Transfusion & Transplantation Safety – American Red Cross Concerns:

Richard J Benjamin MD PhD

Chief Medical Officer

American Red Cross, Biomedical Headquarters

Washington DC

Advisory Committee on Blood Safety and Availability. May 2007.

- What is the current state of safety in transfusion and transplantation safety?
- What are the areas of commonality with blood products, cord, progenitor, bone marrow, tissue and organs?
- Is there scientific/clinical evidence to support a need for a master strategy for transfusion and transplantation safety?

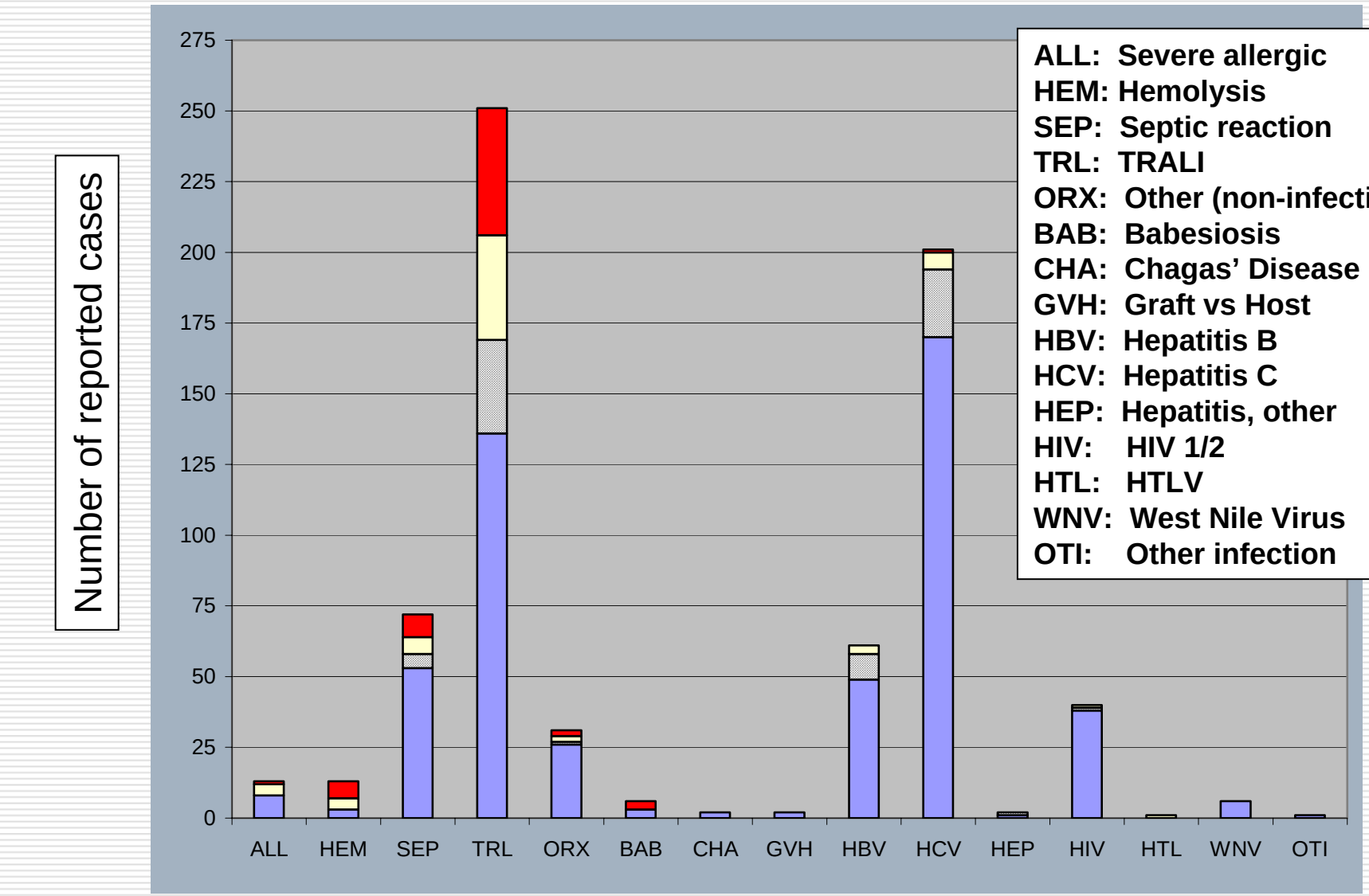
The Committee on Government Reform and Oversight, July 25, 1996.

"The blood supply is safer than it has ever been."

