The background of the slide is a photograph of the Golden Gate Bridge at night. The bridge's towers and suspension cables are silhouetted against a dark blue, misty sky. The water below is also dark and reflects the ambient light. The overall mood is somber and mysterious.

The Trouble with Unreadables

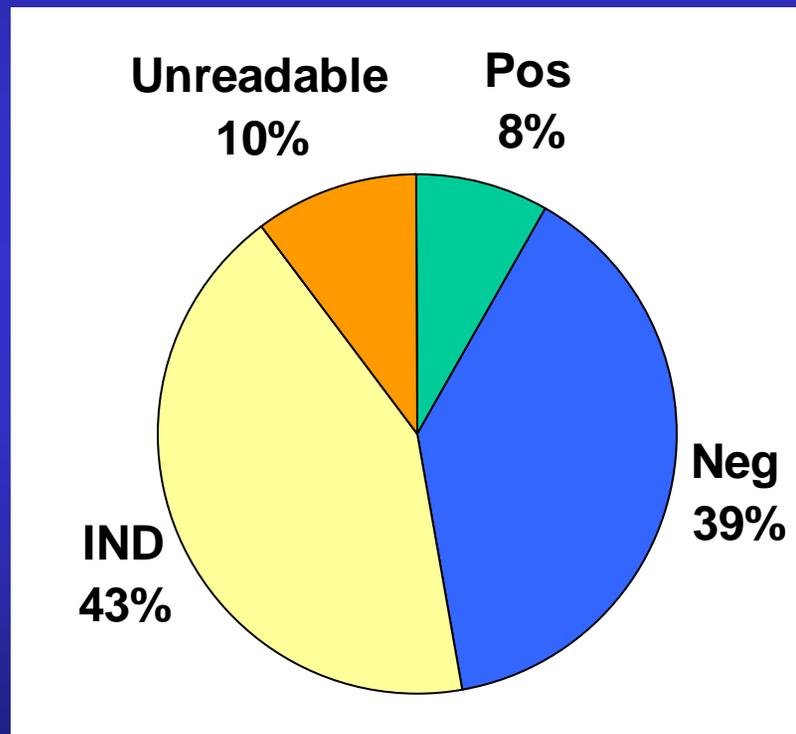
K-A T Nguyen, S Vanderpool,
A Bond, P Lewithan, and H Kamel

Blood Centers of the Pacific
Blood Systems Inc.
October 17, 2005

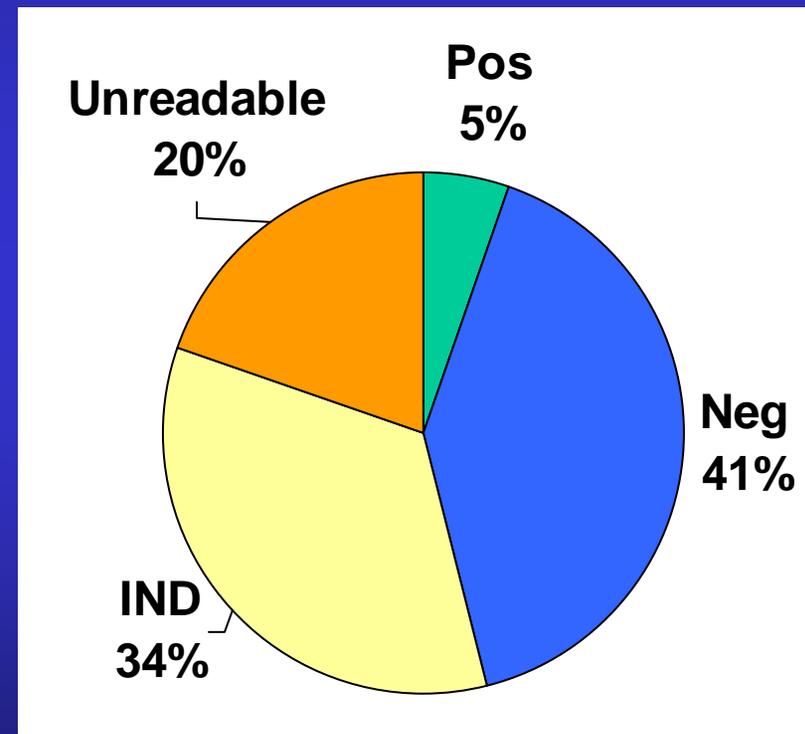
Background

- Federal regulations require confirmatory testing for all HIV screening test Reactive samples
- A very limited number of licensed HIV confirmatory assays are commercially available
- Genetic Systems HIV-1 WB was implemented at Blood Systems Lab in 2002
 - Comparison studies showed performance superior to other available WB
- Since implementation, actual percentage of inconclusive results has increased

