

# **Update on Biovigilance in the US:**

## **Recipient Hemovigilance Organ/Tissue Vigilance**

### **Progress...Slow, But Steady**

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**International Hemovigilance Seminar**

**Brussels, Belgium**

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# Biovigilance and Hemovigilance – what does it mean, and who's responsibility is it in the USA?

The Department of Health and Human Services (HHS) has defined “biovigilance” as a comprehensive and integrated national patient safety program to collect, analyze, and report on the outcomes of collection and transfusion/transplantation of blood components and derivatives, cells, tissues, and organs.

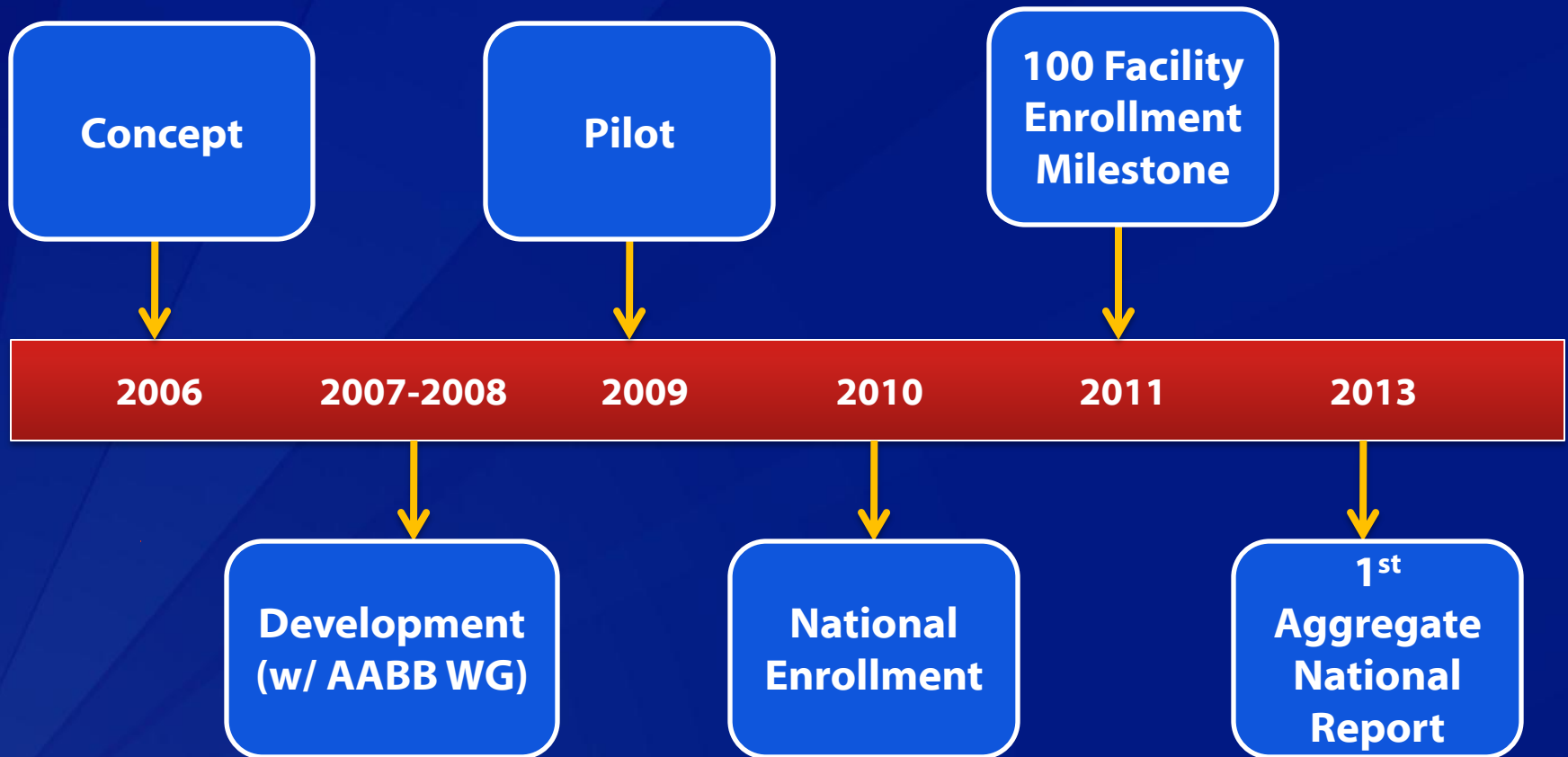
The Department of HHS includes:

- Food and Drug Administration (Regulatory for Blood/Tissue)
- Health Services and Resources Administration (Regulatory for Organs)
- National Institutes for Health (Research)
- Centers for Medicare and Medicaid Services (Reimbursement)
- **Centers for Disease Control and Prevention (SURVEILLANCE)**

# **Transfusion reaction reporting: recipient hemovigilance in the USA**

- ❑ Hospital transfusion services and blood centers each have a regulatory burden**
- ❑ FDA – current regulations require only serious reactions, including fatalities, be reported (likely represents a small proportion of what occurs annually)**
- ❑ National Blood Collection & Utilization Survey estimates 60,000+ transfusion reactions annually**
- ❑ New public health surveillance has been developed to fill gap, with CDC as US government agency in lead**

