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# Do Pathogen Inactivation Systems Offer an Alternative to Platelet Screening?

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# Overview

- Bacterial Risk to Platelets
  - Screening and affect on safety
  - PI principles
  - Our study
  - Outcomes
  - Further work
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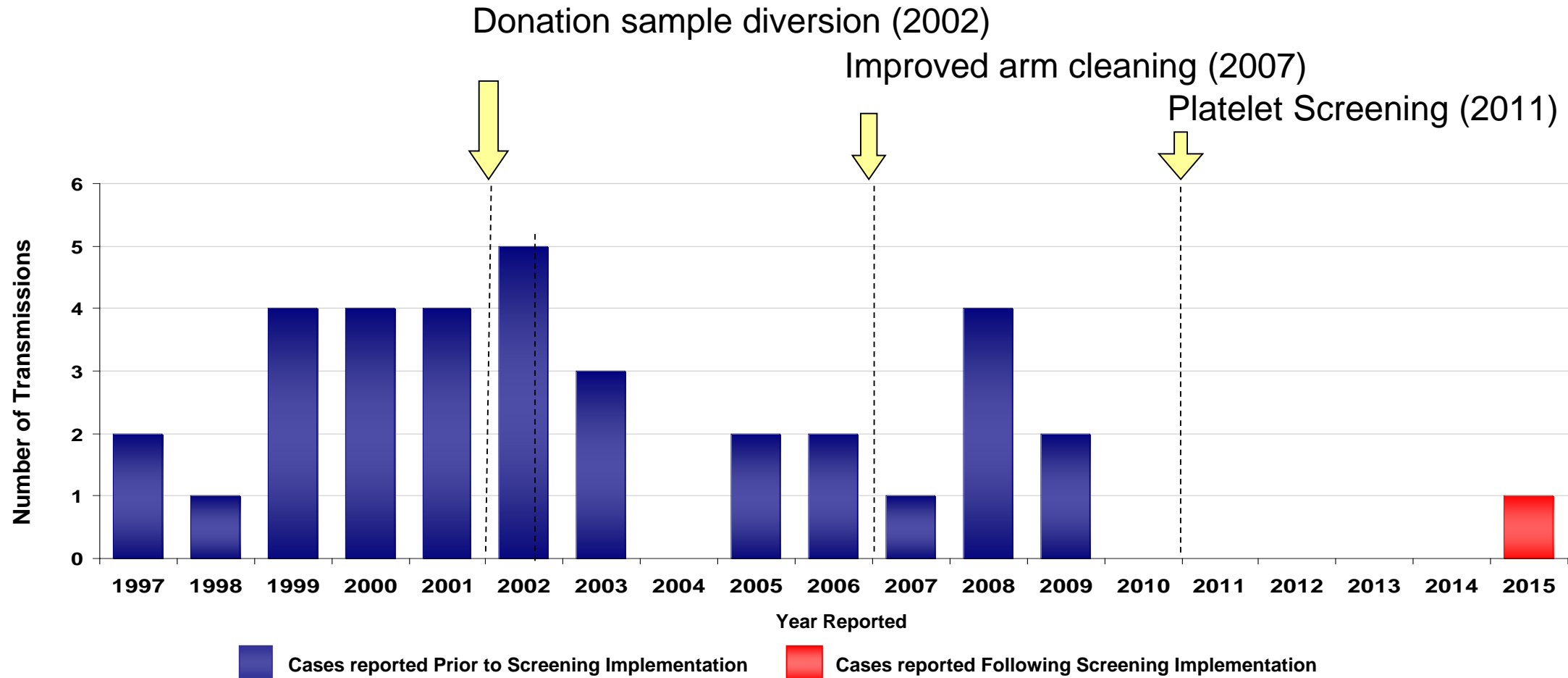
# Bacterial Risk to Platelets

- Platelets at high risk from contamination
- Storage at 22°C
  - maintains platelet viability and function
- UK SHOT reports 1996 - 2010
  - 36 transmissions from platelets
  - 9 deaths (81.8%)
- USA FDA 2005-2013
  - 28 of 32 (87.5%) fatalities