BSI HIV-1 WB Results (Jan, 2004 – Jul, 2005)

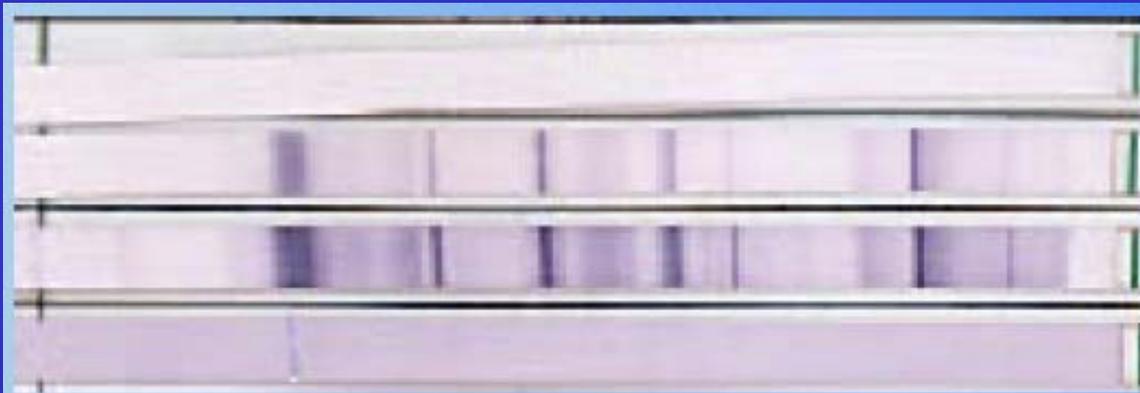


2004
n=798



2005
n=517

Unreadable Western Blot



Strip 1 = Negative

Strip 2 = Weak positive control

Strip 3 = Strong positive control

Strip 4 = Unreadable sample strip

BSL, *Bloodstream* (2004) 17:4.

Factors affecting WB IND/UNR results

- Interpretation of results
 - Negative and Positive criteria are standardized [MMWR 38(S-7): 1-7]
 - There are no standards for interpretation of “indeterminate” vs. “unreadable”
- Test characteristics
- Test kit lot
- Donor related factors

Impact of inconclusive results

- Donor anxiety
- Confusion by consignees
 - Consignees must be notified within 72 hours of an HIV EIA RR
 - If EIA RR component is transfused, consignees must decide whether recipient should be notified
 - Recipient tracing is only required for confirmed HIV Ab positive cases
 - However, transfusion service physicians often feel obligated to notify the recipient in WB UNR cases



More HIV confirmatory results are back!

Study methods

- Study population: UBS and BCP donations
- Study period: Jan, 2004-Jul, 2005
- Genetic Systems HIV-1/2 EIA RR samples -> Genetic Systems HIV-1 WB
- EIA S/CO and NAT results evaluated for WB inconclusive samples
- WB UNR donors contacted for follow-up
- Donor and consignee counseling based on all available data

Screening test vs. WB results

(805 EIA RR in 2004)

