Photochemical Treatment of Platelet Components: A Paradigm Shift in Blood Transfusion Safety

Laurence Corash, M.D.

Cerus Corporation, Concord, CA

University of California, San Francisco

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Agenda

- Rationale for pathogen inactivation
- Technology
- Inactivation spectrum
- Clinical evaluation
- Implementation experience in clinical practice

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Rationale for Pathogen Inactivation

- Testing has improved safety, but limitations remain
- Pathogen inactivation is a prospective complimentary strategy to:
  - Interdict pathogens not tested for
  - Deal with low burden pathogens during window periods: HBV, WNV, CMV
  - Deal with bacteria in all platelet components
  - Deal with emerging pathogens without tests: WNV
  - Inactivate residual CMV and leukocytes for patients not identified as immune suppressed

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Technology

- Amotosalen + UVA light
  - CE Mark - Implemented into clinical practice
  - US PMA review
  - JRC evaluation studies
- Riboflavin + UV light
  - Development - Phase 1

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Activity Spectrum: Amotosalen

Inactivation Activity

- Enveloped viruses
  - HIV, HTLV, HCV, HBV
  - CMV, EBV, HHV-8
  - WNV, SARS, Vaccinia
- Non-enveloped viruses
  - B19, Adenovirus, Reovirus
- Bacteria
- Protozoa
- Leukocytes
- Bio-terrorism agents

Limitations

- Non-enveloped viruses
  - HAV
- Bacterial spores
- Prions

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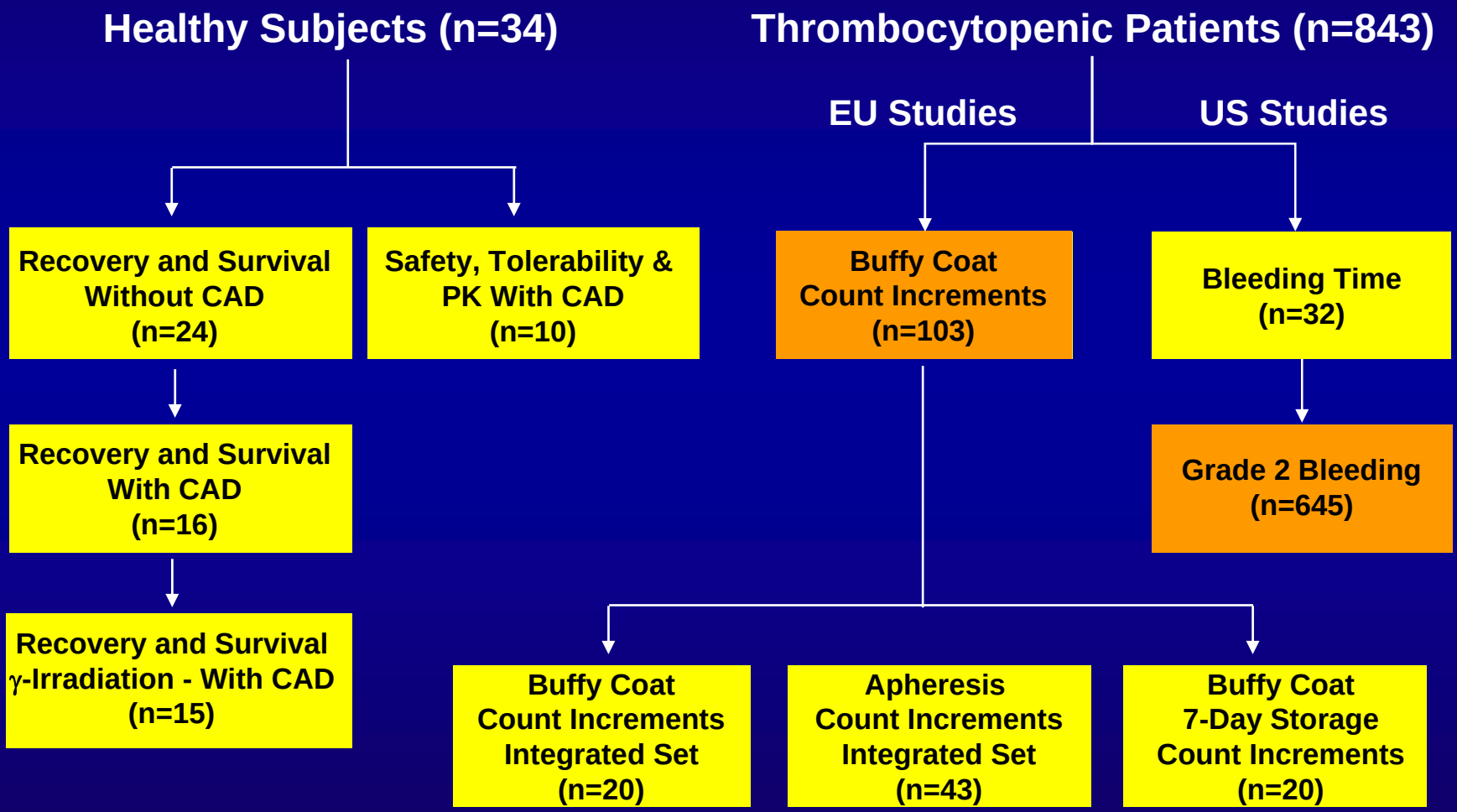
Clinical Trial Experience: Amotosalen