Image: Platelet unit contaminated with *Staphylococcus aureus*

# Confirmed TTI Due to Contaminated Platelets



# Bacterial Screening Provides A Very Safe System

- Over 1.4 million donations screened to date
  - 1 confirmed and 1 “possible” transmission
  - 4 near-misses
    - 3 *Staphylococcus aureus*, 1 *Serratia marcescens*
  - False negative rate of 0.0003%
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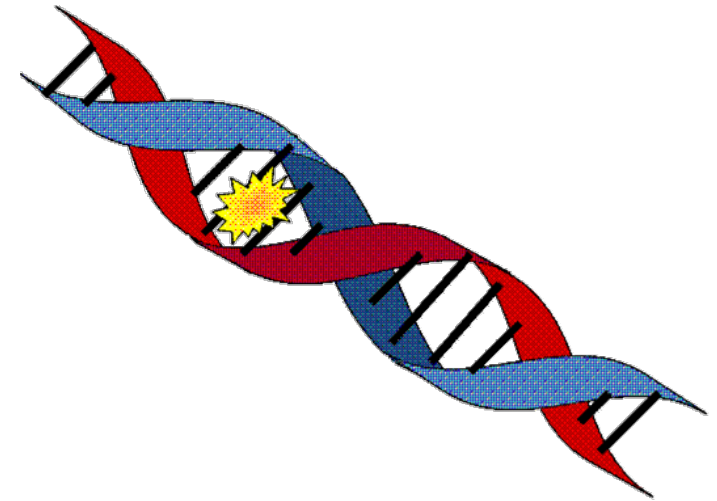
# **Pathogen Inactivation Systems Assessed as an Alternative to Screening for Platelet Components**

Cerus Intercept and TerumoBCT Mirasol systems



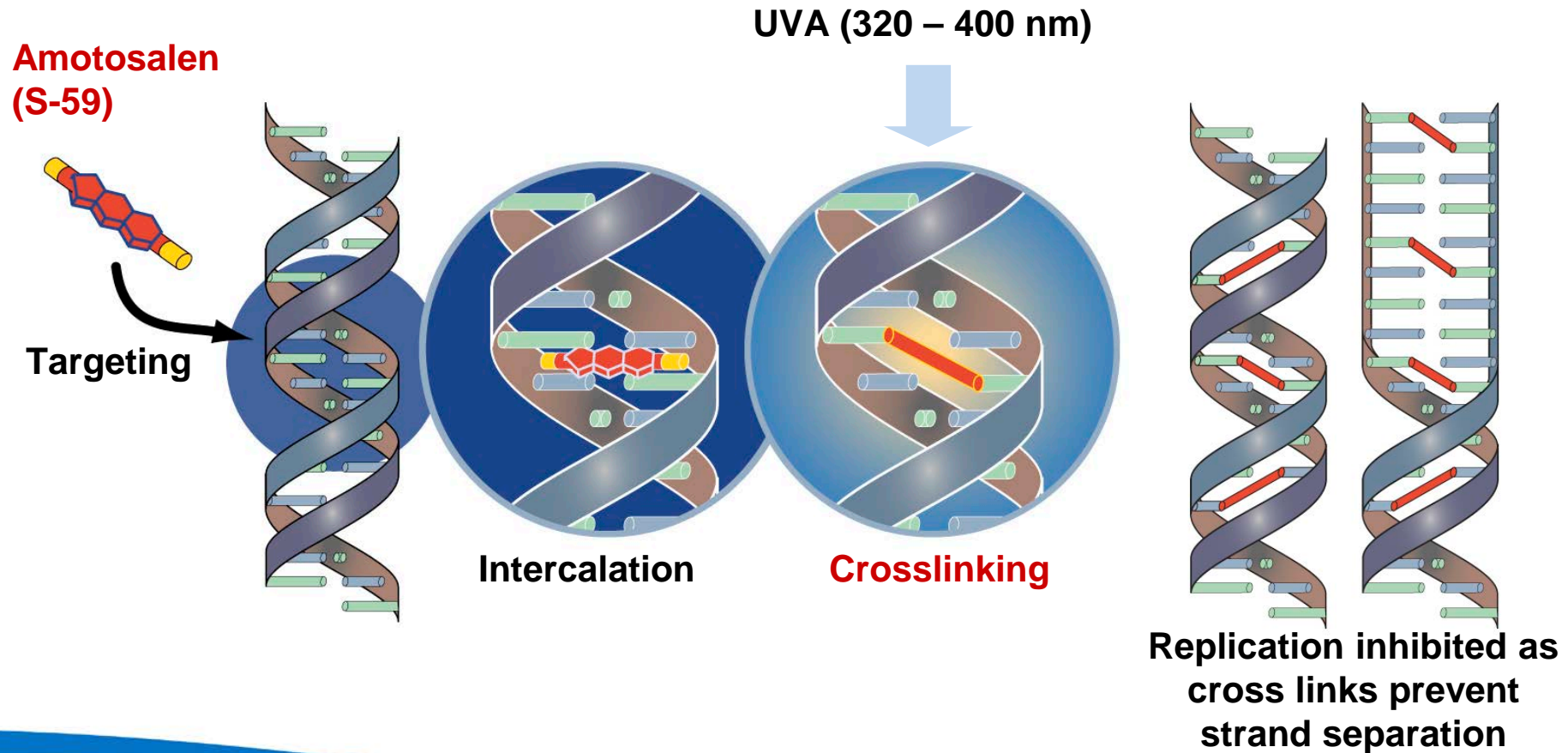
# Pathogen Inactivation

- Treatment of a range of products
  - Platelets and plasma treatment systems commercially available
  - Treatment of red cells and whole blood also in development
- Targets RNA and DNA in the sample
  - Inactivates white cells
  - Prevents bacterial replication
  - Platelets, red cells and plasma unaffected