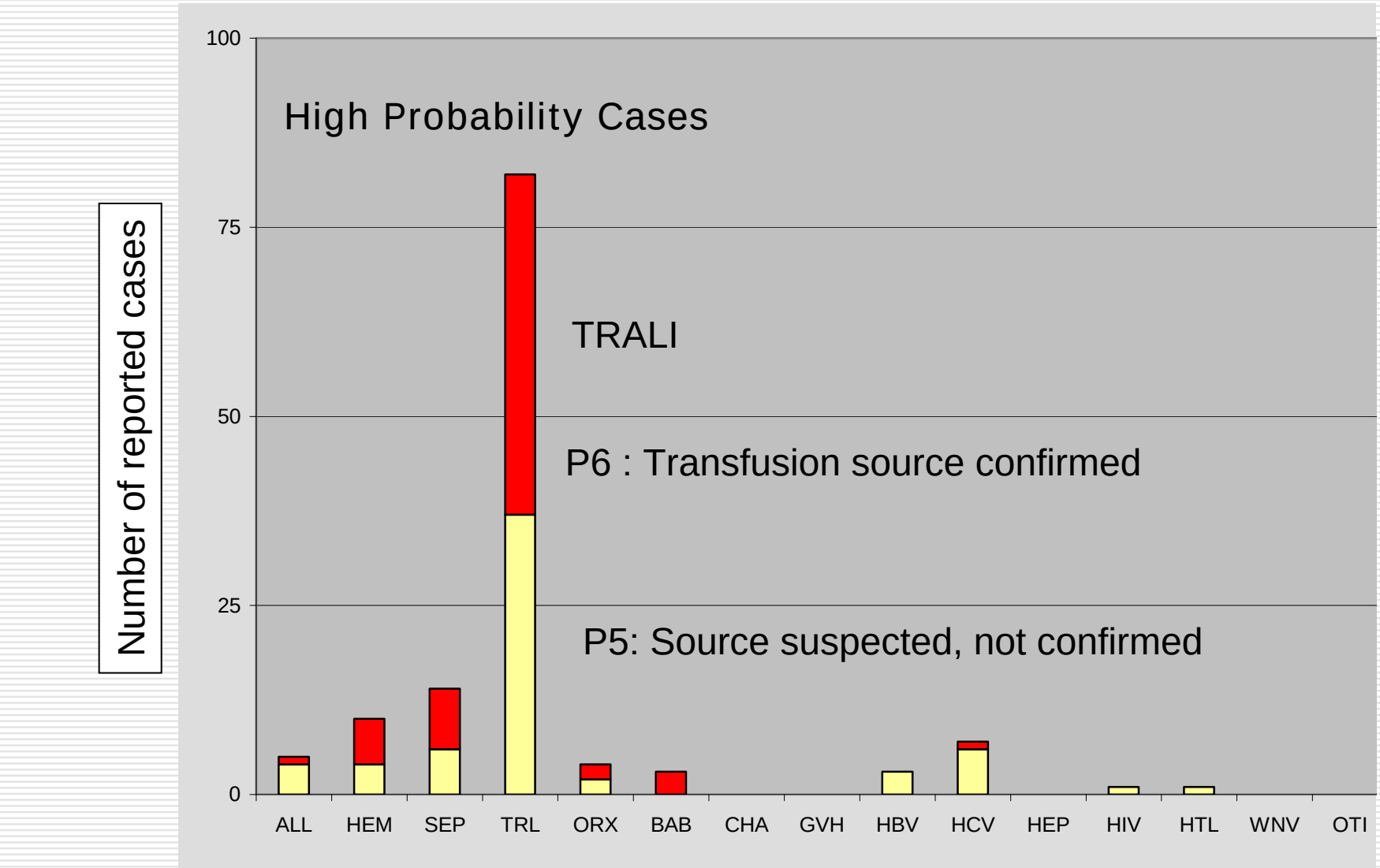
☐ Universal leukoreduction	☐ WNV NAT testing
☐ HIV-1 NAT testing	☐ Bacterial culture
☐ HIV p24 antigen	☐ Chagas disease testing
☐ HCV NAT testing	☐ Male plasma (2007)
☐ Deferrals for vCJD risk	☐ Leukocyte Ab testing (2008)