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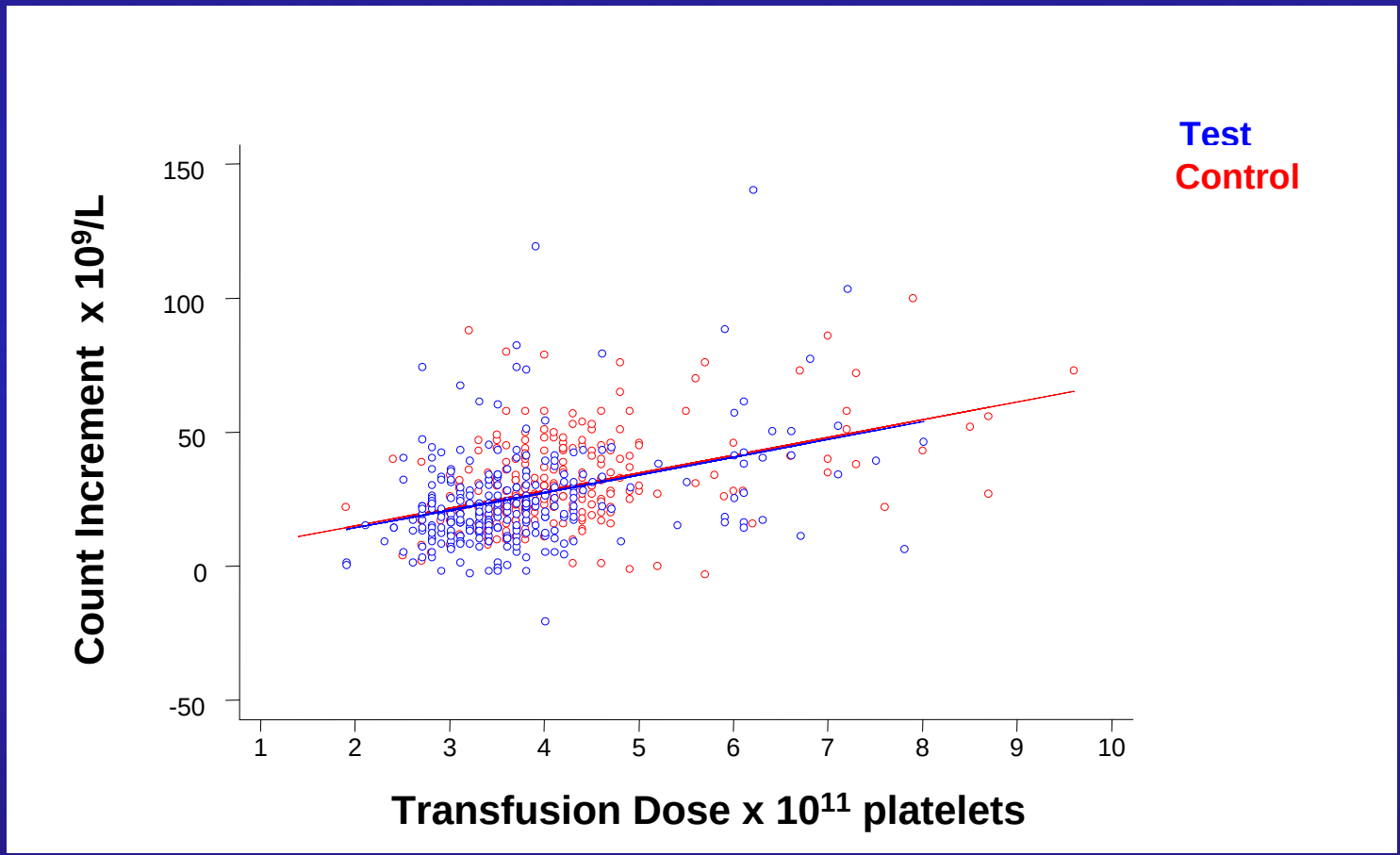
euroSPRITE Primary Endpoint: 1-Hour Count Increment



Blood 2003; 101: 2426-2433

SPRINT: Hemostasis

ENDPOINT	Test (n = 318)	Reference (n = 327)	p-Value
Patients with Grade 2 bleeding (%)	58.5	57.5	0.80
Patients with Grade 3 or 4 bleeding (%)	4.1	6.1	0.37
Number of bleeding sites with Grade 2 bleeding	1.1	1.0	0.24
Proportion of patients with maximum bleeding of Grade 2 (%)	54	52	0.58

Blood 2004; 104: 1534.