# Cerus Intercept Mechanism of Action







# TerumoBCT- Mirasol System for Platelet Components




# NBL Evaluation Method

- Day 1 buffy coat pooled platelets in SSP+ (additive solution)
  - Concentrations assessed:
    - $10^{-1}$  CFU/ml
    - $10^3$  CFU/ml
    - $10^4$  CFU/ml
    - $10^5$  CFU/ml
  - Concentrations cover range of growth possible at time of treatment
  - 3 units per concentration
    - 2 treated “test” units, 1 untreated control
- 

# NBL Evaluation Method

- Pool and split
  - Bags spiked with bacteria and enumerated
  - Stored in a platelet shaker for two hours (22°C)
  - Sampled (enumerated/BacT/ALERT) and treated
  - Sampled immediately post treatment (enumerated/ BacT/ALERT)
  - Stored in a platelet shaker for the remaining shelf life (up to 7 days)
  - At day 7, enumerated/BacT/ALERT
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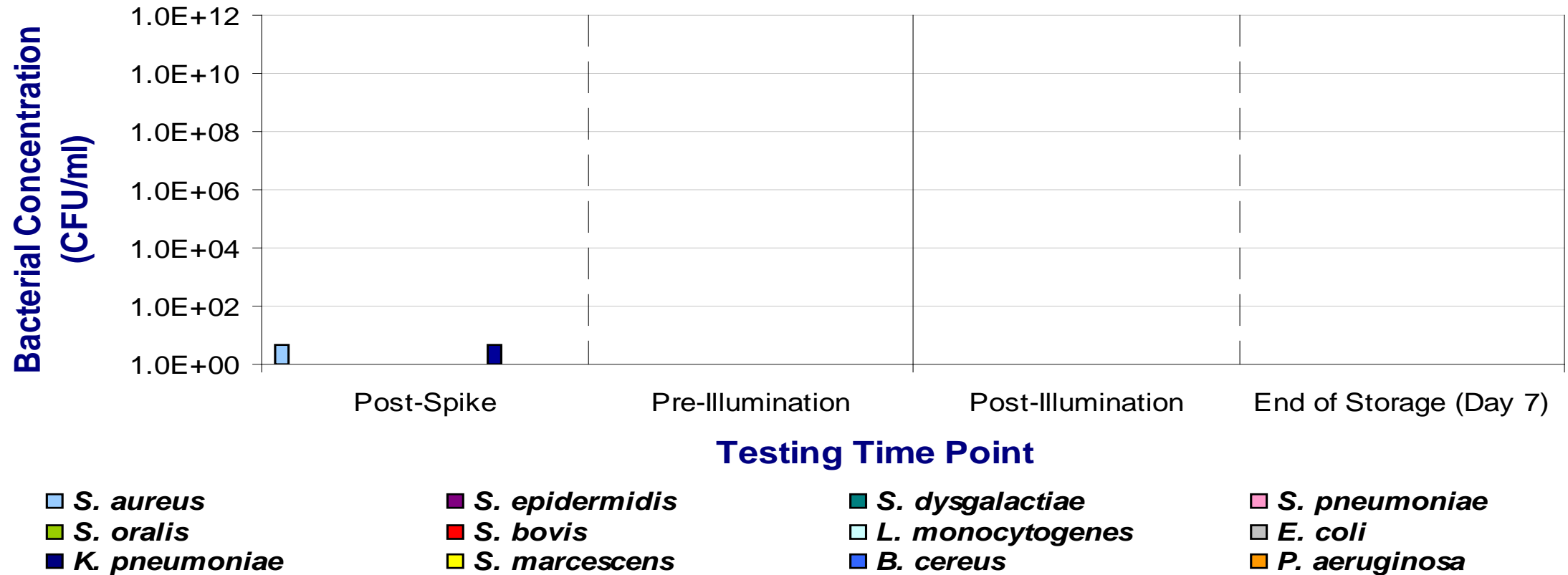
# Organisms assessed

