BIOVIGILANCE IN THE UNITED STATES:

Regulatory Perspective

Alan E. Williams, Ph.D.
Office of Blood Research and Review
Center for Biologics Evaluation and Research
US Food and Drug Administration

15th International Haemovigilance Seminar
Brussels, Belgium
January 20-22, 2013

HHS Biovigilance Gap report: Key Deficiencies of Biovigilance in the United States

http://www.hhs.gov/ash/bloodsafety/biovigilance/index.html

- Gaps Identified…….
  - Patchwork and sometimes fragmented system of adverse event reporting
  - Likely under-reporting of transfusion adverse events
  - Challenges with FDA-required reporting
  - Need for accurate recipient denominator data, precise definitions, and training

HHS Biovigilance Gap report: Key Deficiencies of Biovigilance in the United States

http://www.hhs.gov/ash/bloodsafety/biovigilance/index.html

- Gaps Identified…….
  - No national surveillance of donor serious adverse events other than fatalities
  - Need for accurate donor denominator data, precise definitions, and training
  - Need for accurate tracking of all donor infectious disease data
  - Need for timely analysis of reported data

The Deficiencies in US Biovigilance have Explanations

- There have been very strong programs of investigator-initiated and federally-funded epidemiologic research (*we've done it a little differently*)
- Absence of national blood system
- Transfusion Services and Blood Establishments under tight financial restraints (very few TSOs)
- Barriers to data-sharing
- Lack of targeted investment - especially for "real-time" data analysis/interpretation
- Legal and Regulatory liability

Biovigilance: Regulatory Perspective

- Real-time sentinel signal detection and amplification
- Increased power for surveillance (Severe TRALI vs TRALI fatalities)
- Ability to conduct specific, rapid follow-up to identify and act on unsafe products/practices
- Denominator data to support analysis
- Harmonization of data/definitions/reporting mechanisms
- Universal required reporting from regulated manufacturers, least-burdensome as possible

Biovigilance: Regulatory Perspective

- Why require reporting of severe adverse events?