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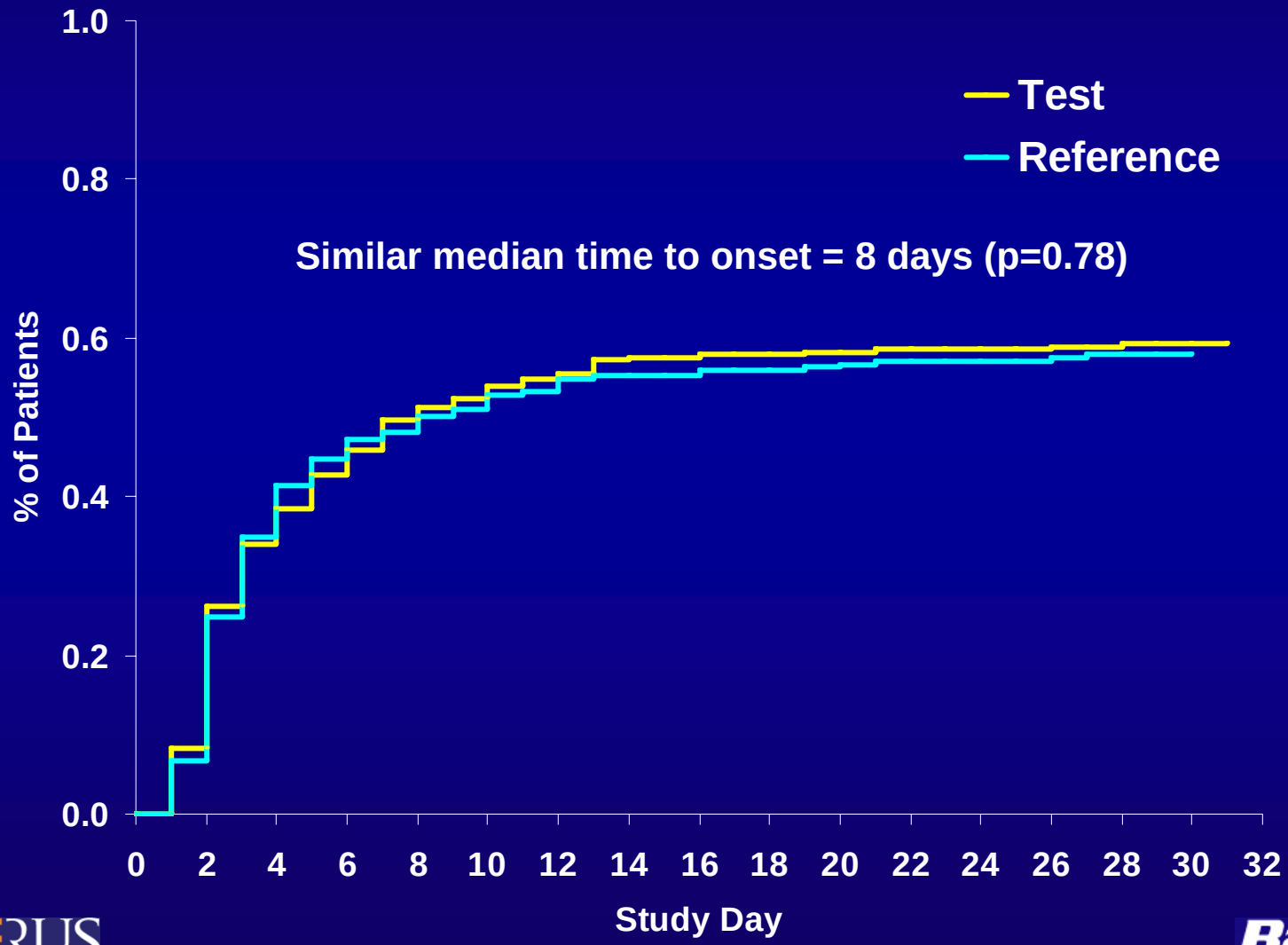
SPRINT: Time to Onset of Grade 2 Bleeding



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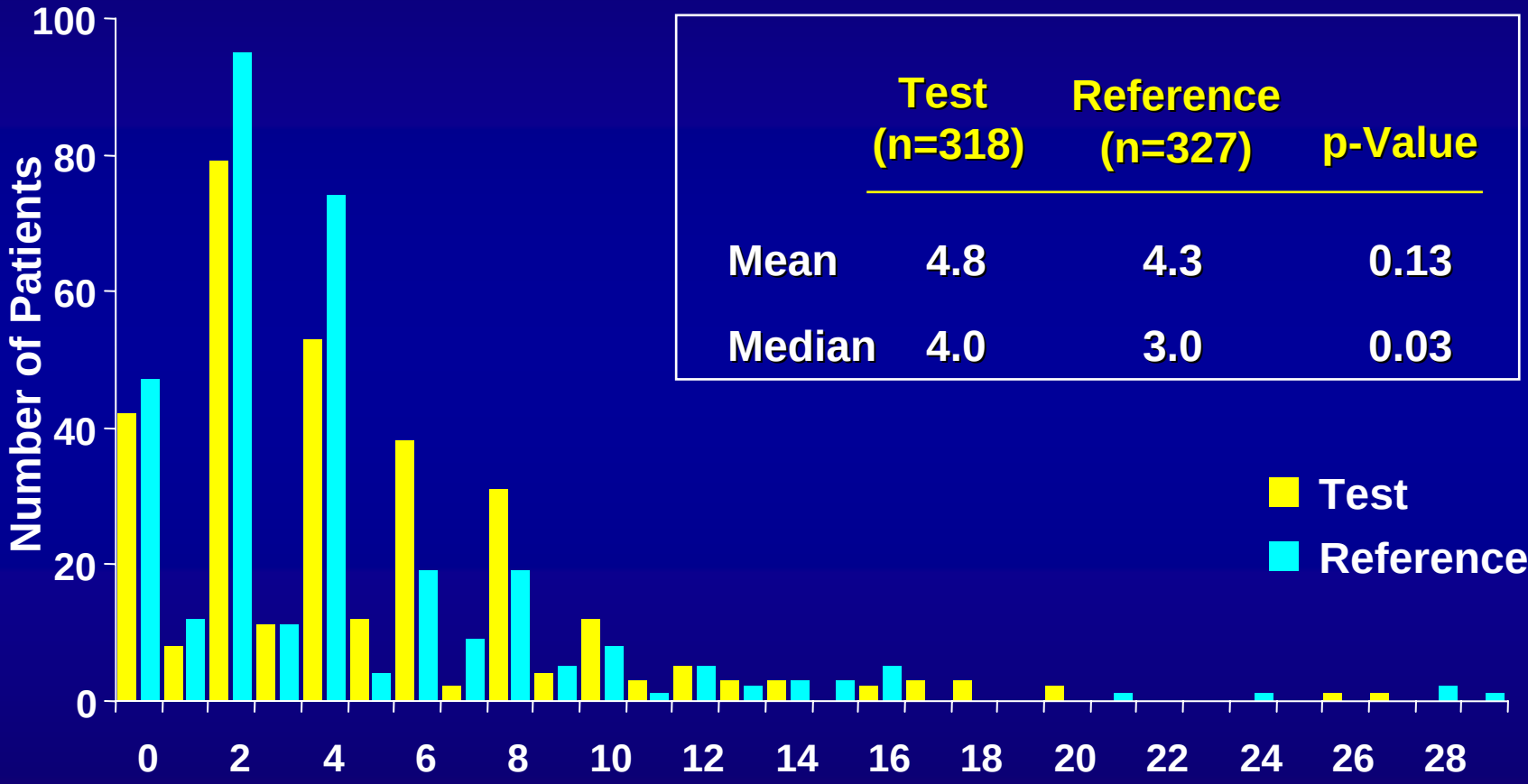
Blood 2004;104:1534

