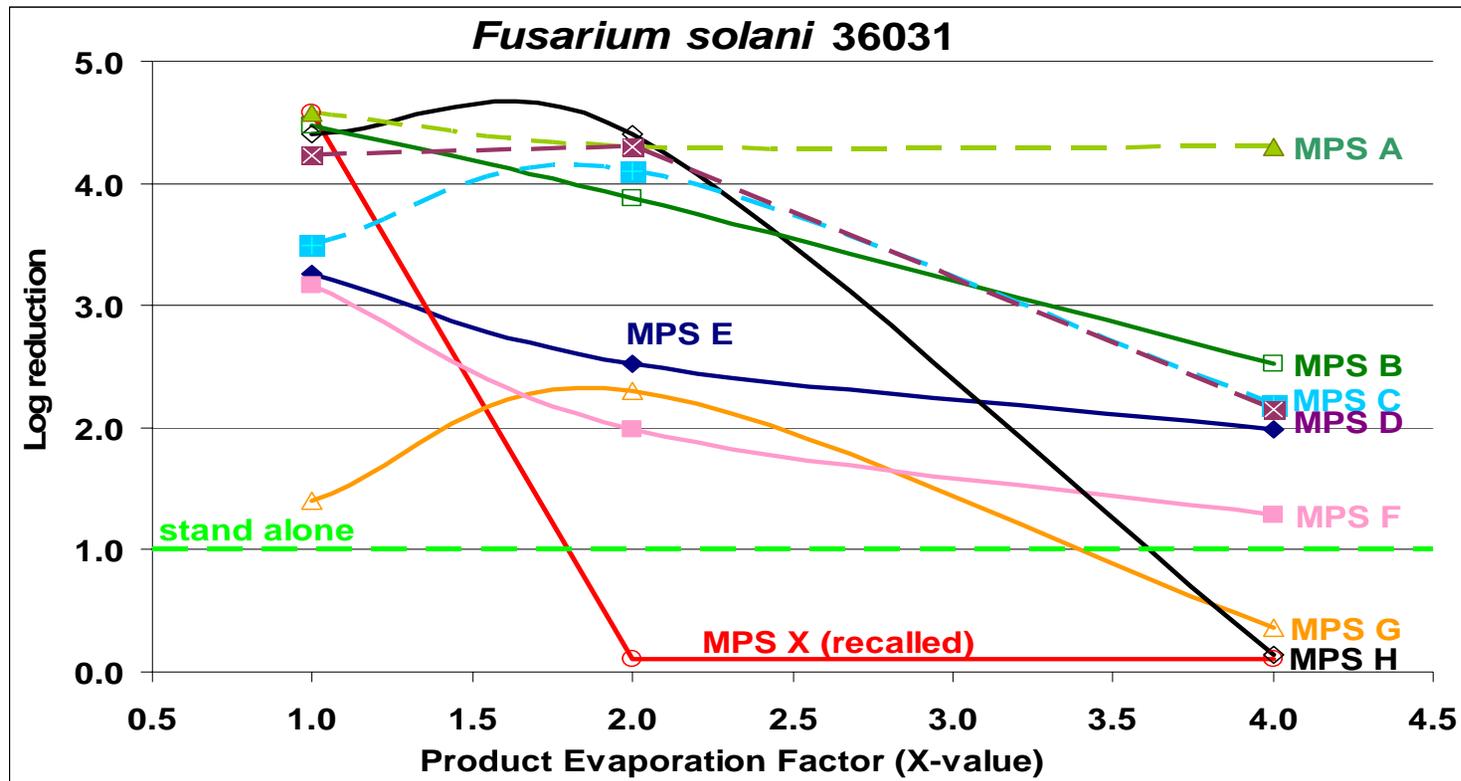
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# Clinical Testing Should Include Worst Case Lenses for Uptake of the Primary Active Entity



Assessing Effective Hydrophobic and Ionic Content of Contact Lenses Based on Uptake/Release of Two Chemically Diverse Active Entities Found in MPS products C.H. Powell, S.W. Huth, J. Lally and L.D. Hoong (BCLA Poster 2008).

# Evaporation Can Reduce Antimicrobial Effectiveness



Helps elucidate ruggedness of a product toward evaporation effects associated with “topping off” and other misuses

Susceptibilities of Various Contact Lens Multipurpose Solutions to Efficacy Diminution When Partially Evaporated, C.H. Powell, S.W. Huth, L.D. Hoong, J. M. Lally, K. Ambrus, ARVO and BCLA Poster 2007