# Timeline – 5 years of USA Recipient Hemovigilance





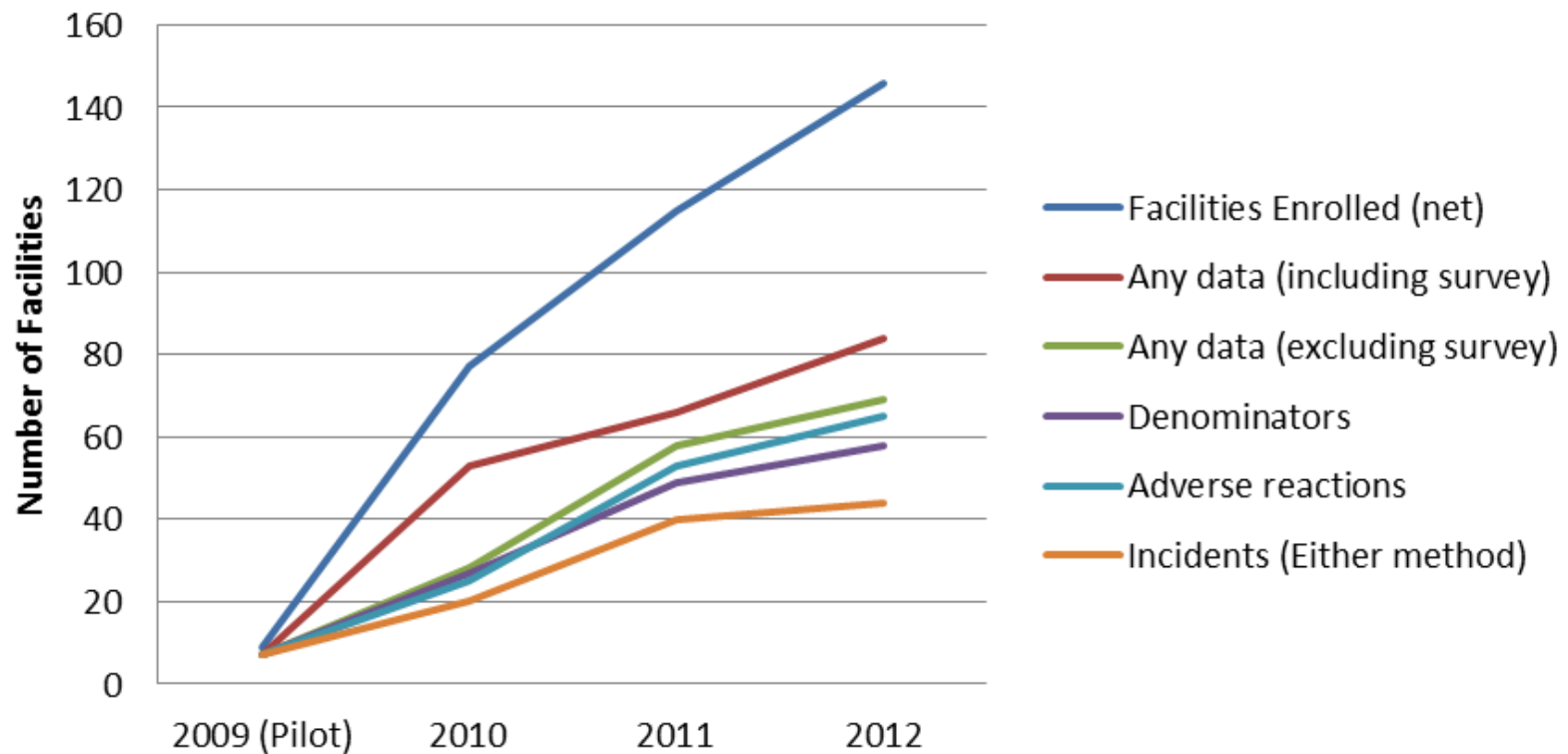
The National Healthcare Safety Network (NHSN) is a secure, internet-based system that integrates patient and healthcare personnel safety surveillance managed by the Division of Healthcare Quality Promotion (DHQP) at CDC.

# **Why Use NRSN as a hemovigilance platform?**

- ❑ Provides standard definitions, protocols and methodology**
  - Adverse reactions
  - Process incidents
- ❑ Not just a reporting tool, comparative rates used for performance improvement**
- ❑ Useful analysis tools are included**
- ❑ CDC provides training and user support**
- ❑ Confidentiality**
- ❑ Ability to share data with other entities (using the group function)**

# Participation is Increasing ...but quality data incoming more slowly

## NHSN HV Module Participation Growth



# Blood Products Transfused, 2010-2012 (approximate estimates)

	<b>2010</b>	<b>2011</b>	<b>2012</b>	<b>Total</b>
	n=27	n=49	n=58	n=69
<b>Red Blood Cells</b>	57%	59%	59%	---
<b>Platelets</b>	20%	16%	17%	---
<b>Plasma</b>	18%	20%	18%	---
<b>Cryoprecipitate</b>	5%	5%	6%	---
<b>Total</b>	430,000	693,000	806,000	1,929,000

## Percentage of US Transfusion Volume Under Surveillance\*

2.0%	3.2%	3.7%
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\*Compared to 2009 NBCUS: National Estimate of US Hospital Transfusions

*Unpublished data.*



# Adverse Reactions, 2010-2012

## Approximate Estimates

	<b>2010</b> n=20	<b>2011</b> n=49	<b>2012</b> n=63	<b>Total</b> n=70
<b>Allergic</b>	54%	48%	43%	---
<b>Febrile, non-hemolytic</b>	32%	34%	38%	---
<b>TACO</b>	3%	4%	4%	---
<b>TRALI</b>	1%	1%	<1%	---
<b>Dyspnea</b>	1%	1%	2%	---
<b>Hypotensive</b>	1%	3%	3%	---
<b>Delayed Serologic</b>	4%	6%	7%	---
<b>Delayed Hemolytic</b>	2%	2%	1%	---
<b>Acute Hemolytic</b>	1%	<1%	1%	---
<b>Infection</b>	1%	<1%	<1%	---
<b>Total</b>	850	1,680	2,500	<b>5,030</b>

Cases graded by definition criteria, severity, and imputability.