SPRINT: RBC Transfusions



	Test (n=318)	Reference (n=327)	p-Value
Mean	4.8	4.3	0.13
Median	4.0	3.0	0.03

Number of RBC units transfused

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Blood 2004;104: 1534

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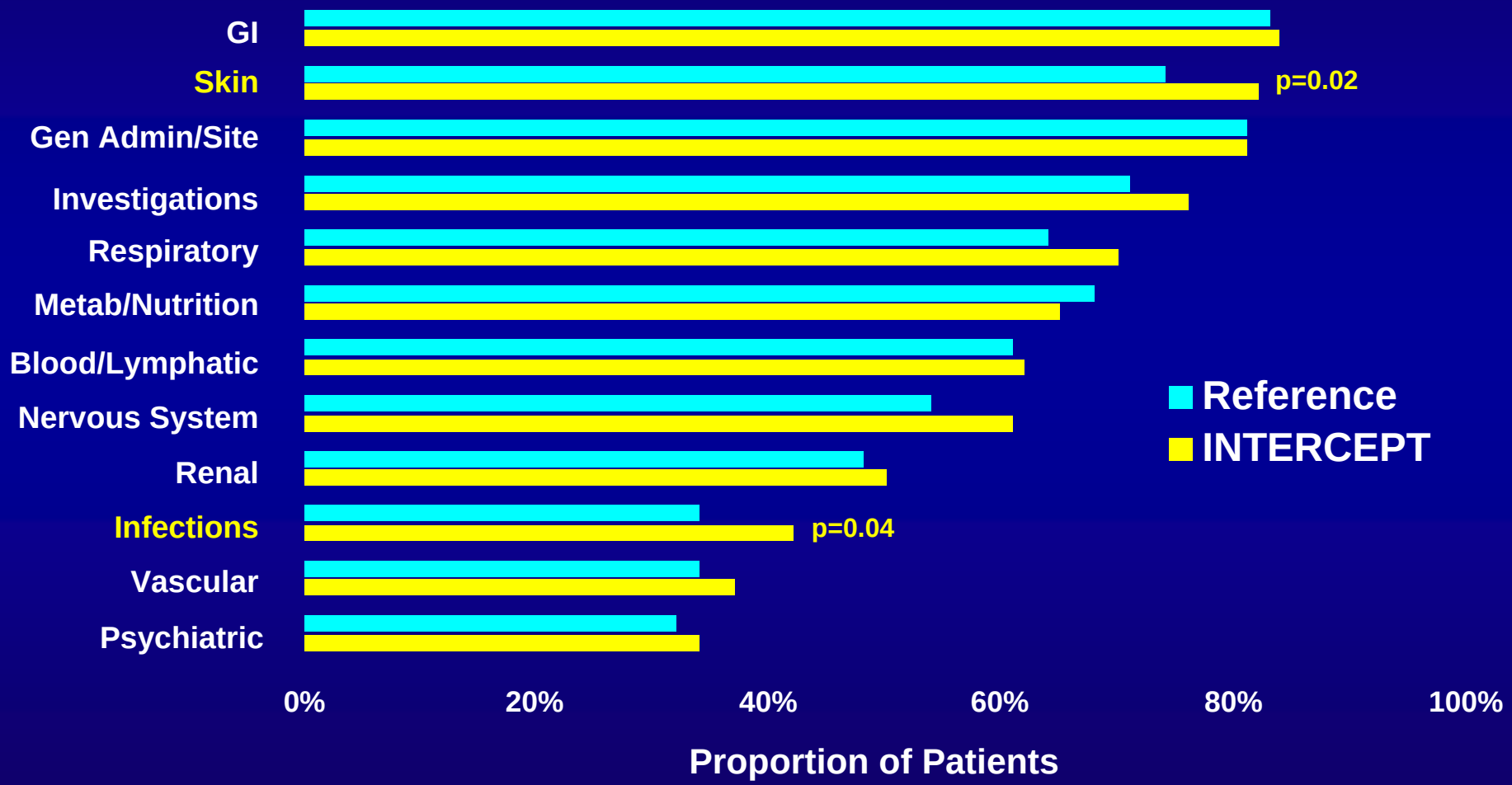
Adverse Events by System Organ Class: *SPRINT*