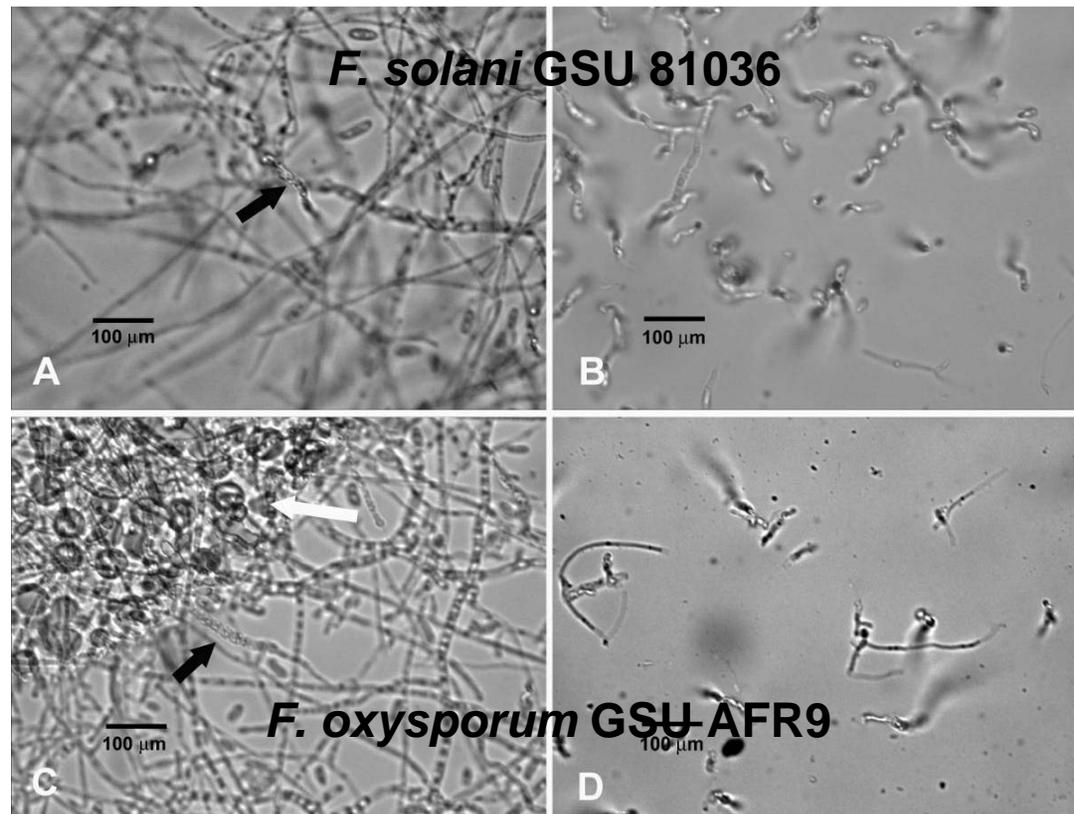


# Progress in *Acanthamoeba* Testing

- **Non-standardized microbiological methods for SCL disinfection efficacy against *Acanthamoeba* continue to produce highly variable data from study to study.**
  - *Acanthamoeba*: A Review of its Potential to Cause Keratitis, Current Lens Care Solution Disinfection Standards and Methodologies, and Strategies to Reduce Patient Risk, C Anger and J.M. Lally, Eye and Contact Lens, In-Press
  
- **Recommended that all lens care products be tested for propensity to induce *Acanthamoeba* encystment**
  - Encystment of *Acanthamoeba* During Incubation in Multipurpose Contact Lens Disinfectant Solutions and Experimental Formulations, S. Kilvington, W. Heaselgrave, J. M. Lally, K. Ambrus and H. Powell, Eye and Contact Lens, May/June 2008
  
- ***Acanthamoeba* is ubiquitous and reducing the incidence of *Acanthamoeba* keratitis is multifaceted. Includes:**
  - Education of SCL wearers in the hygienic wear and care of their lenses
  - Implementation of standardized solution disinfection requirements

# Rubbing Lenses Reduces Fungal Colonization

Rinse



Rub and Rinse

Firm Attachment to and Penetration of Silicone Hydrogel Contact Lenses by Representatives of *Fusarium oxysporum* - *F. solani* Complexes, S. Zhang, R. B. Simmons, D. G. Ahearn, R. D. Stulting, B. L. Schwam, G. E. Pierce, S. A. Crow.

## Rinse *versus* Rub/Rinse

- Rub step provides added safety margin in real-life settings

	<u>Direct Inoculation Method (10min)</u> Log Redn in CFU or PFU /Lens			<u>Lens Immersion Method (Overnight)</u> Log Redn in CFU or PFU/Lens		
	Rinse	Rub/ Rinse	Additional log reduction from rub step	Rinse	Rub/ Rinse	Additional log reduction from rub step
<i>A. polyphaga</i> trophs ATCC 30461	>3.5	>3.5	0 log	2.6	>3.5	0.9 log
<i>S. marcescens</i> ATCC 13880	>5.0	>5.0	0 log	3.2	3.9	0.7 log
<i>S. aureus</i> ATCC 6538	4.3	5.4	1.1 log	2.8	4.8	2.0 log

Using a Novel Method to Test the Effectiveness of the Rub-Rinse Step to Reduce Microbial Load,  
N. Brady, K. S. Ambrus, N. Azizi, ARVO Poster 2008



# Summary

- **Contact lens care products must provide effective disinfection yet maintain corneal integrity**
- **2Hr Short-term staining does not correlate with clinical cytotoxicity**
- **Disinfection effectiveness testing must address real-life patient use, lack of standardized *Acanthamoeba* testing, and non-compliance.**
- **Scientific data supports a rub and rinse regimen in reducing microbial load and enhancing effectiveness of all lens care solutions**