*Unpublished data.*

# Summary Incidents Reported, 2010-2012

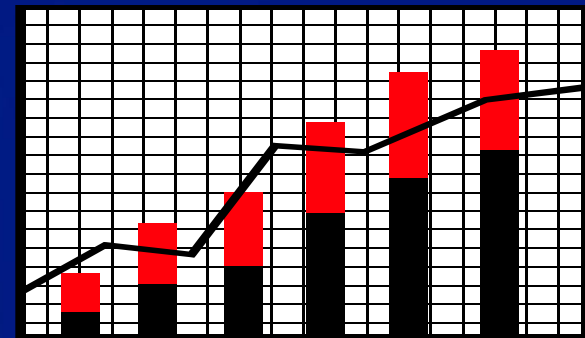
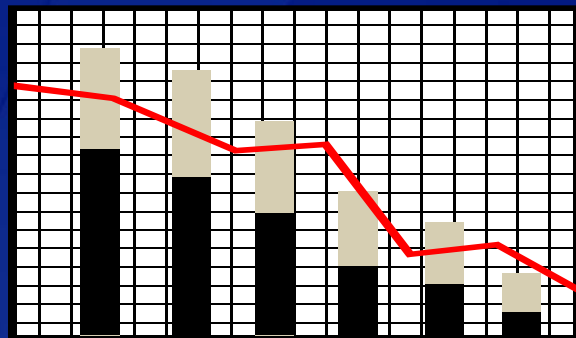
## Approximate Estimates

	2010	2011	2012	Total	Adverse Reactions
<b>Product Check-In</b>	1%	2%	1%	---	1
<b>Product/Test Request</b>	2%	7%	10%	---	2
<b>Sample Collection</b>	36%	33%	37%	---	5
<b>Sample Handling</b>	42%	29%	19%	---	12
<b>Sample Receipt</b>	<1%	1%	3%	---	1
<b>Sample Testing</b>	2%	5%	4%	---	4
<b>Product Storage</b>	1%	2%	1%	---	0
<b>Available for Issue</b>	<1%	1%	<1%	---	0
<b>Product Selection</b>	1%	1%	<1%	---	1
<b>Product Manipulation</b>	1%	2%	1%	---	0
<b>Pick-Up Request</b>	3%	3%	2%	---	1
<b>Product Issue</b>	1%	2%	1%	---	1
<b>Product Admin</b>	10%	13%	16%	---	11
<b>Miscellaneous</b>	1%	2%	4%	---	7
<b>Total</b>	6,000	10,120	16,580	<b>32,700</b>	46

*Unpublished data.*

# Hemovigilance Module Data Analysis

- Facilities can analyze their data as soon as it is entered
- Benchmarking capabilities are planned, but will not be available with rates until adequate data have been entered
- CDC plans to publish a Public Health Report with aggregate national data for 2010-2012 (late 2013)



# US Hemovigilance: Issues for Discussion

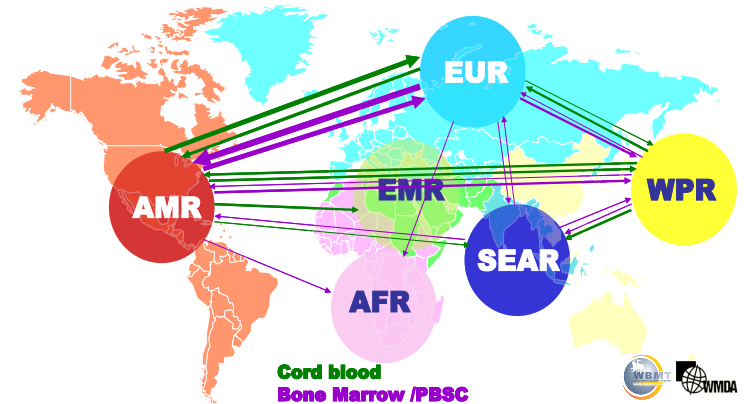
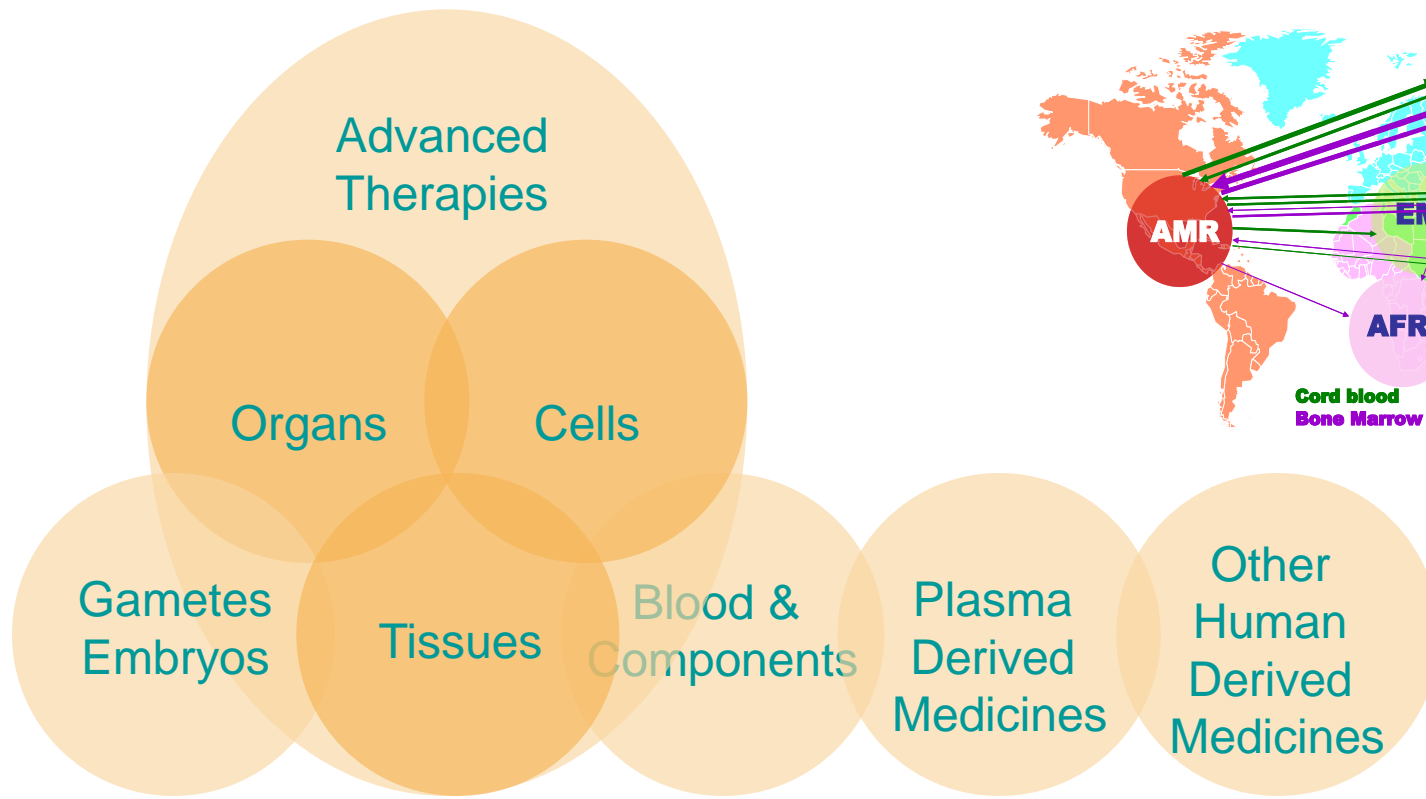
- Participation
  - Create incentives for participation
  - Reduce burden of reporting\*
  - Make data more usable for facilities (e.g., benchmarking)
- Interoperability
  - Harmonize definitions
  - Make data more easily entered for reporting
  - Improve understanding of group function to share data