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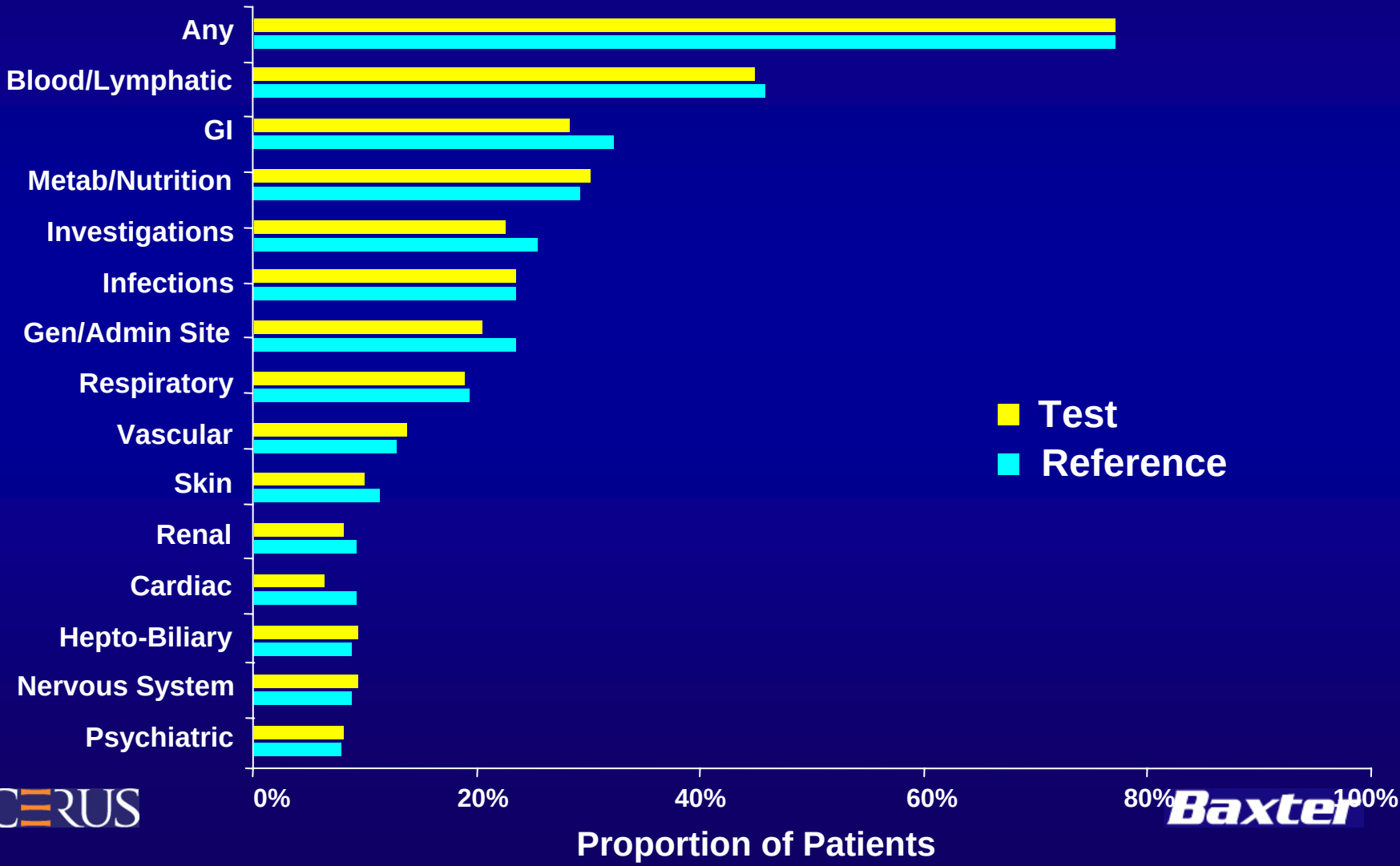
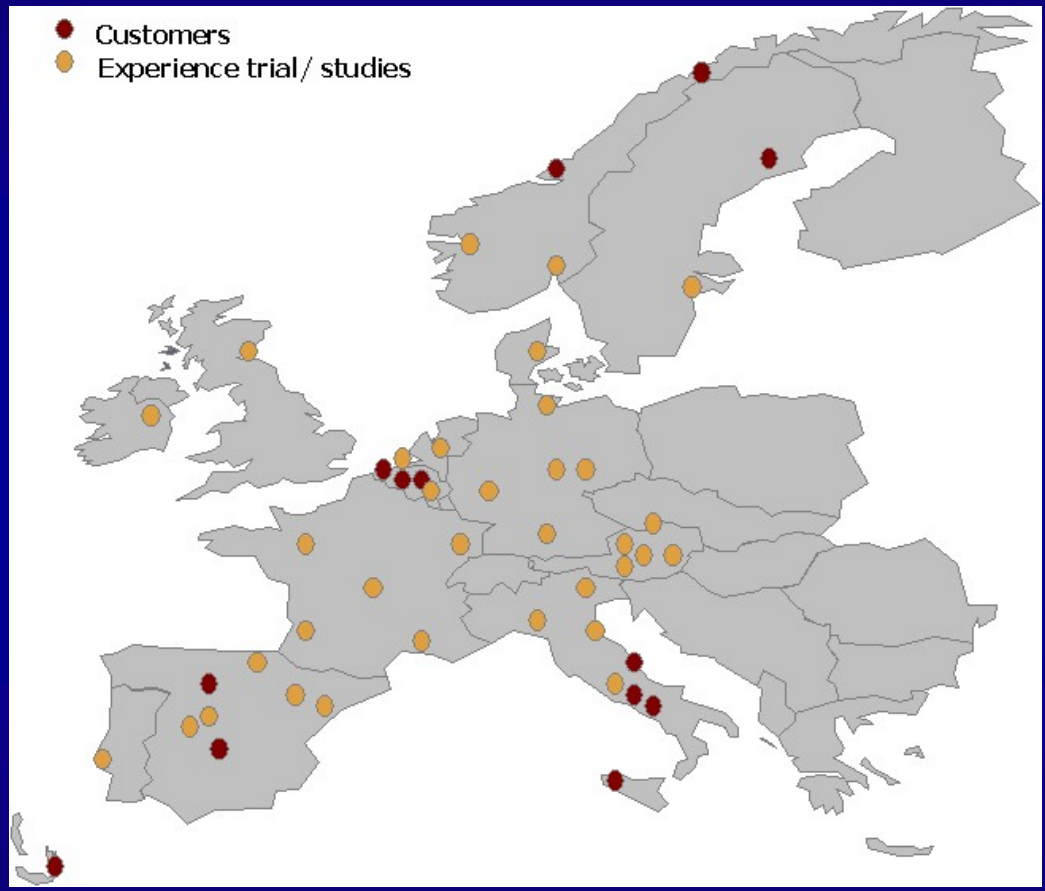
Transfusion 2005; in press