Processes introduced since 1996

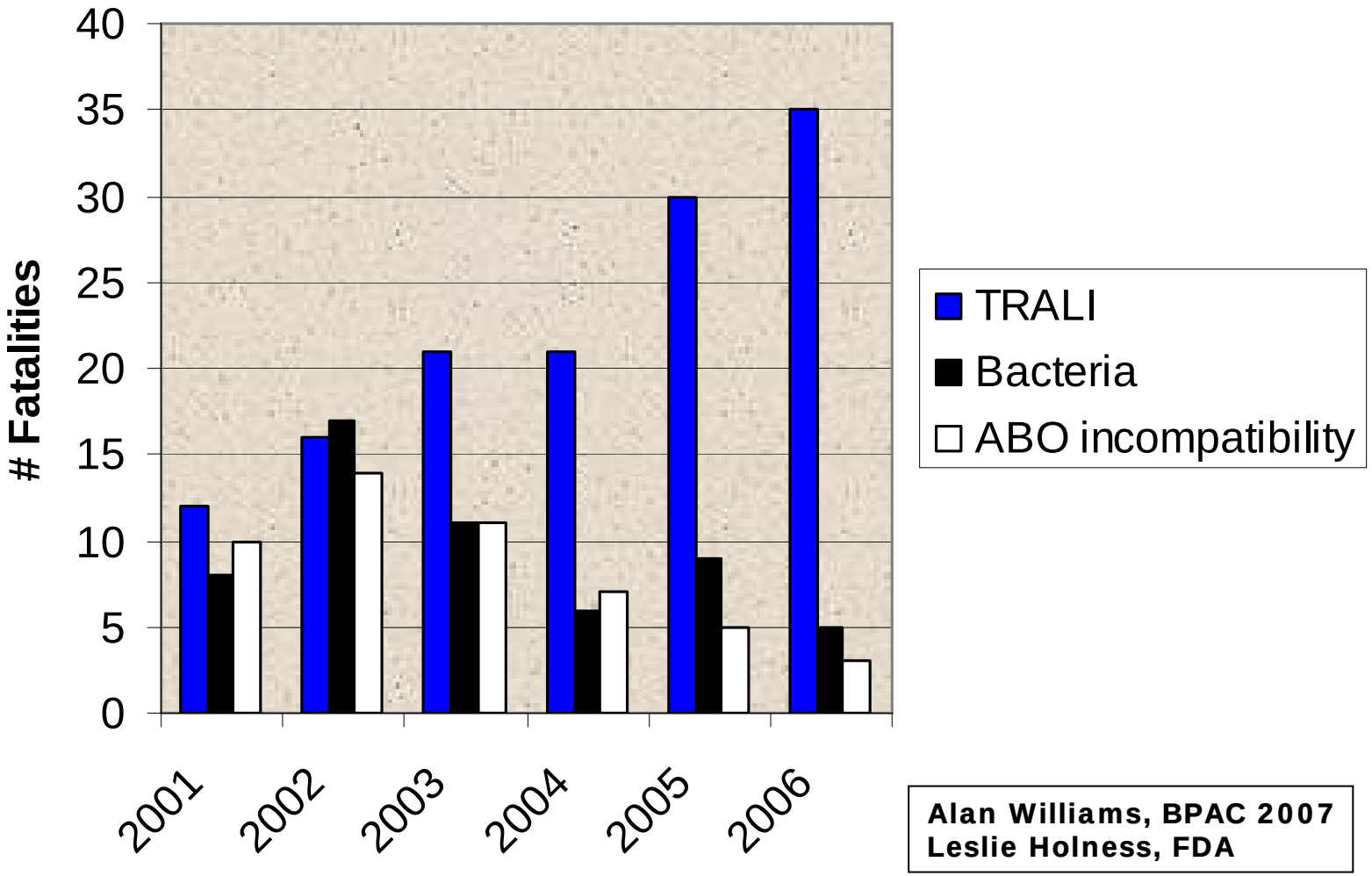
American Red Cross Hemovigilance, 2006



American Red Cross Hemovigilance, 2006



FDA Reported Fatalities (2001-6)



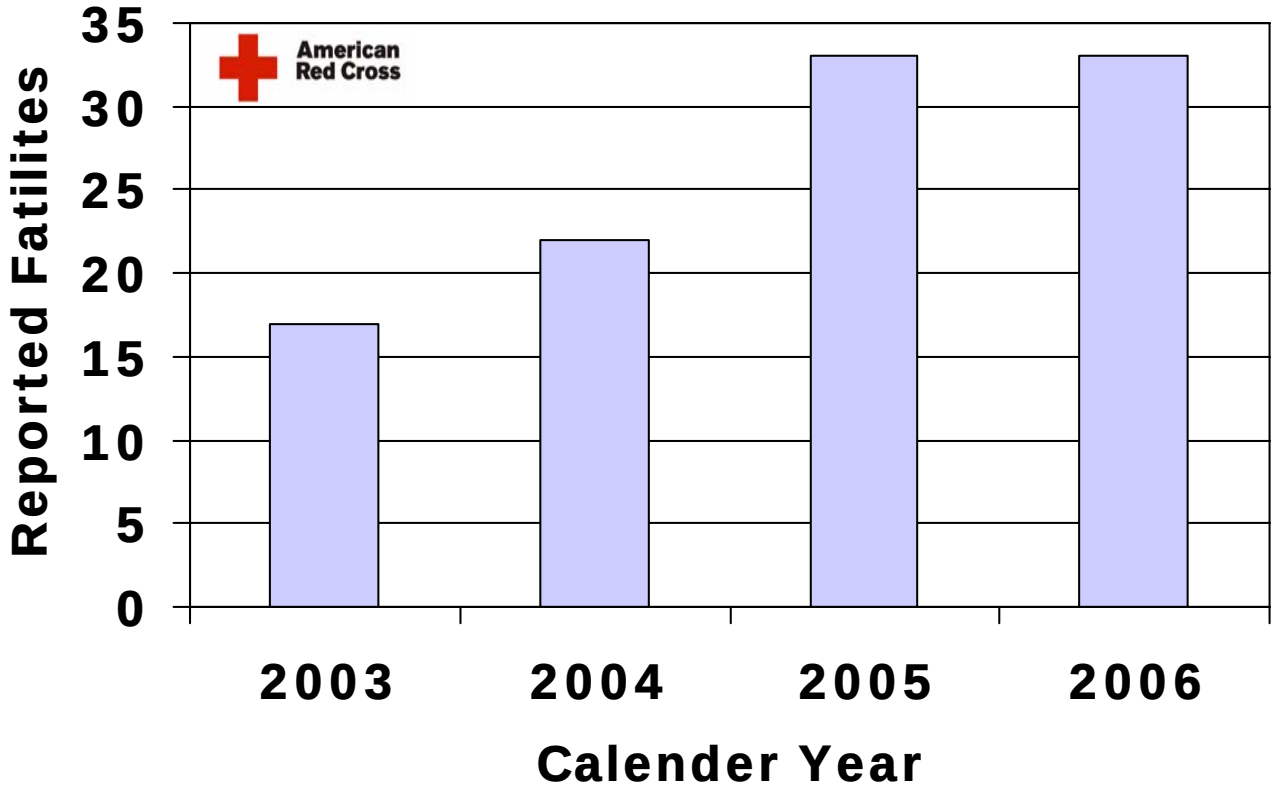
Alan Williams, BPAC 2007
Leslie Holness, FDA