\*protocol as of Jan 1, 2013 only requires serious allergic reaction reporting, and incidents associated with adverse reactions

# Hemovigilance Summary

- ❑ **NHSN Hemovigilance Module enrollment is growing, although data reporting is inconsistent (or nonexistent) for many facilities**
- ❑ **Simplifications have been introduced to the surveillance protocol, aimed at improving participation and data quality**
- ❑ **Partnering needed**
  - Facilitating reporting to multiple entities on adverse events in transfusion (e.g., NHSN, regulatory entities, blood centers)
  - Harmonize definitions, nationally and internationally
  - Compare data across facilities and between national hemovigilance systems when rates are available

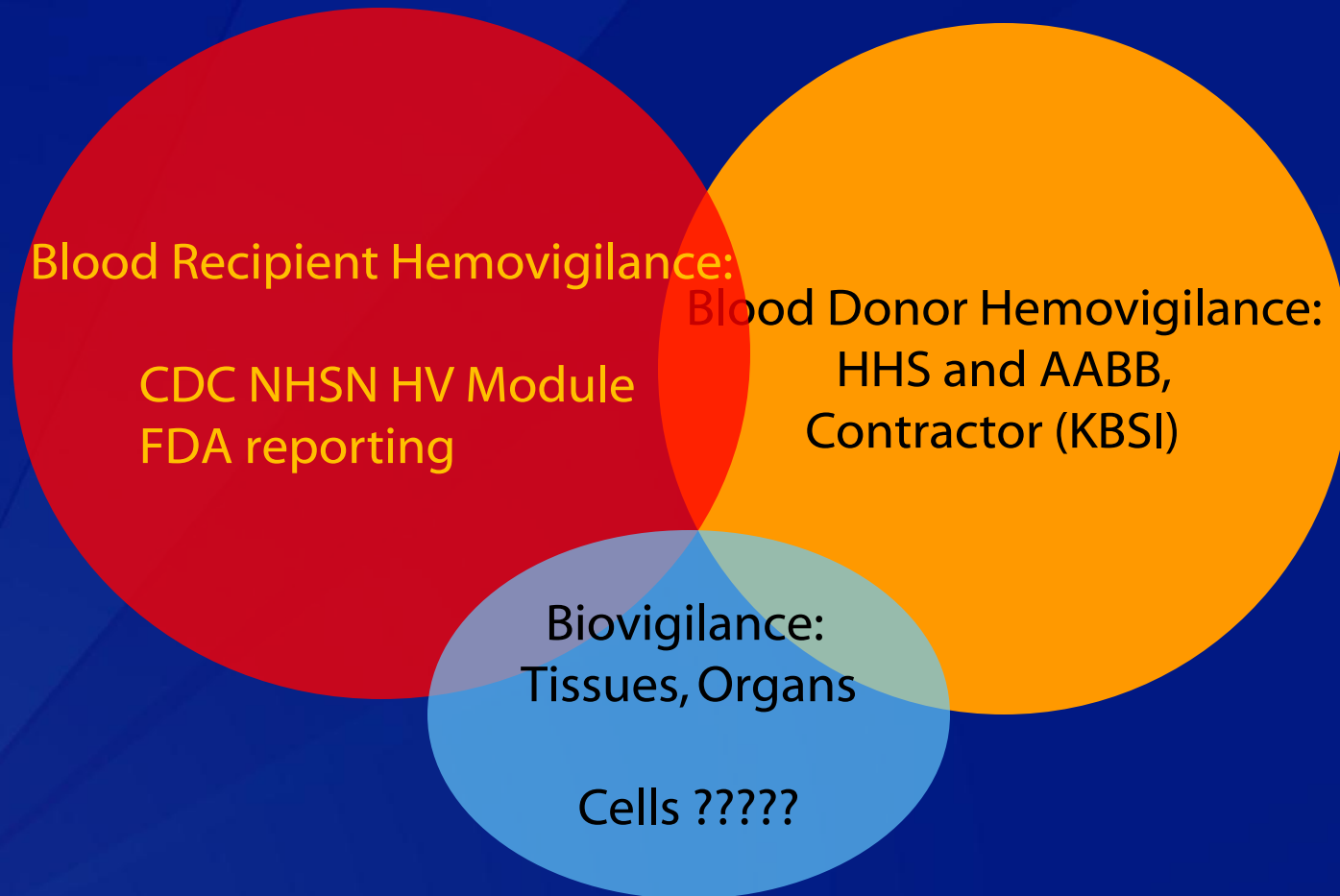
# Medical Products of Human Origin - MPOHO -