FDA Blood Safety Required Reporting

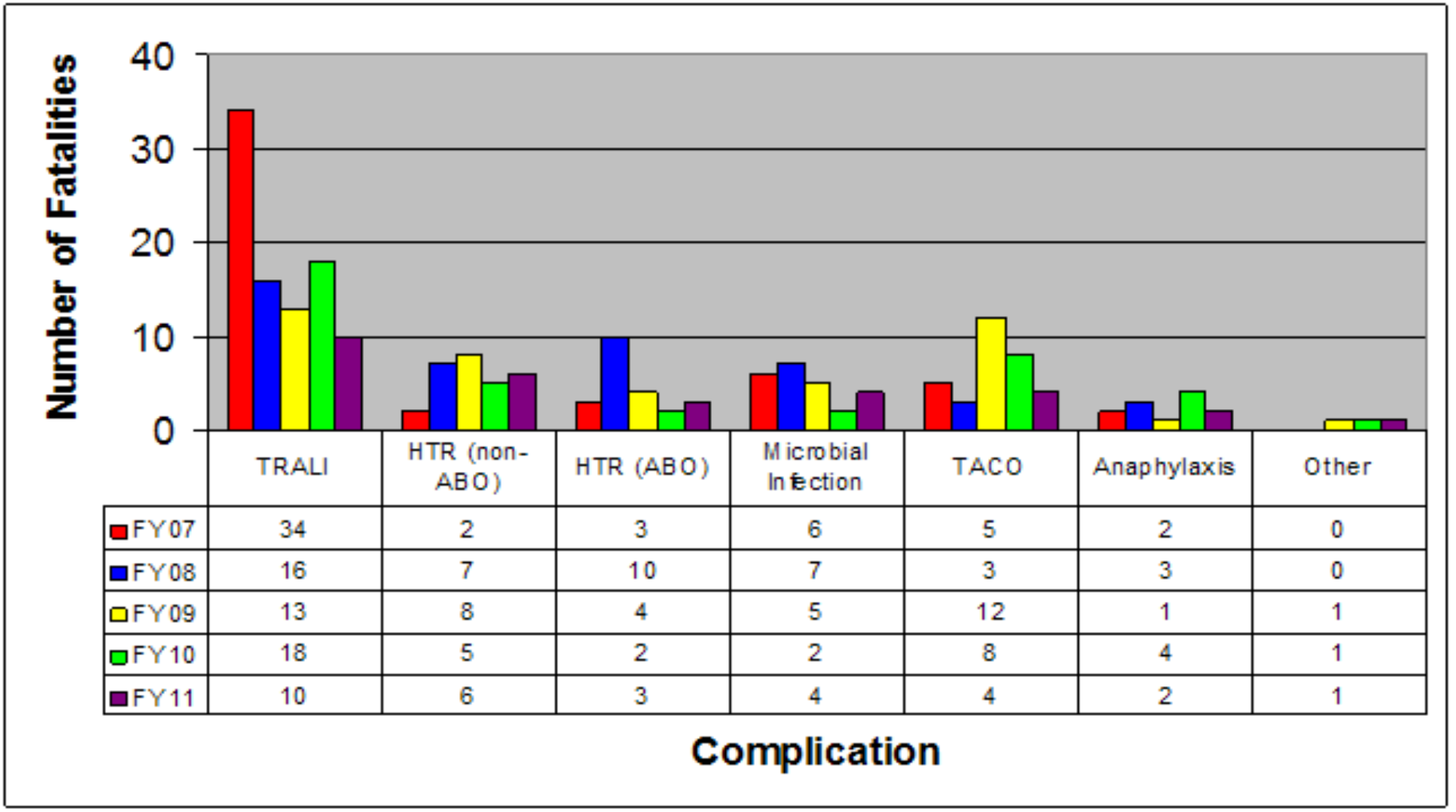
Product deficiencies

- Biological product deviation (BPD) reports
- Medical device reports

Fatalities (donors & recipients)

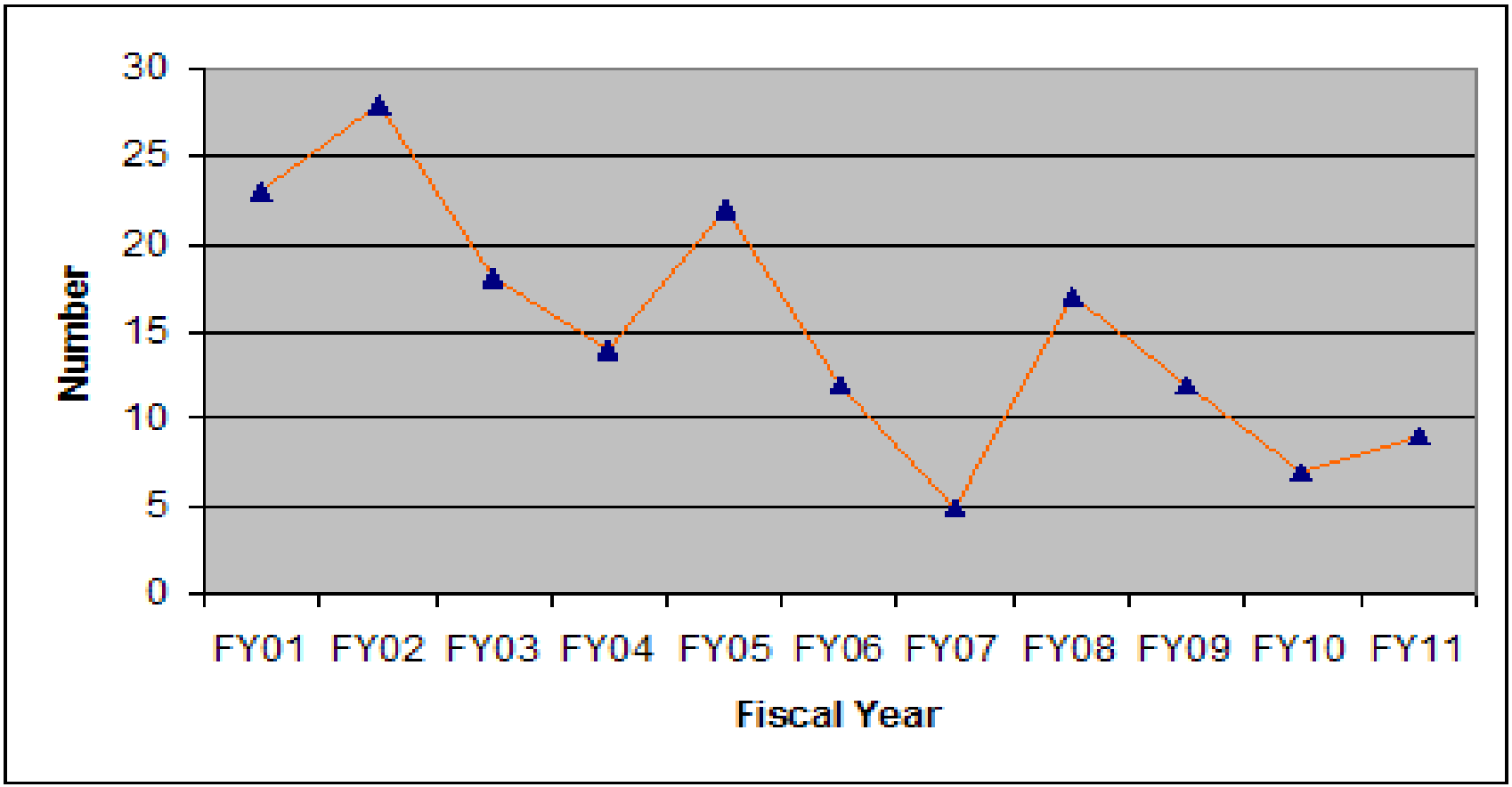
(Severe Adverse Events – Pending)