- *Escherichia coli*
  - *Klebsiella pneumoniae*
  - *Listeria monocytogenes*
  - *Serratia marcescens*
  - *Staphylococcus aureus*
  - *Staphylococcus epidermidis*
  - *Streptococcus bovis*
  - *Streptococcus dysgalactiae*
  - *Streptococcus oralis*
  - *Streptococcus pneumoniae*
  - *Pseudomonas aeruginosa* (Intercept only)
  - *Bacillus cereus* (Intercept only)
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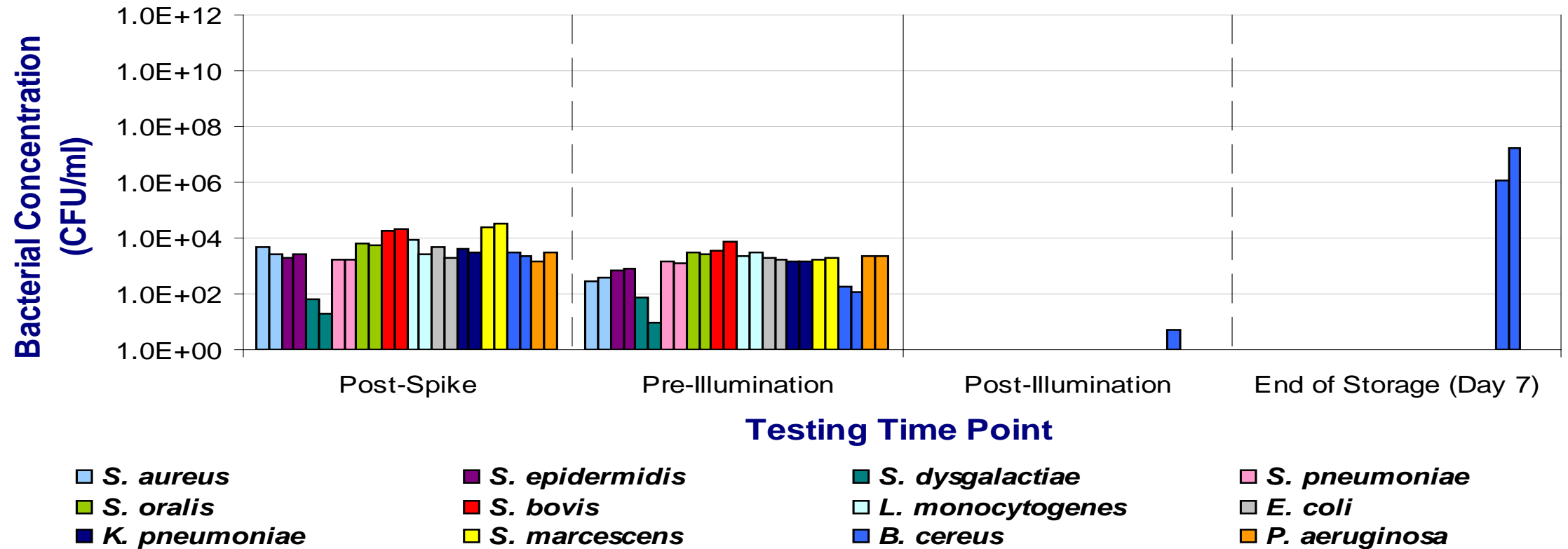
# Cerus Intercept Results