Grade 3/4 Adverse Events by System Organ Class: *SPRINT*



Implementation in Europe



- Approximately 12,000 INTERCEPT doses transfused as of March 2005

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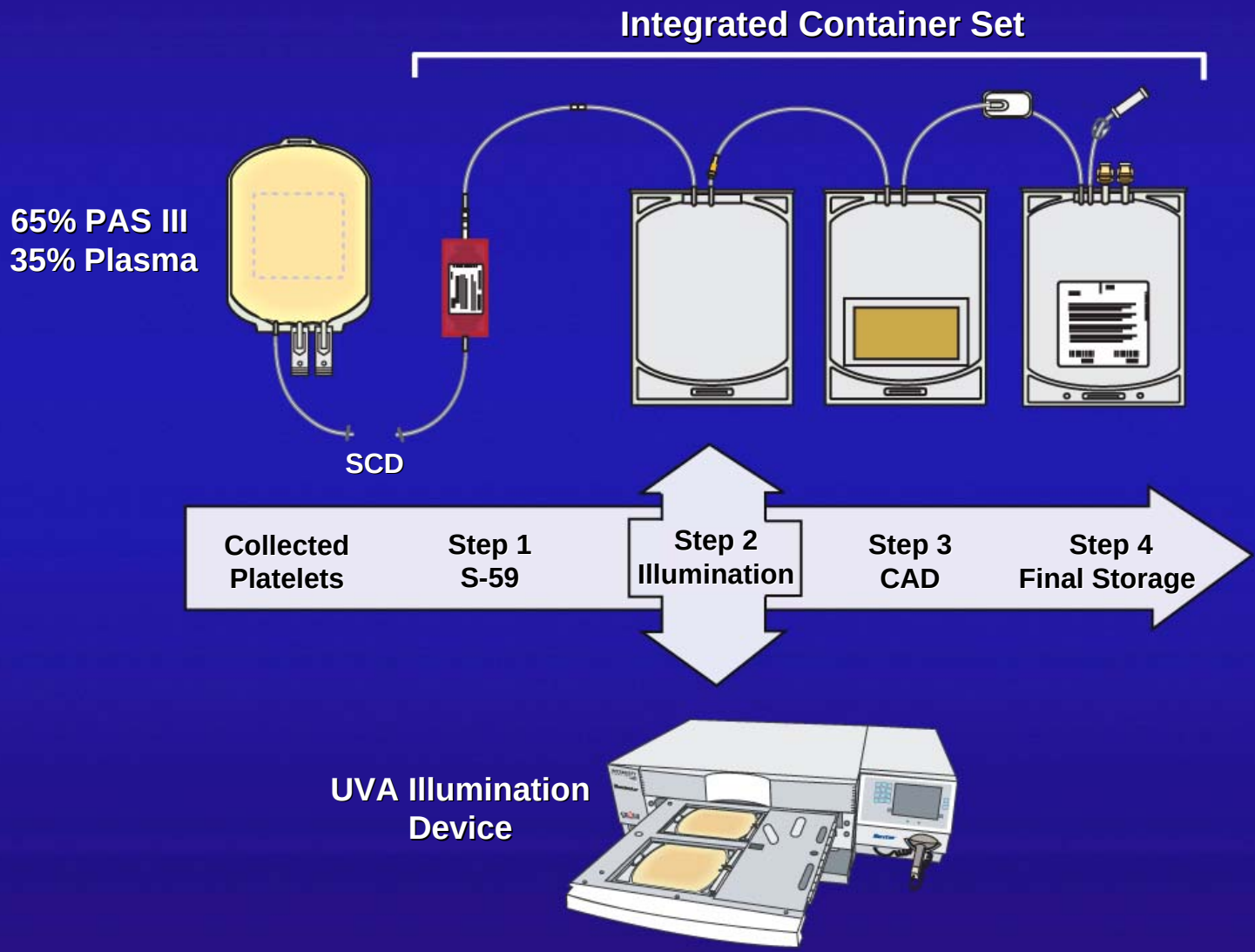
Photochemical Treatment



European Post Marketing Studies

- Pathogen inactivation versus bacterial detection
  - Provides for effective 4 day shelf life
- Hemovigilance study: 5,000 transfusions
  - Interim analysis of 2,512
- Platelet utilization
- Pediatric transfusion experience
  - 300 transfusions, 42 patients

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Bacterial Detection

- 3 European studies of over 175,000 platelet components have shown that only a minority of contaminated products can be detected before transfusion
- In the US, bacterial detection methods are not well suited to whole blood platelets
- A European study was designed to compare bacterial detection and pathogen inactivation