Current Major Risks of Transfusion:

- TRALI & TACO (fluid overload)
- Bacterial contamination
- ABO incompatibility and ID issues (bedside safety)
- Emerging infectious diseases

Transfusion Related Acute Lung Injury

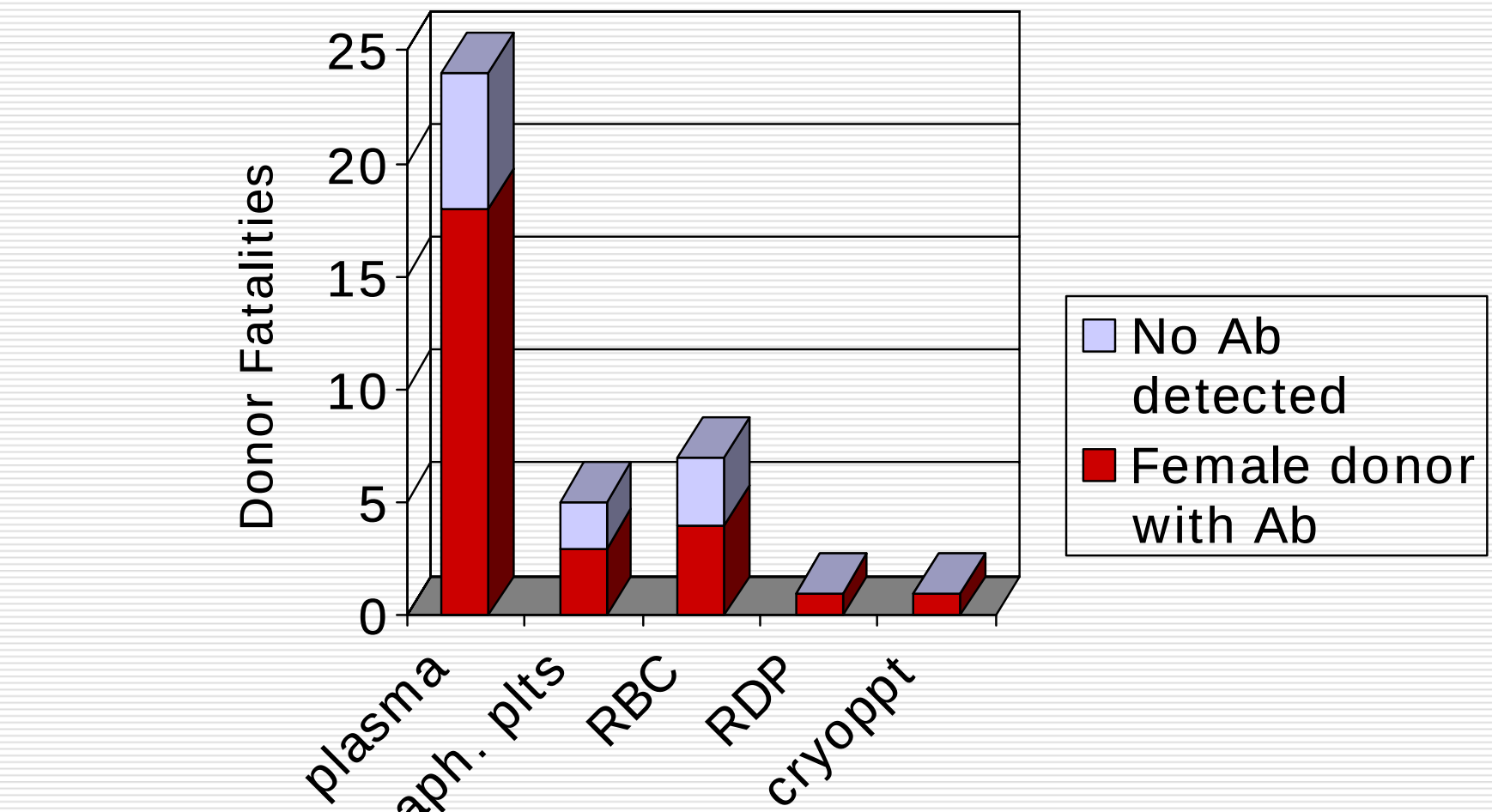
Red Cross Suspected TRALI Fatalities



105 reported Fatalities (2003-2006)

Updated from Eder et al Transfusion 47(4):599-607;2007

Probable TRALI by Implicated Component:



Eder et al Transfusion 47(4):599-607;2007

TRALI and TACO