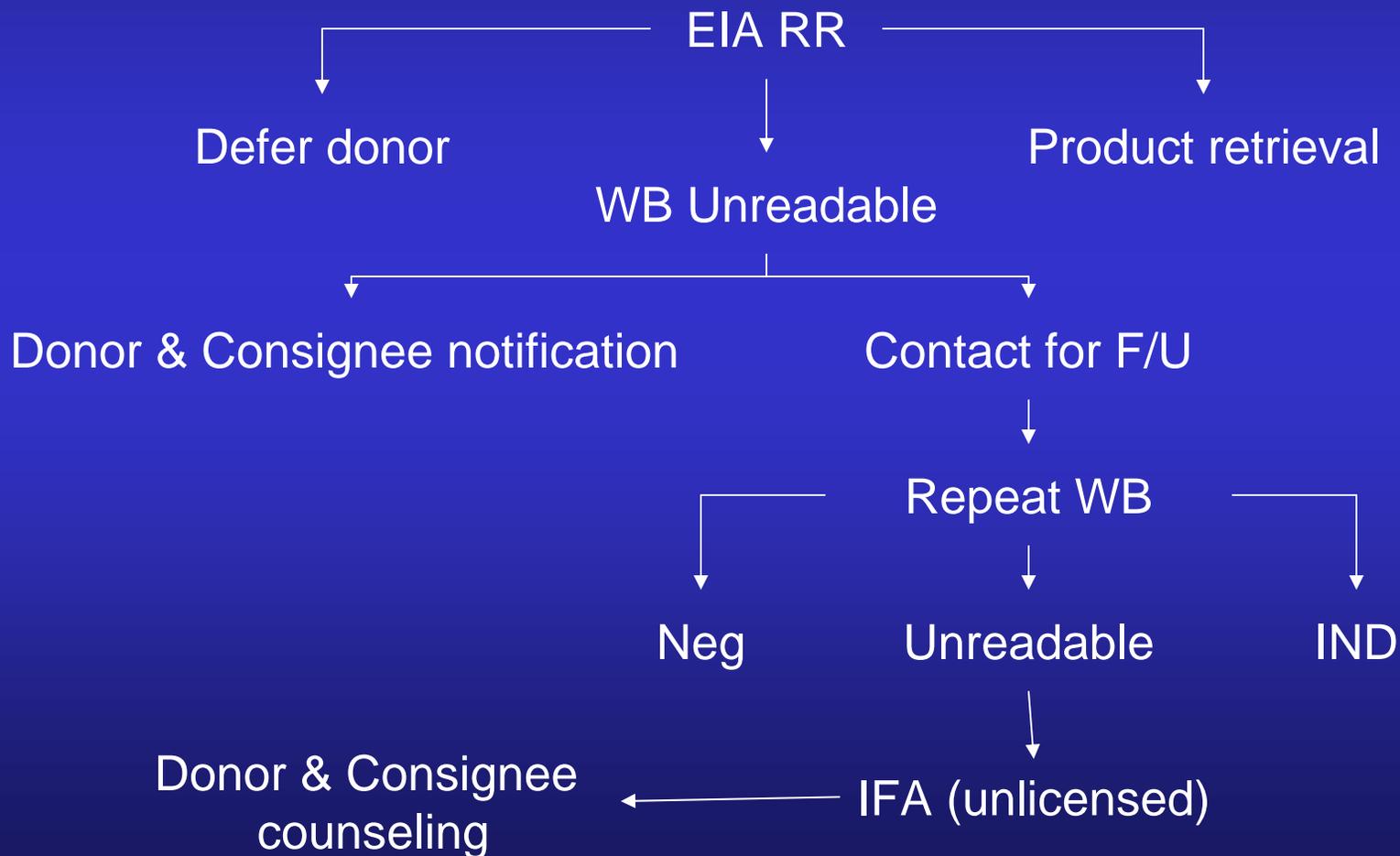
	UNR	IND	Neg	Pos
WB result	83 (10%)	339 (43%)	310 (39%)	66 (8%)
NAT	83 NR	339 NR	310 NR	-
# EIA S/CO Analyzed	76	38	32	36
Av S/CO	1.47 ± 0.8	2.11 ± 1.4	1.99 ± 1.2	6.44 ± 1.2