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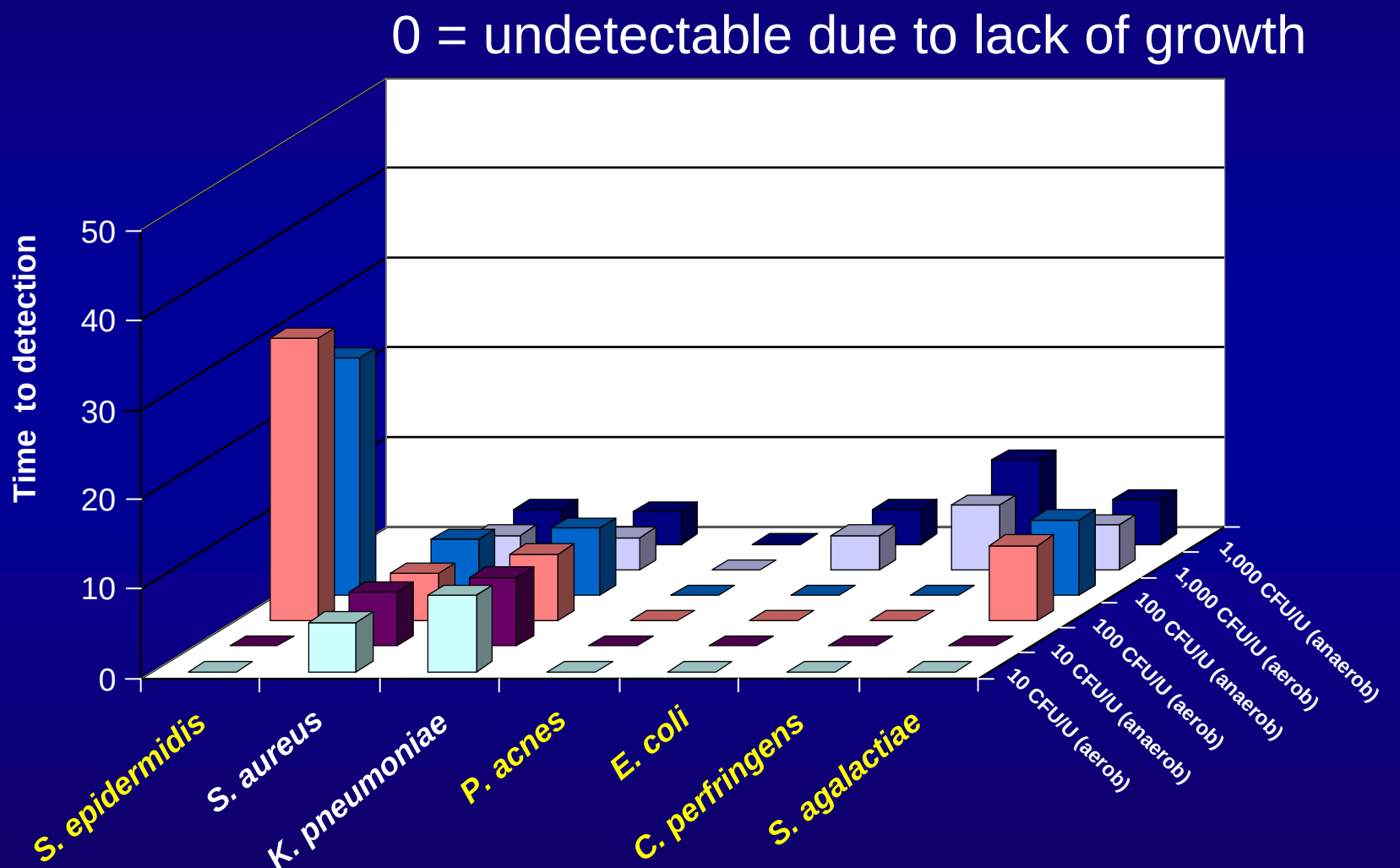
Bacterial detection in untreated platelet concentrates after 1 day of storage