# The current state of transplantation: technological advances and challenges

- >2,000,000 tissue allografts distributed annually
  - tissues (musculoskeletal, skin, heart valves, vascular tissues constitute majority of allografts)
  - ~50,000 corneas
- >25,000 solid organs transplanted
- “Composite” allografts are now possible
  - entire face, hand, or foot
  - nerve, vessel complexes
  - defined as organs

# *USA Biovigilance: A work in progress*



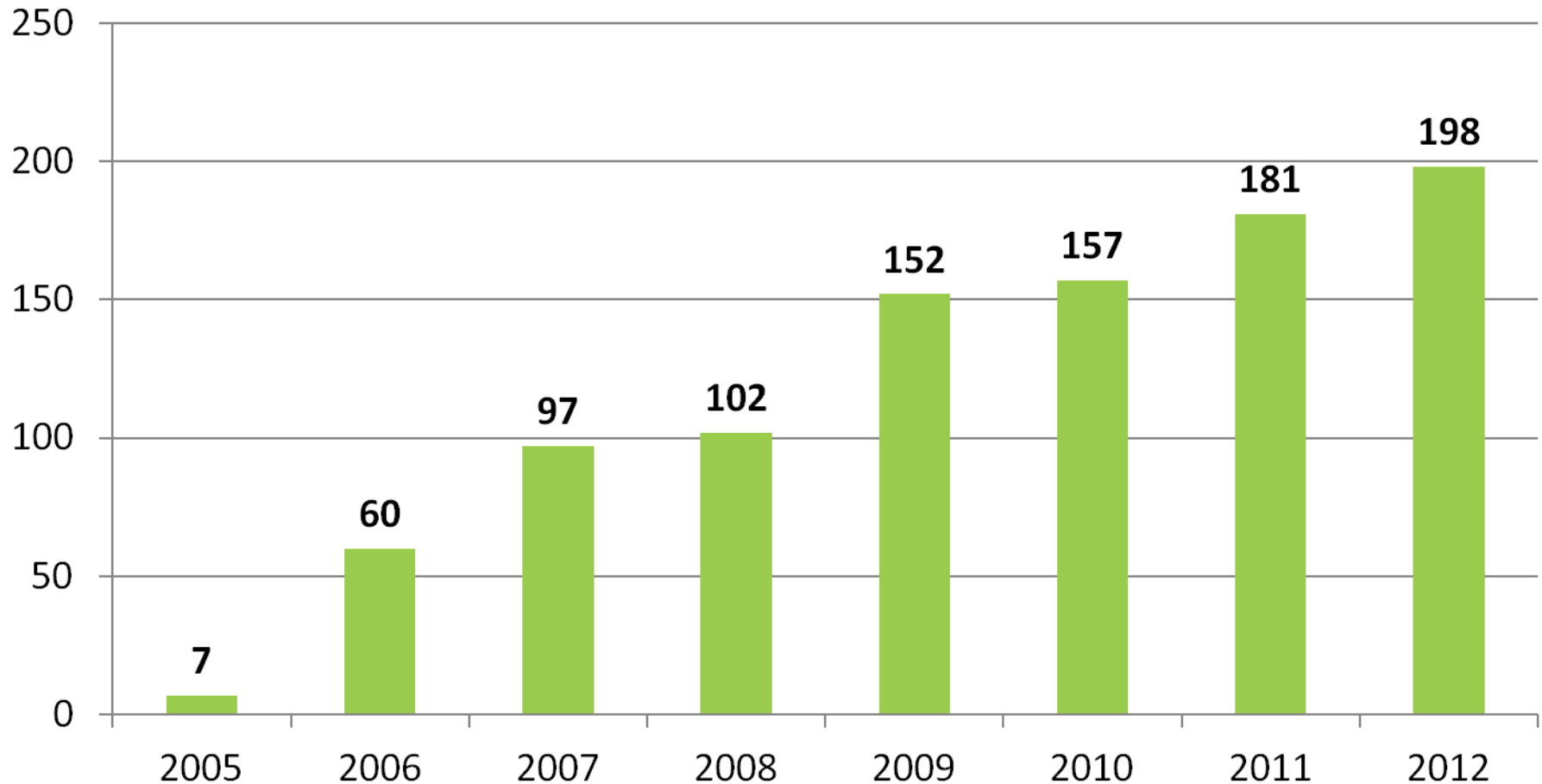


# *Biovigilance efforts in the U.S.*

## *Organ/Tissue Transplantation*

- Example Initiative: Tissue and Organ Donor Epidemiology Study (TODES)
  - Collect information on infectious disease screening laboratory test results, obtained from potential organ and tissue donors in a consistent and standardized manner
- HRSA regulates solid organs (through contract with UNOS/OPTN)
  - Disease Transmission Advisory Committee (DTAC) of UNOS/OPTN (for organs)
  - DTAC examines potential disease transmission cases in an effort to confirm organ transplant transmission cases
- FDA regulates tissues (HCT/Ps)
  - Reporting is required from tissue banks but not by clinicians, and for a narrow spectrum of reactions
  - Regulation only applies to tissue banks, and not to recovery entities or to healthcare facilities
  - There is an FDA Tissue Safety Team, but not a similar categorization effort for possible transmission cases as with organ transplantation

# Potential Donor Derived Transmission Events Reviewed by DTAC, 2005-2012



# Notable Organ Transplant-Transmitted Infections Investigated by Public Health Authorities, 1985-2012

- HIV, 1985, Hepatitis C (HCV), 2000
- Chagas Disease, 2001
- West Nile Virus (WNV), GA 2002
- Lymphocytic Choriomeningitis Virus (LCMV), WI 2003
- Rabies, 2004
- LCMV, MA/RI 2005
- WNV, NY/PA 2005
- Chagas, CA 2006
- HIV/HCV, IL 2007
- Tuberculosis (TB), OK/TX 2007
- LCMV, MA 2008
- Babesiosis, WI/MN, 2008
- WNV, 2008
- Zygomycosis, Coccidioidomycosis, TB, 2009
- *Balamuthia mandrillaris*, HIV in a living donor, 2010
- HCV organ/tissue 2011
- Microsporidiosis 2012