- Respiratory compromise after transfusion represents the biggest current risk of transfusion
- Current strategies to reduce TRALI only address ~60% of the fatal cases
- There is an urgent need for:
  - A better understanding of cause of TRALI
  - Greater physician awareness of TACO (fluid overload)
  - Evidence based guidelines for transfusion

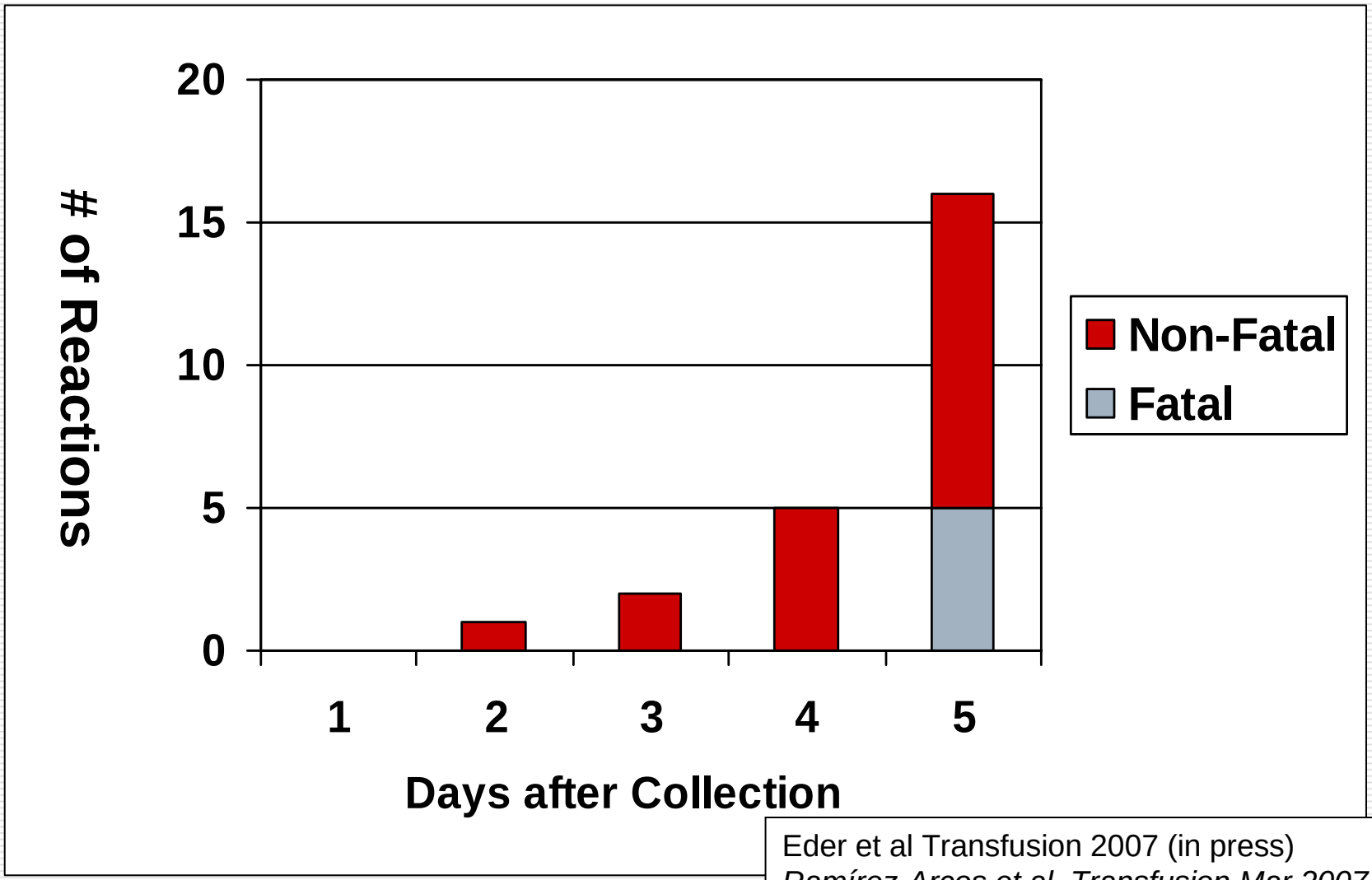
Bacterial Contamination

March 1, 2004 to May 31, 2006
1,004,206 apheresis platelet donations, 1,496,134 components