Screening test vs. WB results

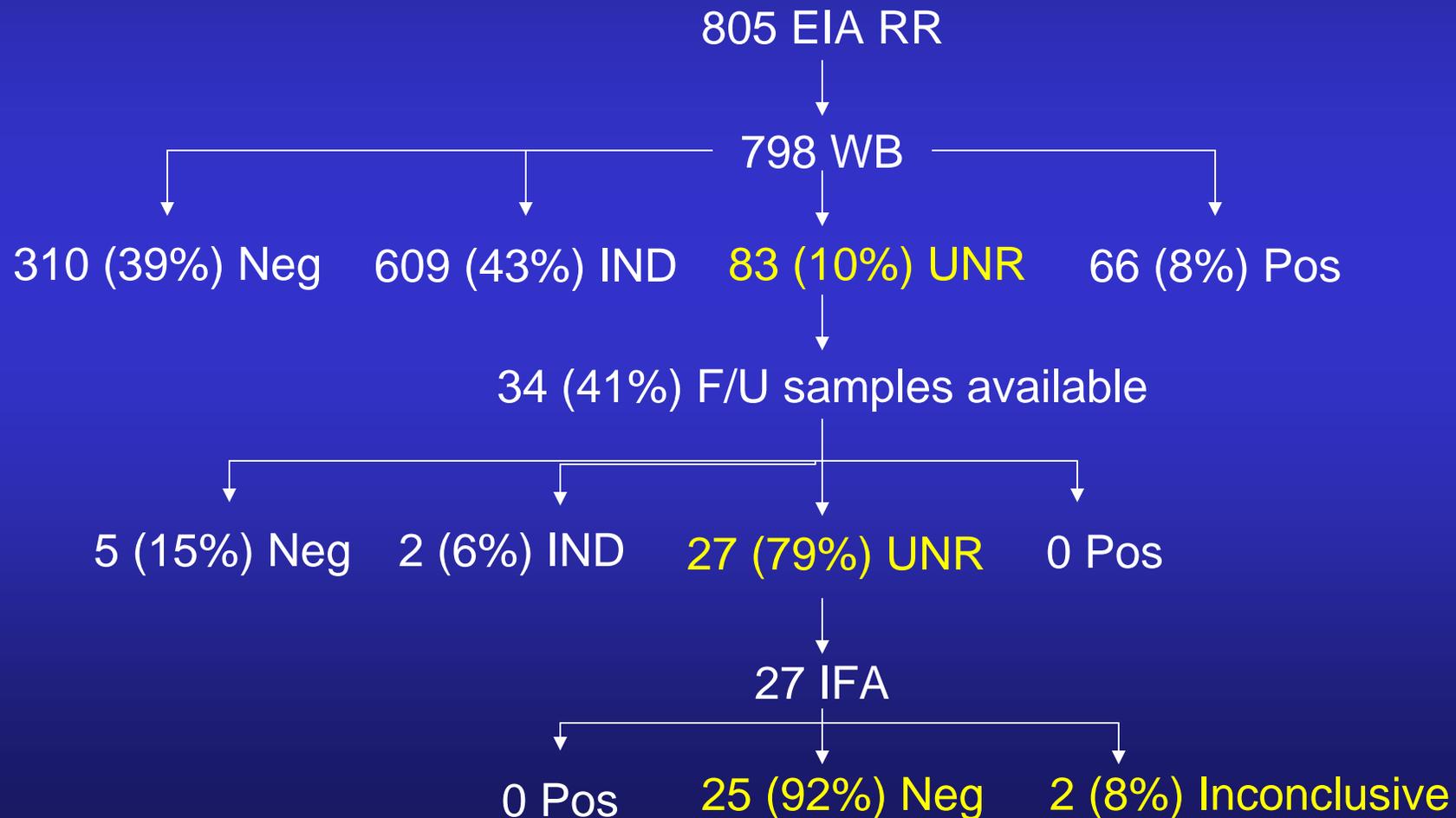
(805 EIA RR in 2004)

	UNR	IND	Neg	Pos
WB result	83 (10%)	339 (43%)	310 (39%)	66 (8%)
NAT	83 NR	339 NR	310 NR	-
# EIA S/CO Analyzed	76	38	32	36
Av S/CO	1.47 ± 0.8	2.11 ± 1.4	1.99 ± 1.2	6.44 ± 1.2

Follow-up testing algorithm



Follow-up testing results, 2004



Conclusions

- Only 41% of donors returned for follow-up
 - Average F/U period 28 days, range 7-141 days
 - Follow-up sample often WB Unreadable
- No follow-up WB progressed to positive
- IFA resolved 92% of WB UNR to negative
 - No follow-up sample was IFA positive
 - Donor management continued to be based on licensed HIV-1 WB results

Alternative HIV confirmatory tests

- FDA licensed: Fluorognost™ HIV-1 IFA
 - Fewer IND/UNR than licensed WB
 - Subjective interpretation, labor intensive
- Proposed: NAT & alternate HIV-1/2 EIA
 - For EIA RR/NAT NR donations
 - Sensitivity 100%, specificity 98.4%
 - Would eliminate 98.5% of WB, 98.6% of IND WB

[S Stramer, SM Owen, presentations at *HIV Diagnostics: New Developments and Challenges*, Orlando, FL, March, 2005]

Draft FDA guidance on HIV re-entry

- Donors eligible for re-entry if EIA RR, NAT NR, and:
 - WB Neg, IND, or ND
 - IFA Neg, IND, or ND
 - p24 Neg or ND
- Test follow-up 8 weeks post-index
- If NAT NR/EIA NR, re-enter
- If NAT NR/EIA RR, then may perform WB
 - If WB Neg, or IND not progressed, eligible for re-entry after another 8 weeks