Estimated risk of unintended disease transmission – 1% of recipients (includes malignancies)

# Risks of Tissue Use: Not well defined

- Risk of disease transmission not well quantified
- Processing can mitigate risk, but techniques are not standardized and efficacy not well-defined
- Investigations of tissue-transmitted infection
  - Hepatitis C virus (most recent)
  - Group A Streptococcus
  - *Clostridium sordellii*
  - Clostridial endophthalmitis
  - *Chryseobacterium meningosepticum*  
(nka *Elizabethkingia meningoseptica*)
  - *Candida albicans*
  - Improper donor screening or tissue processing  
(e.g., BTS, DRS recalls)

Estimated risk of transmission –  
UNKNOWN



TRANSPLANTATION TRANSMISSION SENTINEL NETWORK



Welcome to the TTSN Web site

Please login to get started

#### SECURE LOGIN

Username

Password

Login

This section is password-protected for secure data entry by authorized users. Contact your site administrator for information on becoming an authorized user of this system or click the following link to [create a new account](#).

#### About TTSN

The Transplantation Transmission Sentinel Network (TTSN) was established by a CDC cooperative agreement in September 2005. The United Network for Organ Sharing (UNOS), in an alliance with Association of Organ Procurement Organizations (AOPO); American Association of Tissue Banks (AATB); Eye Bank Association of America (EBAA); American Society of Transplantation (AST); and American Society of Transplant Surgeons (ASTS), was awarded the cooperative agreement. The purpose of the Sentinel Network is to establish a network for detecting, communicating, and tracking allograft donors to recipients.

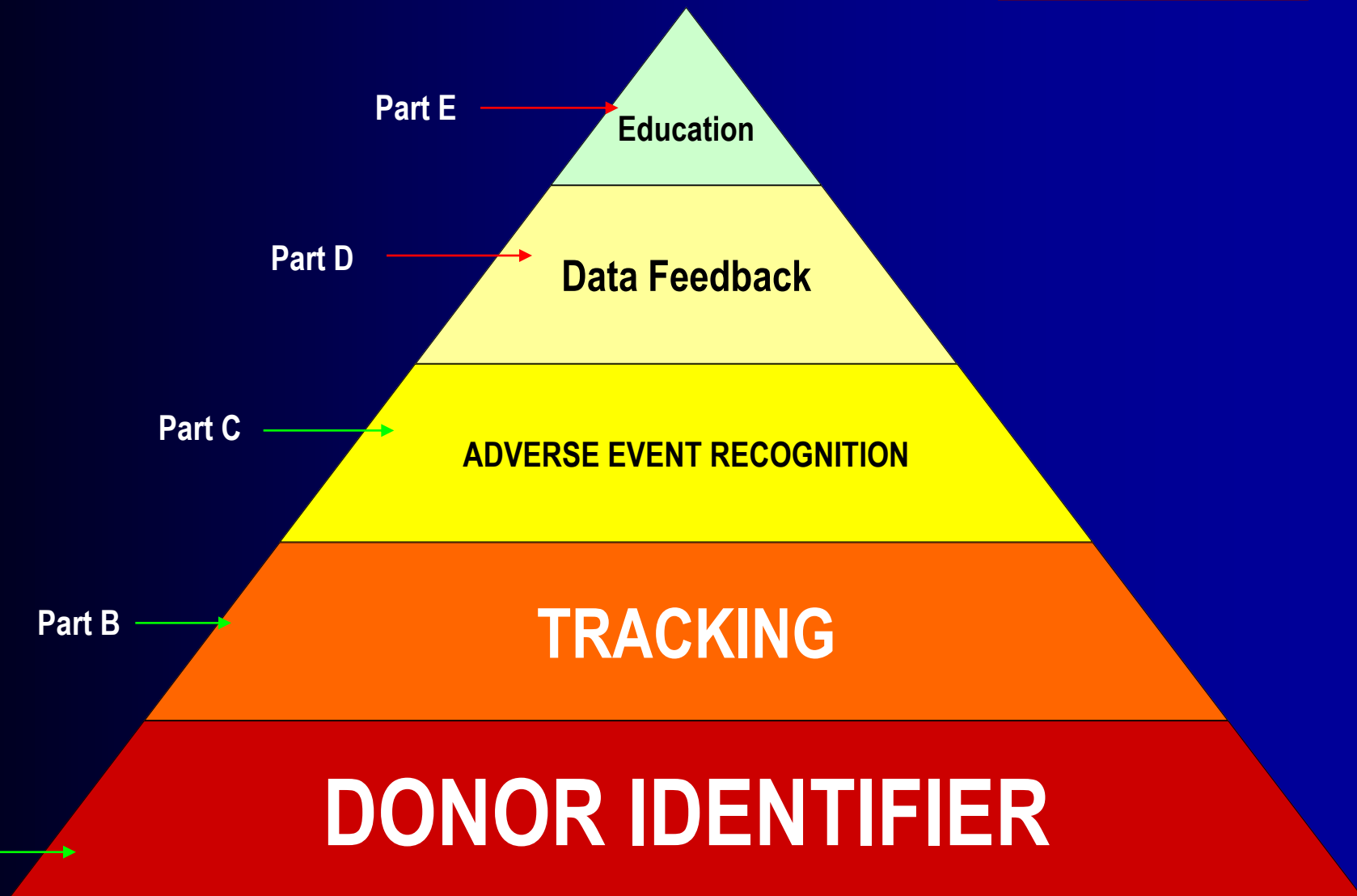
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# The TTSN Task Pyramid