Result	Number (%)	Rate per 10^5 donations	Risk per donation
Confirmed positive	**186 (30.3)**	**18.5**	**1:5,399**
False positive, total	348 (57.0)	34.7	1:2,886
Sampling contamination	198 (32.4)	19.7	1:5,072
Instrument error	150 (24.5)	14.9	1:6,695
Indeterminate	78 (12.6)	7.8	1:12,874
Total positive donations	612	60.7	1:1,646

Eder et al Transfusion 2007 (in press)

US, German & Canadian Septic Transfusion Reaction Experience, after BacT/ALERT:



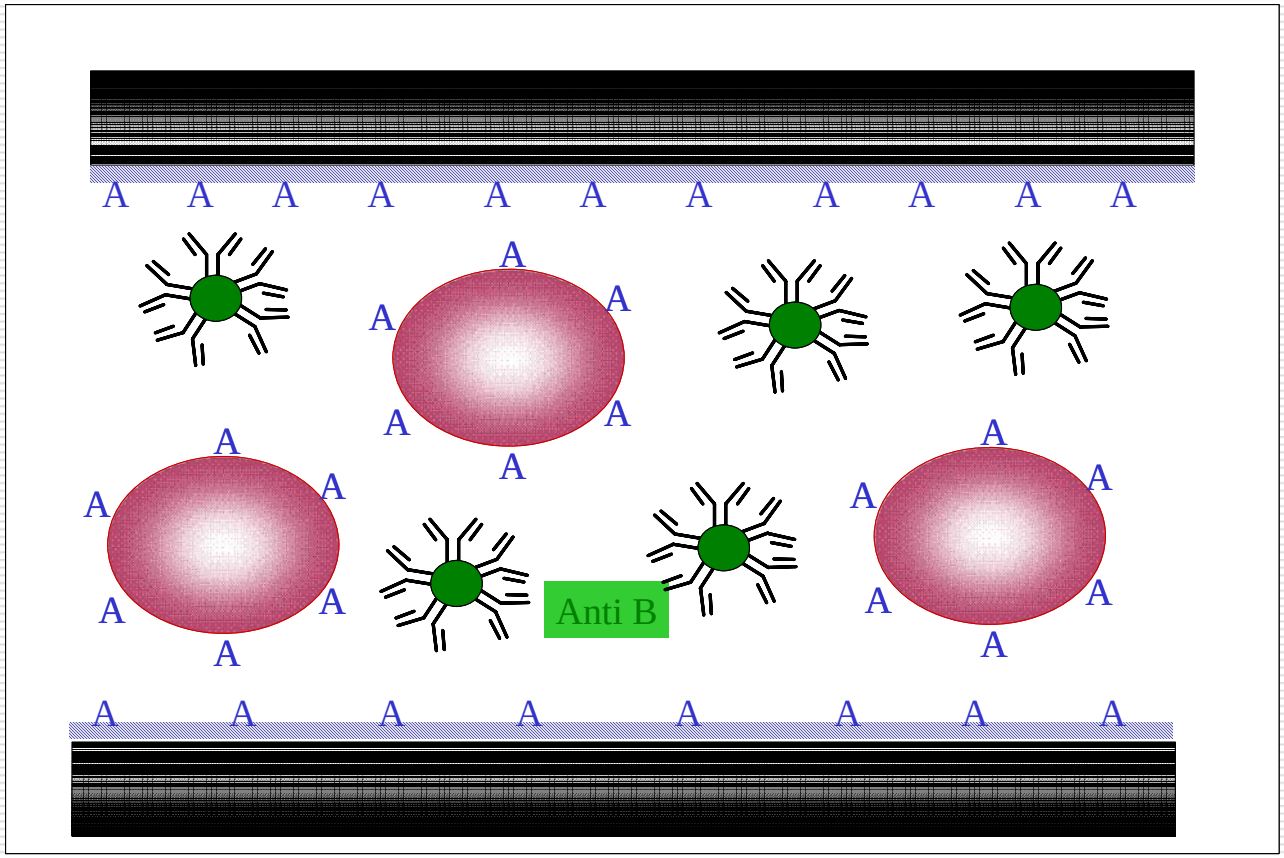
Eder et al Transfusion 2007 (in press)
Ramírez-Arcos et al, Transfusion Mar 2007
Schmidt et al, Vox Sanguinis 2007 (online)

Bacterial Testing

- Whole blood derived platelets continue to be screened with insensitive, unlicensed methodologies
- Culture systems at time of manufacturing cannot guarantee product sterility
- Current systems may fail to detect 30-50% of contaminated products (Benjamin & Wagner, Transfusion 2007, in press)
- Urgent need for:
  - Improved skin decontamination
  - Mandated sample first/diversion strategies
  - Sensitive point of issue testing
  - Pathogen inactivation strategies