Transfusion-Related Fatalities by Complication FY2007 through FY2011

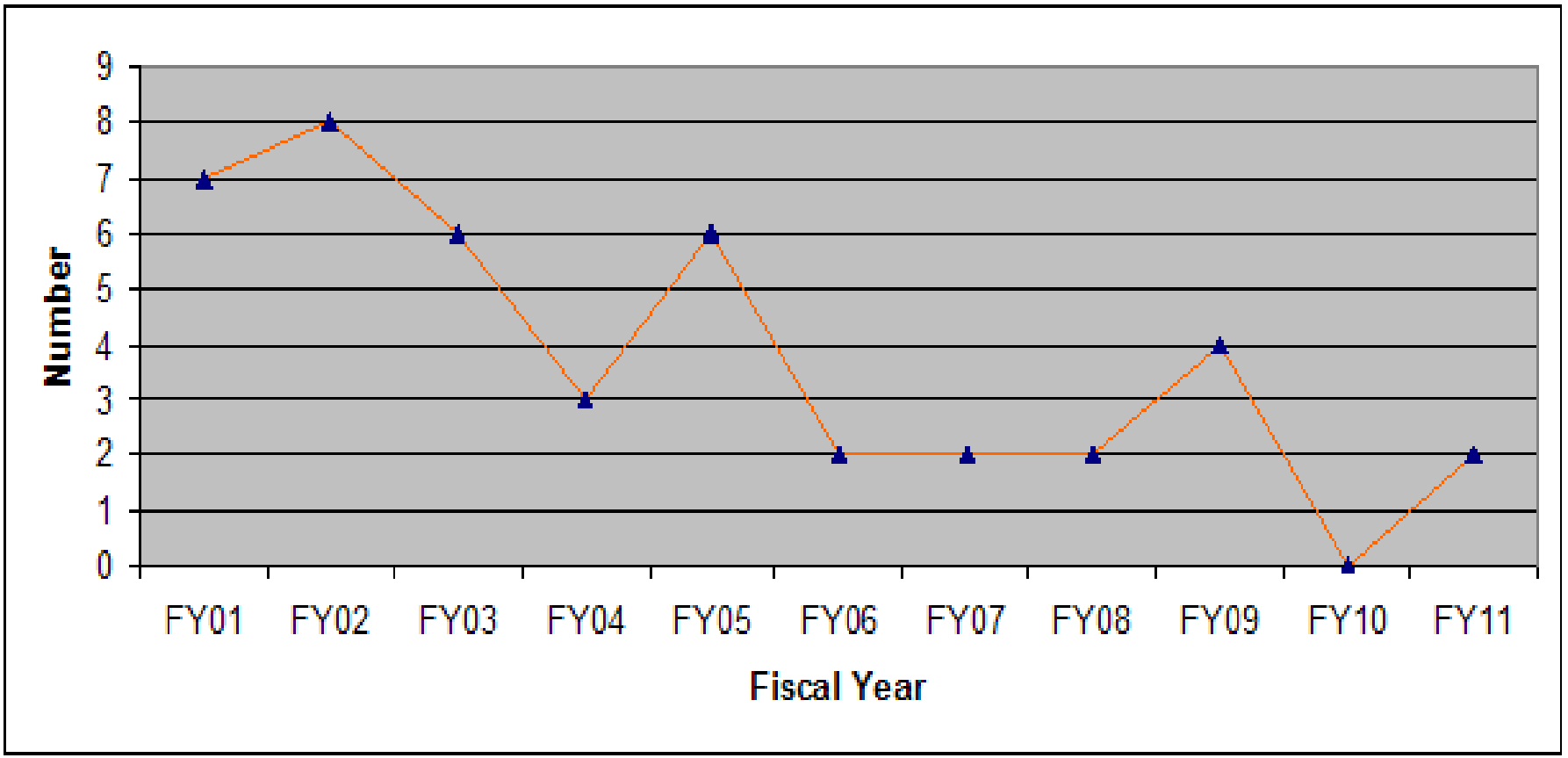


	TRALI	HTR (non-ABO)	HTR (ABO)	Microbial Infection	TACO	Anaphylaxis	Other
FY07	34	2	3	6	5	2	0
FY08	16	7	10	7	3	3	0
FY09	13	8	4	5	12	1	1
FY10	18	5	2	2	8	4	1
FY11	10	6	3	4	4	2	1