# Effect of Intercept Treatment on Bacterial Growth in Units Inoculated to Achieve $10^{-1}$ CFU/ml



# Effect of Intercept Treatment on Bacterial Growth in Units Inoculated to Achieve $10^3$ CFU/ml





**Bacterial Concentration (CFU/ml)**

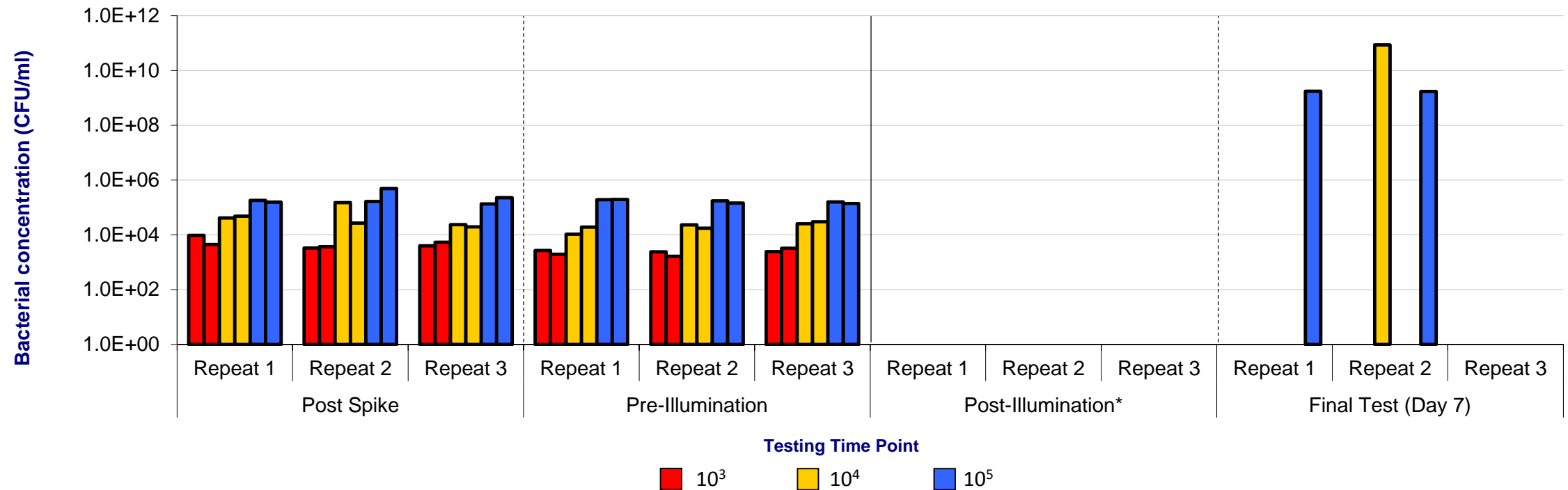
**Testing Time Point**

**Legend:**

- S. aureus* (light blue)
- S. epidermidis* (purple)
- S. dysgalactiae* (teal)
- S. pneumoniae* (pink)
- S. oralis* (green)
- S. bovis* (red)
- L. monocytogenes* (light blue)
- E. coli* (grey)
- K. pneumoniae* (dark blue)
- S. marcescens* (yellow)
- B. cereus* (blue)
- P. aeruginosa* (orange)

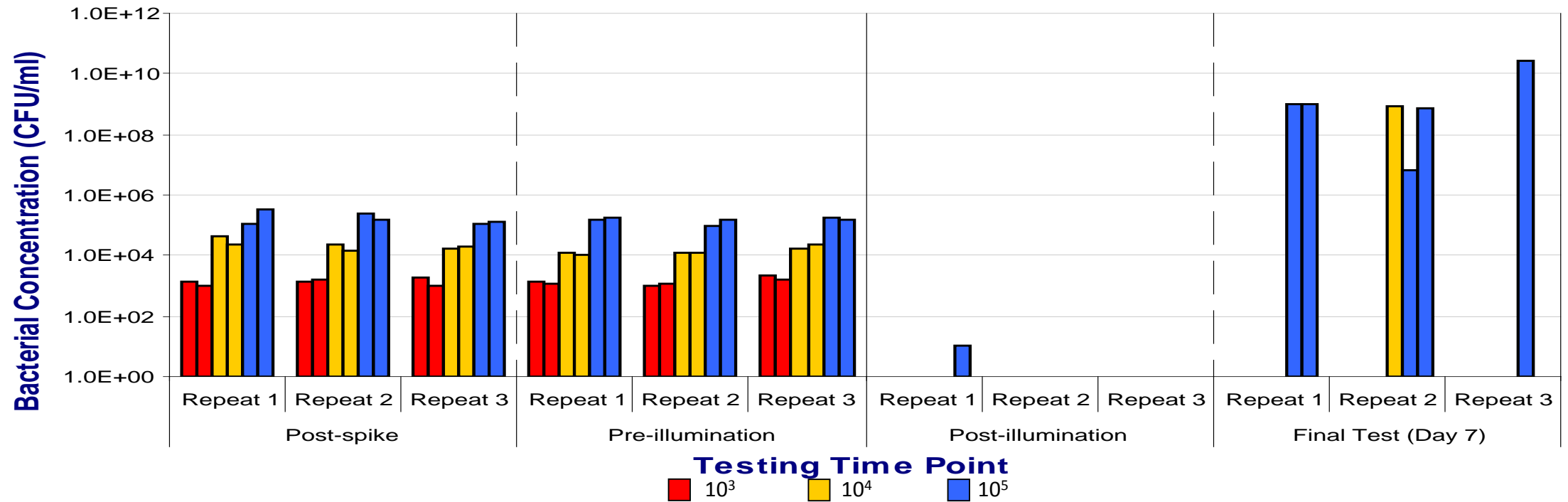
Species	Post-Spike	Pre-Illumination	Post-Illumination	End of Storage (Day 7)
<i>S. aureus</i>	~1.0E+06	~1.0E+05	~1.0E+01	~1.0E+10
<i>S. epidermidis</i>	~1.0E+05	~1.0E+05	~1.0E+01	~1.0E+01
<i>S. dysgalactiae</i>	~1.0E+05	~1.0E+05	~1.0E+01	~1.0E+01
<i>S. pneumoniae</i>	~1.0E+05	~1.0E+05	~1.0E+01	~1.0E+01
<i>S. oralis</i>	~1.0E+05	~1.0E+05	~1.0E+01	~1.0E+01
<i>S. bovis</i>	~1.0E+06	~1.0E+05	~1.0E+01	~1.0E+01
<i>L. monocytogenes</i>	~1.0E+06	~1.0E+05	~1.0E+01	~1.0E+01
<i>E. coli</i>	~1.0E+06	~1.0E+05	~1.0E+01	~1.0E+01
<i>K. pneumoniae</i>	~1.0E+06	~1.0E+05	~1.0E+01	~1.0E+01
<i>S. marcescens</i>	~1.0E+06	~1.0E+05	~1.0E+01	~1.0E+01
<i>B. cereus</i>	~1.0E+05	~1.0E+05	~1.0E+01	~1.0E+01
<i>P. aeruginosa</i>	~1.0E+05	~1.0E+05	~1.0E+01	~1.0E+01