ABO incompatibility

- ABO is the major histocompatibility antigen for both transfusion and organ transplantation



Transfusion Errors

TABLE 1. Frequency of erroneous administration of RBCs in New York State, 1990 through 1999

	Number	Frequency
ABO-incompatible	237	1/38,000
ABO-compatible	221	1/41,000
Total†	462	1/19,000
Adjusted total‡	659	1/14,000
Fatal reaction	5	1/1,800,000

Jean Linden et al Transfusion 1999

Parents of dead child sue over liver transplant mistake

Wednesday, March 12, 2003 Posted: 9:15 AM EST (1415 GMT)

DALLAS, Texas (AP) -- The parents of a 17-month-old girl who died last summer after receiving a transplanted liver that didn't match her blood type are suing two Dallas hospitals and three surgeons who were involved.

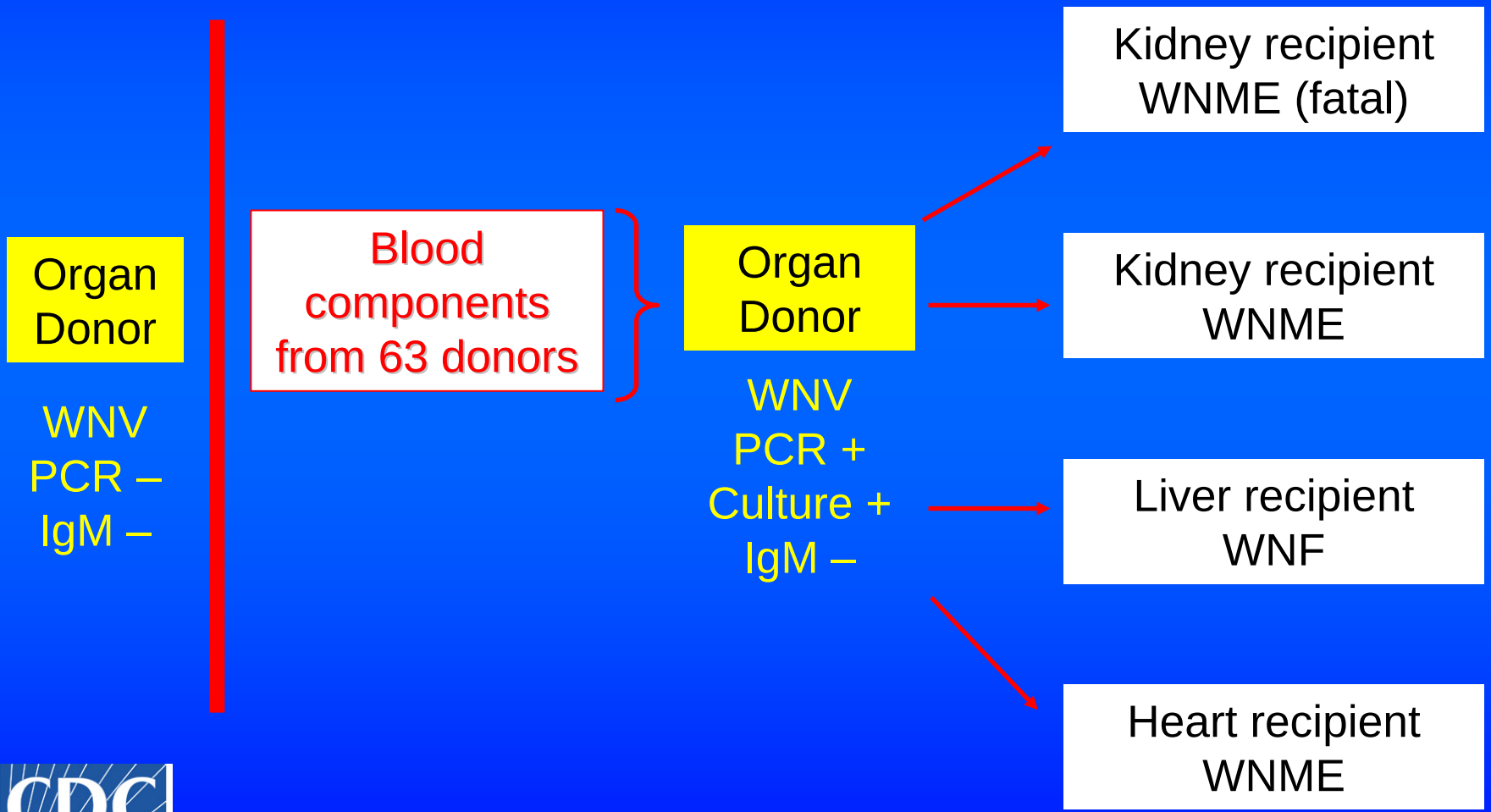
The lawsuit alleges that doctors mistakenly gave XXXXX XXXX a liver transplant from her father instead of from her mother. The mother and child had type O blood; the father is type A.