Part A →

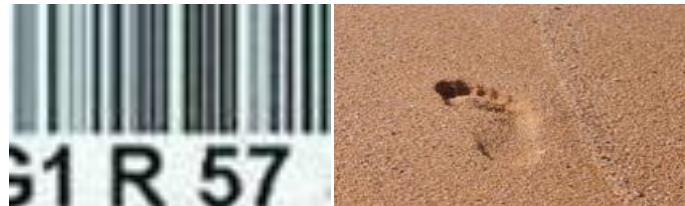
# Challenges in the Hospital – Tracking Tissues

**“The beginning of  
wisdom is to call things  
by their right names.”**

*- Chinese Proverb*

# Consistent Global Nomenclature and Coding Systems

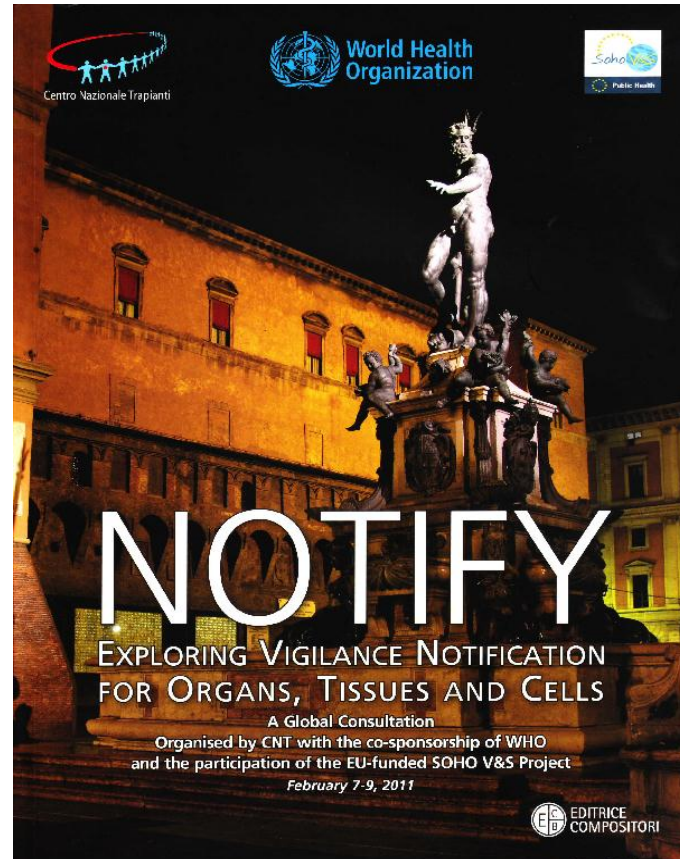
- Indisputable **need** for globally standardized description and coding for Medical Products of Human Origin
- **Opportunity** to work in a harmonized way before individual countries or regions develop disparate systems
- A global review shows that promoting **ISBT128** is the best way to achieve global consistency of coding across all medical products of human origin (Commitment of AABB, global cell therapy community)
- Working relationship between WHO and ICCBBA maintaining ISBT 128: global nomenclature, access for LMIC
- **WHO SONG project: Standardization of Organ Nomenclature Globally**  
[http://www.who.int/transplantation/tra\\_song/en/index.html](http://www.who.int/transplantation/tra_song/en/index.html)





# Report of the Bologna Consultation - NOTIFY

## Exploring Vigilance Notification for Organs, Tissues and Cells



Detailed Meeting Report with 4 didactic documents  
published in a Special Edition  
Organs Tissues & Cells. 2011, November, 14, 3: Supp.

# Biovigilance Summary

- ❑ **USA making progress, but has a patchwork approach to blood, organ, tissue, and cell surveillance**
- ❑ **While recipient hemovigilance is operational, biovigilance with organ and tissue not yet underway**
- ❑ **Standard coding and nomenclature needed to allow traceability for tissues**
  - Efforts being made in public and private sectors
  - Global solutions and cooperation underway
- ❑ **Partnering needed**
  - Harmonize adverse event definitions, nationally and internationally
  - Compare data globally...but for now, start with case descriptions and numerator counts, and then construct rates for benchmarking

# **CDC's Office of Blood, Organ, and Other Tissue Safety**

## ***Resources***

**<http://www.cdc.gov/bloodsafety>**

**<http://www.cdc.gov/nhsn/bio.html>**

## ***Questions?***

**[bloodsafety@cdc.gov](mailto:bloodsafety@cdc.gov)**  
**[nhsn@cdc.gov](mailto:nhsn@cdc.gov)**



# **Introduction: General Country Information**

- ❑ **No national blood program in the USA**
- ❑ **~12 million donations, ~24 million blood components collected and transfused**
- ❑ **Blood collected by multiple organizations**
  - American Red Cross (~45%)
  - America's Blood Centers (~45%)
  - Dept of Defense and others, including hospitals (<10%)
- ❑ **Transfusion services**
  - >4,000 inpatient facilities, in addition to outpatient centers

# Adverse Transfusion Events in the US: How common are they?

**Table 7-2. Transfusion-Related Adverse Reactions Reported to the Transfusion Service**

<b>Adverse Transfusion Reactions</b>	<b>Number of Occurrences</b>	<b>Reactions: Components Transfused (n=23,669,000 total components)</b>
Total number of reactions that required any diagnostic or therapeutic intervention	60,110	1:394
Febrile, nonhemolytic transfusion reaction	28,997	1:816
Severe allergic reactions	6,555	1:3,611
Delayed serologic transfusion reaction	2,143	1:11,044
Transfusion-associated circulatory overload (TACO)	1,417	1:16,706
Transfusion-associated dyspnea	1,150	1:20,588
Hypotensive transfusion reaction	1,140	1:20,757
Delayed hemolytic reaction	819	1:28,887
Posttransfusion purpura	493	1:47,993
Transfusion-related acute lung injury (TRALI)	460	1:51,443
Acute hemolysis (due to ABO incompatibility)	39	1:606,978
Acute hemolysis (due to other causes)	143	1:164,936
Posttransfusion sepsis	32	1:738,437
Transfusion-associated graft-vs-host disease	0	—
Reactions that were life-threatening, requiring major medical intervention following the transfusion; eg, vasopressors, blood pressure support, intubation, or transfer to the intensive care unit	169	1:139,908