# Effect of Intercept Treatment on Growth of *Serratia marcescens* in Units Inoculated with $10^3$ , $10^4$ and $10^5$ CFU/ml



\*Enrichment culture (Bact/ALERT) detected at  $10^5$  cfu/ml in one replicate of repeat 1 and 2.

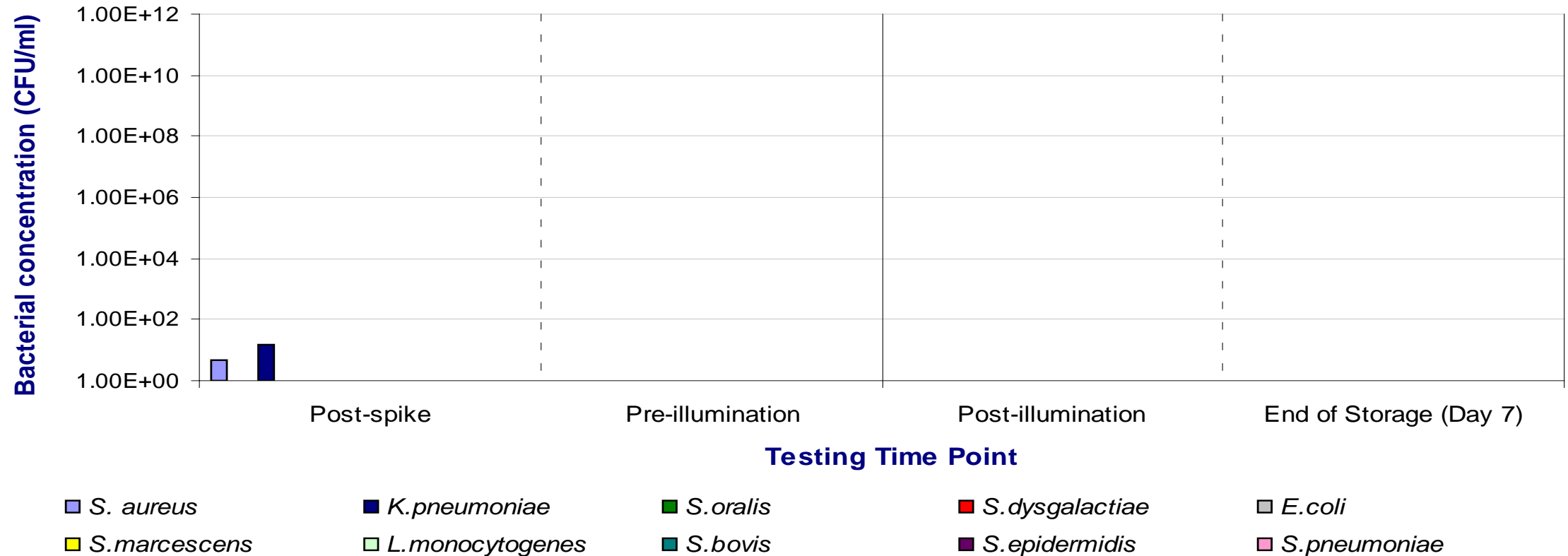
# Effects of Cerus Intercept Treatment on Growth of *Pseudomonas aeruginosa* in Units Inoculated with $10^3$ , $10^4$ and $10^5$ CFU/ml