Hemolytic Transfusion Reaction Deaths FY2001 - 11



Bacterial Infection Fatalities (Apheresis Platelets) FY2001 - 11



Data collection form for required reporting of FDA-approved pharmaceuticals

Currently supports voluntary reporting to FDA for Blood Donors and Recipients

Voluntary FDA MEDWATCH Reports for Blood and Blood Components - Calendar Year 2007

(Compare to 60,000+ AE reports in 2007 NBCUS Report)

Products	US	Foreign	Total
Fresh frozen plasma	4	1	5
Platelets	4	3	7
Red blood cells	14	1	15
Blood derivative	9	7	16
Whole blood + other components	3	3	6

- Safety Reporting Requirements for Human Drug and Biological Products – proposed rule, March 2003.

  Investigational New Drug Safety Reporting Requirements for Human Drug and Biological Products……..September 29, 2010

  Final Rule for Post-Marketing Safety Reporting Requirements –Pending (includes blood and blood (components)

Integration of Voluntary and Mandatory Hemovigilance Reporting

- Goal is to establish a comprehensive system for simultaneous end-user reporting in support of multiple applications

- CDC NHSN System
  - Voluntary, functionally anonymous, mostly surveillance design

- FDA Safety reporting rule (under development)
  - Identity linked (to permit follow-up)
  - Combines sentinel with surveillance reporting
  - Some serious AEs reported/investigated in real time (e.g. fatalities, and unexpected serious adverse events)

Development of a nationwide electronic safety monitoring system

Under FDAAA, section 905, FDA was required to link to disparate sources of safety data in order to access 25 million patient records by 2010 and 100 million by 2012

Enable FDA to partner with existing data owners (e.g., insurance companies with large claims databases, owners of electronic health records)

Strengthens FDA's ability to monitor postmarket performance of a product

HHS/AABB Donor Hemovigilance

Focus on Donor Adverse Reactions

National Standards for Donor Reaction Data Collection

- Data Elements and Definitions
- Reactions and Reaction Categorization

Systemic, Standard Mechanism to Calculate Donor Reaction Rates

- Trends at Facility, Organization, Region and Nation Levels
- Comparison With Peers, Region and Nation

Points to consider

Certain elements of hemovigilance (but not biovigilance) have been very strong in the US for the past 25 years, but have not been not well-coordinated nationally

Examples of Hemovigilance-Related Elements Operational in the United States:

Epidemiologic research

Major blood organizations and certifying bodies (donors)

Individual and organized hospital entities and certifying bodies (recipients)

Exceptionally Strong Hemovigilance-Related Research Has Been Operational in the United States

Recent examples…..

Federal Agency Partnerships

- NHLBI REDS I, REDS II, REDS III
- NHLBI Repositories
- National Blood Collection and Utilization Survey (NBCUS)

Investigator-Initiated Studies

- Donor reactions

Summary

- Biovigilance in US does exist, but national coordination has been sub-optimal
  - Each PHS Agency and numerous private entities have created systems of data collection to meet their specific mission and objectives. There is non-complementary overlap (e.g. same design with different definitions)

Summary (cont.)

Improvements are on the horizon

- Broad interest in a centralized data entry portal that can be accessed by multiple stakeholders

- Required reporting of a subset of donation and transfusion outcomes may be necessary to obtain representative data and support follow-up investigations

For More Information

Biovigilance Gap Report

http://www.hhs.gov/ash/bloodsafety/biovigilance/index.html

FDA Mini-Sentinel - http://mini-sentinel.org/about_us/

FDA Fatality Reporting - http://www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/ReportaProblem/TransfusionDonNational

For More Information (cont.)

National Blood Collection and Utilization Survey

http://www.aabb.org/programs/biovigilance/nbcus

FDA MedWatch

http://www.fda.gov/Safety/MedWatch

Donor HART

http://www.aabb.org/programs/biovigilance/us/components/donor