- Reliable methods to identify and track patients, samples and products are needed to reduce errors in the hospital setting.

Emerging Pathogens:

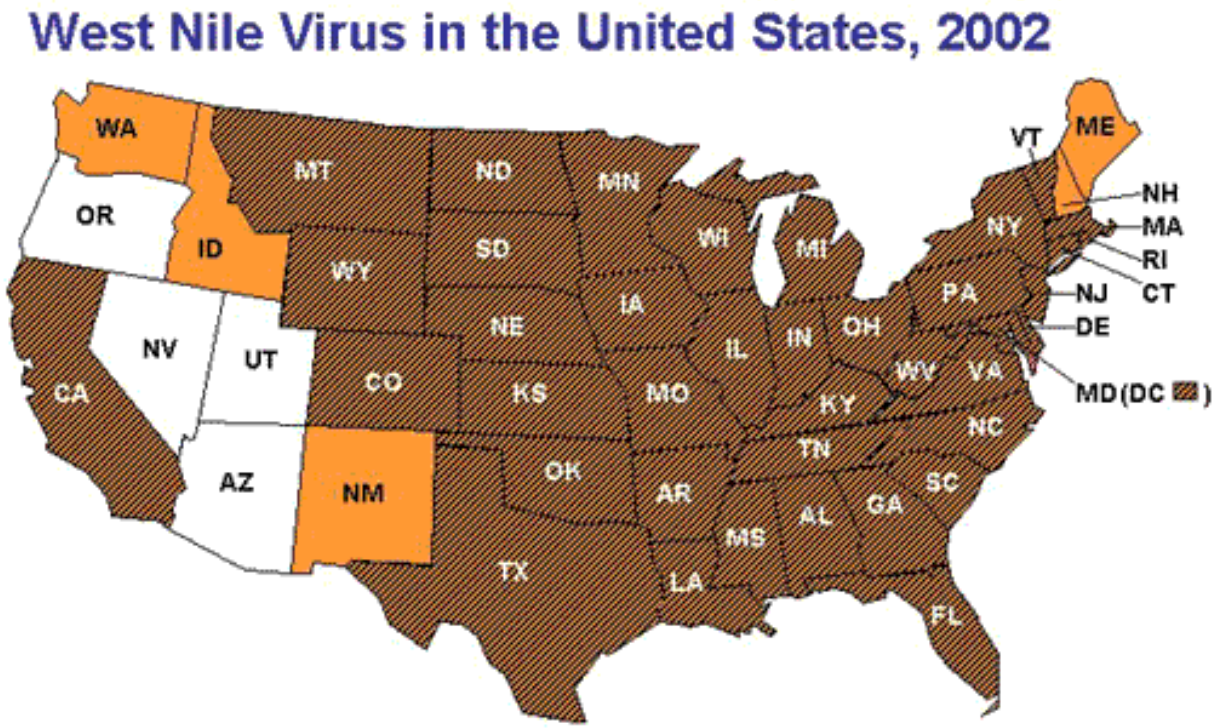
- West Nile virus- paradigm for emerging threats
- Babesiosus
- Dengue Fever
- HHV8
- Chickungunya
- Avian Flu
- SEN-V / TTV
- Chagas in Heart Transplants, CA. MMWR 2007
- Rabies, Dallas, TX MMWR July 9, 2004
- LCMV, Providence, RI NEJM 354:2231, 2006
- and many more….

West Nile Virus Infection in an Organ Donor and Four Transplant Recipients August 2002



CDC
Centers for Disease Control and Prevention

The WNV Paradigm:



- 400,000 Americans infected
- 23 confirmed transfusion-transmitted cases
- ~200 transfusion-transmitted cases estimated by the CDC
- Implemented WNV NAT, prevented ~700 infections in 2003

The WNV Paradigm:

- The Transfusion Community is reactive to threats
- Many patients are infected before a technological solution becomes available
- The technological solution is often incomplete.

"A total of 23 confirmed WNV transfusion-transmitted cases were reported in 2002, before screening was implemented; six probable or confirmed cases were detected in 2003 after MP-NAT screening was initiated, one was detected in 2004, and none were detected in 2005 (*7*).

In 2006, two immunosuppressed patients had onset of West Nile neuroinvasive disease (WNND) after receiving blood products from a single infected donor despite a negative MP-NAT result at the time of donation."
MMWR Feb 2, 2007

Conclusions:

- Blood is “Low Risk” but under constant threat.
- We can measure yesterdays risk, but can only determine today’s risk retrospectively.
- We need a global view of safety.
  - Products — FDA
  - Process — AABB, CAP
  - Bedside safety — JCAHO
- Mandated and funded hemovigilance program
- Evidence-based transfusion guidelines
- Bedside IT solutions for tracking patients, samples and products
- Proactive pathogen avoidance strategies