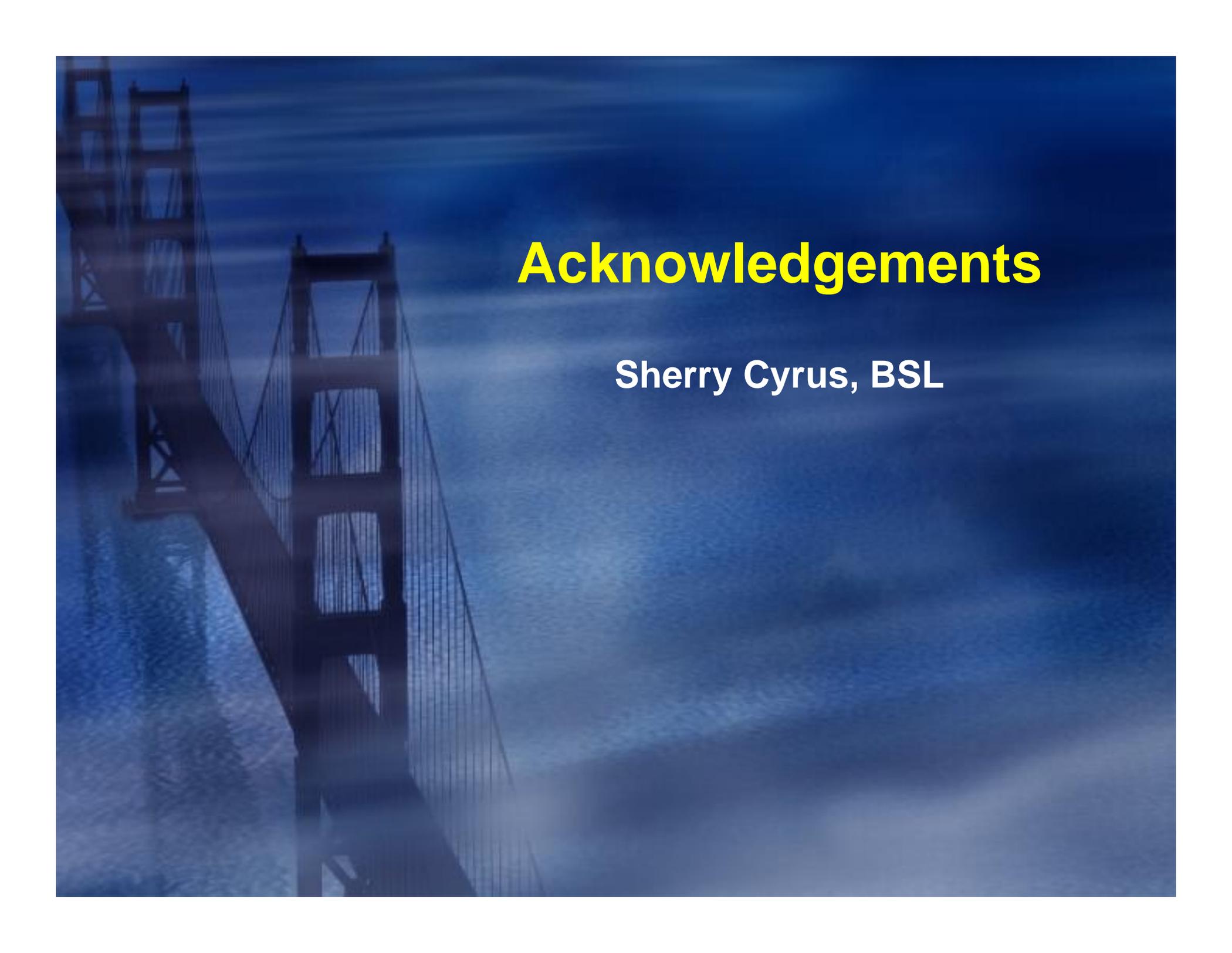
[Guidance for Industry. Nucleic Acid Testing (NAT) for Human Immunodeficiency Virus Type 1 (HIV-1) and Hepatitis C Virus (HCV): Testing, Product Disposition, and Donor Deferral and Reentry. July, 2005.]

BSI proposed approach

- EIA RR/ WB UNR or IND index donation samples reflex to HIV-1 IFA assay
 - Donor and consignee counseling based on all results
- EIA RR/ WB UNR donors should be eligible for re-entry similar to EIA RR/ WB IND donors
 - WB UNR result on follow-up sample → donor eligible for re-entry with another follow-up sample

Captain, the IFA
appears to be
negative.



A photograph of the Golden Gate Bridge at night, with the bridge's towers and suspension cables silhouetted against a dark blue sky and water. The bridge spans across the frame from the left side towards the center.

Acknowledgements

Sherry Cyrus, BSL