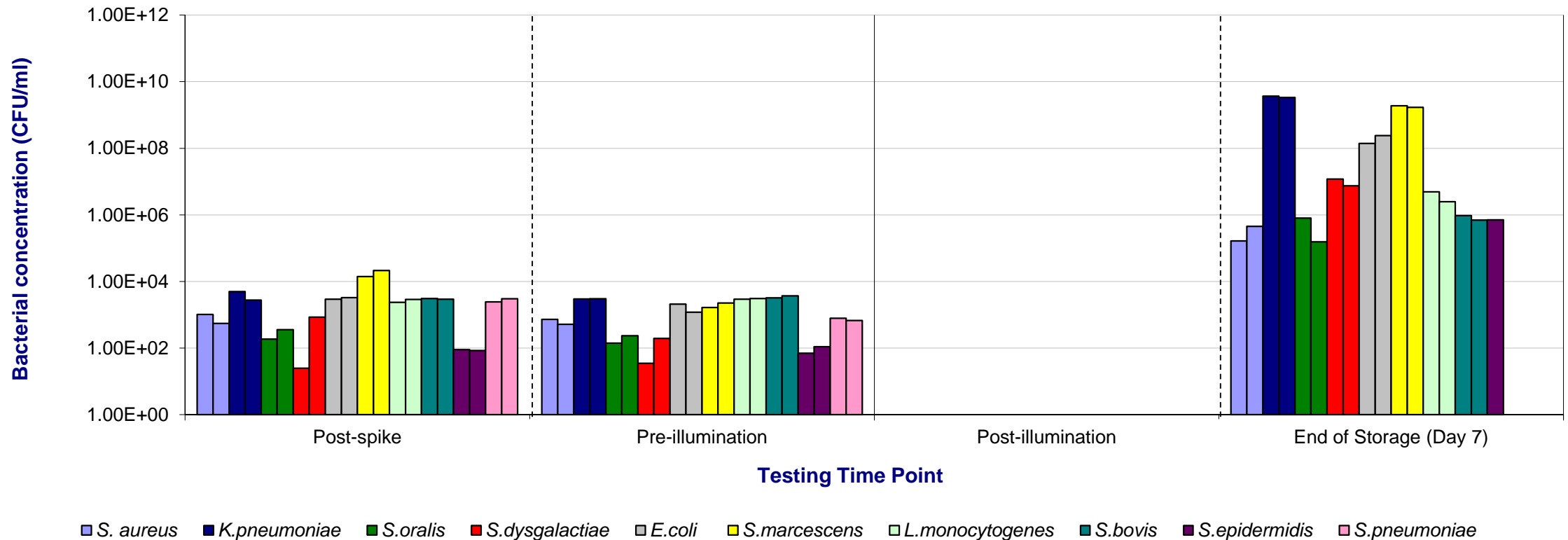
# TerumoBCT Mirasol Results



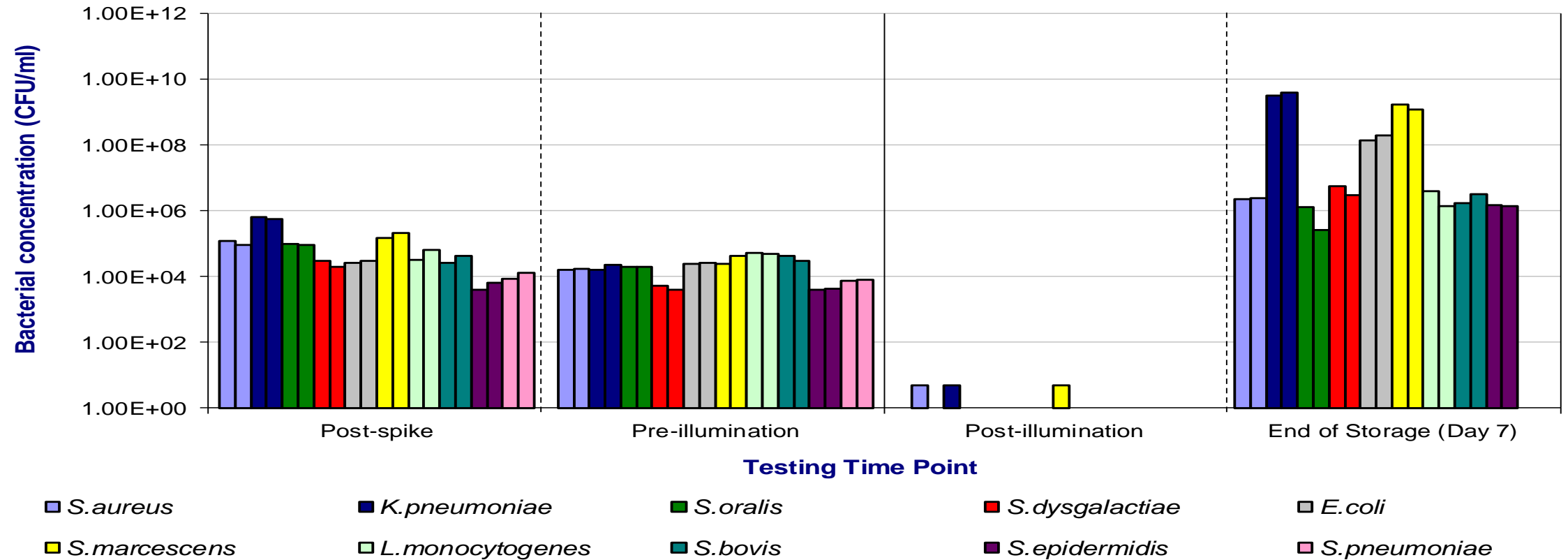
# Effects of Mirasol Treatment on Bacterial Growth in Units Inoculated to Achieve $10^{-1}$ CFU/ml