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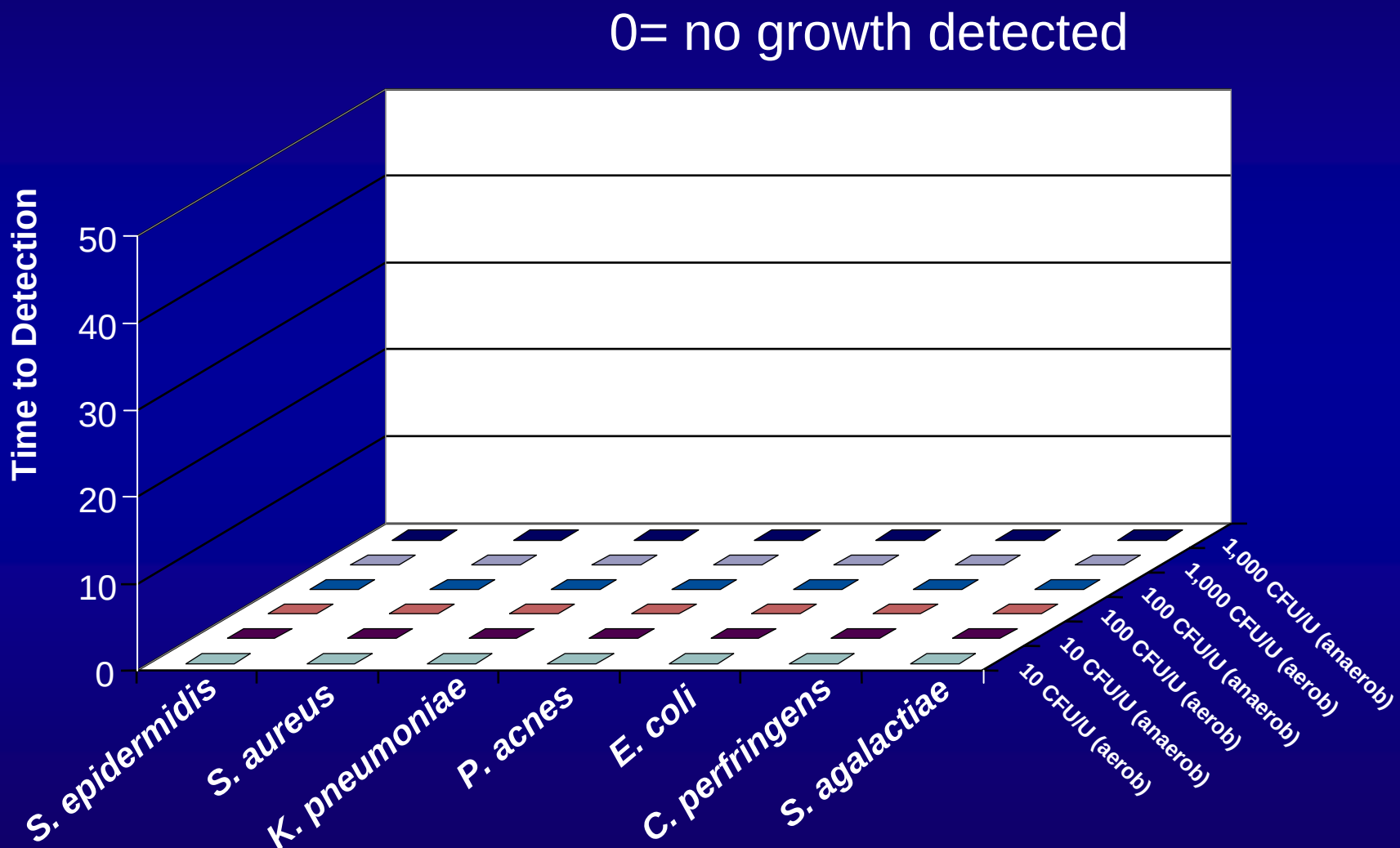
Bacterial detection in treated platelet concentrates after 5 days of storage



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Platelet Utilization

Before and After Implementation

Period	2002	2003
Components[1]	C-PLT	PI-PLT
Transfusions	2,349	2,965
Patients	174	203
Units / Patient	13.5	14.6

[1]C = conventional platelets, PI = Pathogen inactivation platelets
Pathogen inactivation replaced bacterial detection, CMV serologic testing, and gamma irradiation.

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Summary :Pathogen Inactivation

- Broad spectrum of inactivation
- Prospective approach to safety
- Addresses the limitations of bacterial testing
  - Components available earlier
  - Compatible with whole blood platelets
- Implementation into European clinical practice
  - Allowed for earlier release of products

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Key Publications

1. Lin, L., D.N. Cook, G.P. Wiesehahn, et al: Photochemical inactivation of viruses and bacteria in platelet concentrates by use of a novel psoralen and long-wavelength ultraviolet light. *Transfusion* 1997;37:423-435.
2. Lily Lin, Roberta Dikeman, Barbara Molini, Sheila A Lukehart, Robert Lane, Kent Dupuis, Peyton Metzel, and Laurence Corash. Photochemical treatment of platelet concentrates with amotosalen and UVA inactivates a broad spectrum of pathogenic bacteria. *Transfusion* 2004;44:1496-1504.
3. Jorden CT, Saakadze N, Newman JL, et al: Photochemical treatment of platelet concentrates with amotosalen hydrochloride and ultraviolet A light inactivates free and latent cytomegalovirus in a murine transfusion model. *Transfusion* 2004;44:1159-1165.
4. Grass, J.A., T. Wafa, A. Reames, D. Wages, L. Corash, J. L.M. Ferara, and L. Lin: Prevention of Transfusion-Associated Graft-Versus-Host Disease by Photochemical Treatment. *Blood* 1999;93:3140-3147.

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Key Publications

1. Lily Lin, Hanson CV, Alter HJ, Jauvin V, Bernard KA, Murthy K, Peyton Metzel, and Laurence Corash. Inactivation of viruses in platelet concentrates by photochemical treatment with amotosalen and UVA. *Transfusion* 2005;45:580-590 .

2. D. van Rhenen, H. Guilliksson, J.P. Cazenave, D. Pamphilon, P. Ljungman, H. Klüter, H. Vermeij, M. Kappers-Klunne, G. de Greef, M. Laforet, B. Lioure, K. Davis, S. Marblie, V. Mayaudon, J. Flament, M. Conlan, L. Lin, P. Metzel, D. Buchholz and L. Corash: Transfusion of pooled buffy coat platelet components prepared with photochemical pathogen inactivation treatment: the euroSPRITE trial. *Blood* 2003;101:2426-2433.

3. McCullough J, Vesole DH, Benjamin RJ, et al: Therapeutic efficacy and safety of platelets treated with a photochemical process for pathogen inactivation: The SPRINT Trial, *Blood.* 2004;104:1534-1541.

4. Bell CF, Botteman MF, Gao X, et al: Cost-effectiveness of transfusion of platelet components prepared with pathogen inactivation treatment in the United States. *Clinical Therapeutics.* 2003;25: 2464-2486.

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