# Effects of Mirasol Treatment on Bacterial Growth in Units Spiked to Achieve $10^3$ CFU/ml

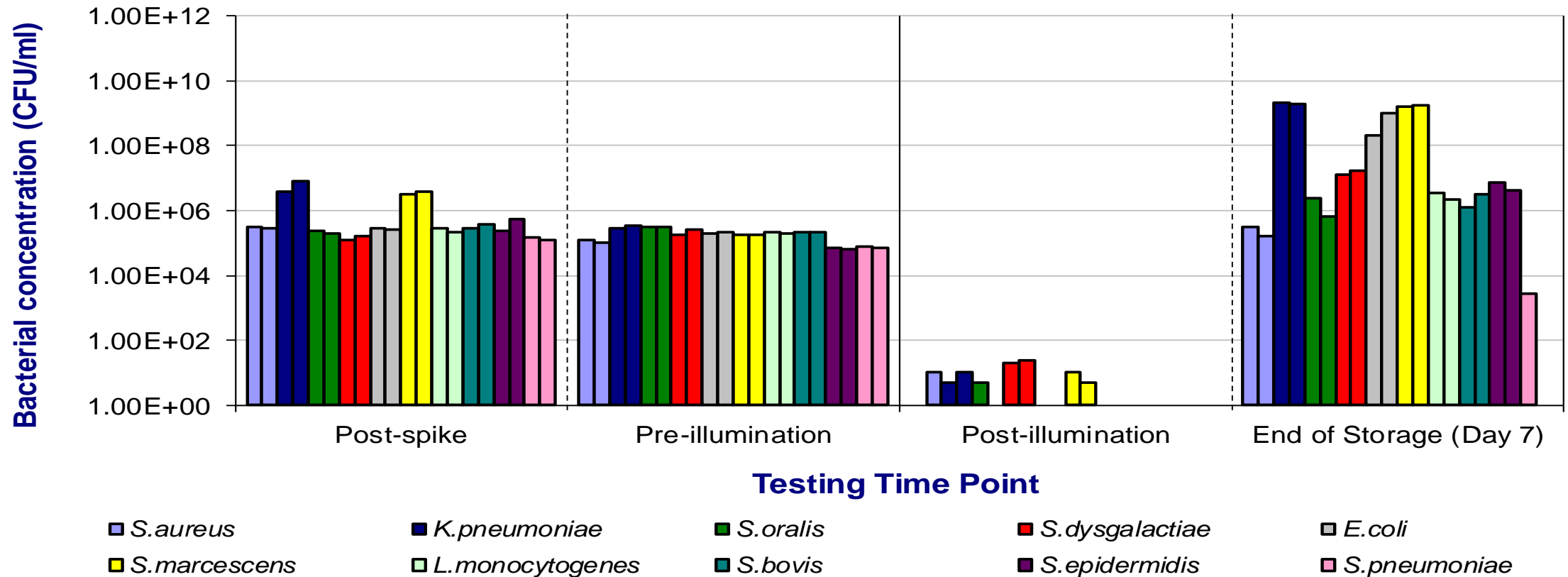


# Effects of Mirasol Treatment on Bacterial Growth in Units Spiked to Achieve $10^4$ CFU/ml







# Effects of Mirasol Treatment on Bacterial Growth in Units Spiked to Achieve $10^5$ CFU/ml



# Conclusion

- All organisms inactivated at low concentrations
  - Treatment most appropriate nearer to the point of donation
  - Log reduction data is misleading
  - Terminal sterility needs to be gold standard for system validation
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# Future PI Studies

- Assess effect of range of treatment times within guidelines
    - Ensure maximal effectiveness for NHSBT
    - Consideration of current logistics limits
  - Breakpoint concentrations
    - Provide assurance as to capabilities of system
  - Evaluation of treatment of platelets in 100% plasma
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Bacterial Screening or PI will not be perfect

Both, if used appropriately, will significantly  
reduce morbidity and mortality in patients



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**THANK YOU**

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