# Organ and Tissue Safety

## Reporting - current systems and gaps

- Suspected organ transplant-related disease is reported through HRSA/OPTN by transplant centers and organ procurement organizations (OPOs)
- If organs and tissues are recovered from a donor, the OPO should report suspected transplant-related transmission to the tissue bank, otherwise the tissue bank may not be aware
- Tissue regulations extend only to “hospital door”
  - FDA regulates tissues through tissue banks, but have no jurisdiction once the product leaves the tissue bank
  - “implant card” return by clinicians are voluntary

# **Challenges: Healthcare facilities have multiple obligations for reporting**

## **❑ Voluntary Reporting**

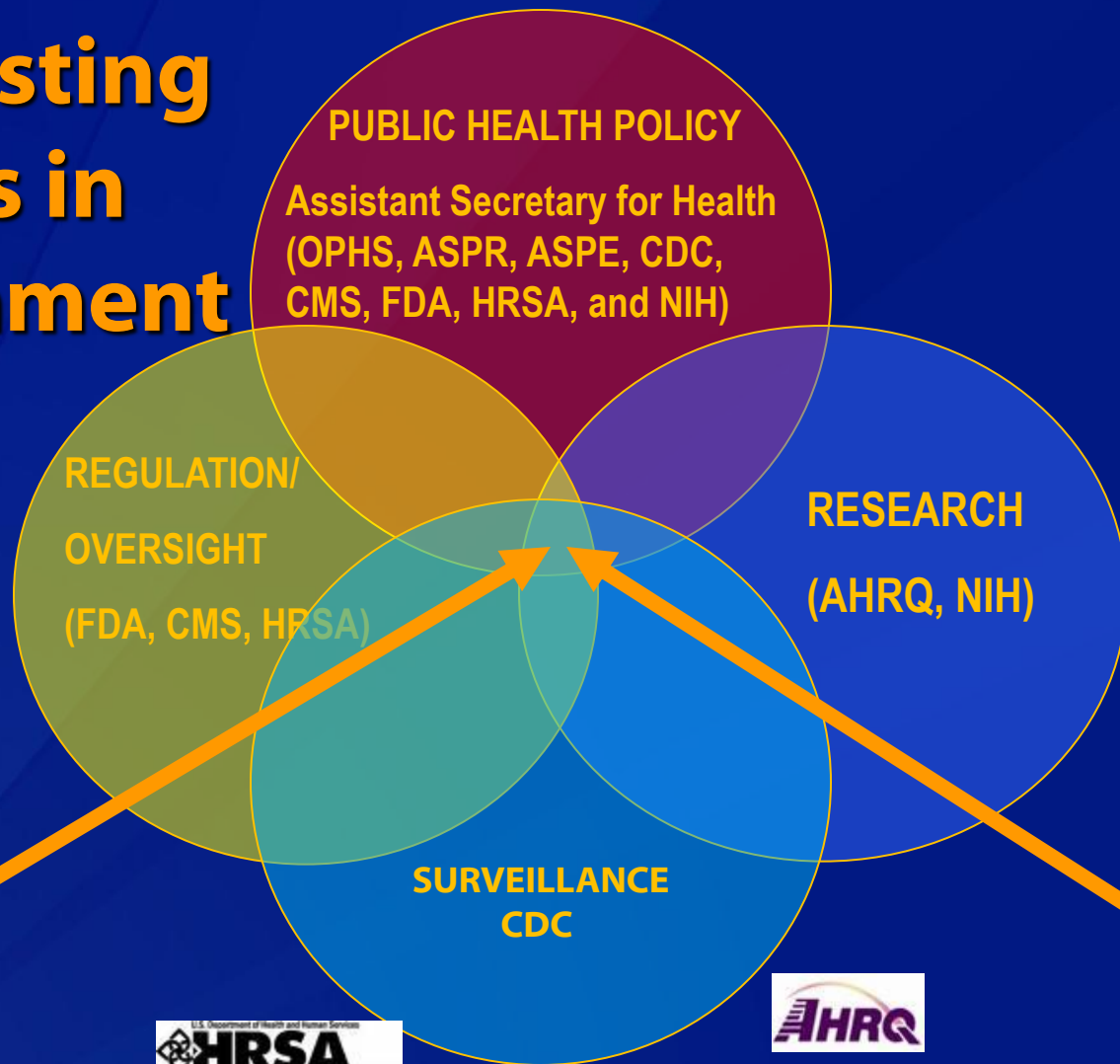
- ❑ NHSN Hemovigilance Module**
- ❑ FDA (MedWatch for clinicians)**
- ❑ Joint Commission (Sentinel Event)**

## **❑ Required Reporting**

- ❑ FDA (for Deaths, Biologic Product Deviations)**
- ❑ Facility Quality Assurance**
- ❑ Supplying Blood Center**
- ❑ State Compliance Authorities**



# Biovigilance: Contrasting Roles in Government





# **Hemovigilance Module**

## **Patient Adverse Reactions**



- ❑ Allergic reaction
- ❑ Acute hemolytic transfusion reaction (AHTR)
- ❑ Delayed hemolytic transfusion reaction (DHTR)
- ❑ Delayed serologic transfusion reaction (DSTR)
- ❑ Hypotensive transfusion reaction
- ❑ Febrile non hemolytic transfusion reaction (FNHTR)
- ❑ Post transfusion purpura (PTP)
- ❑ Transfusion associated circulatory overload (TACO)
- ❑ Transfusion associated dyspnea (TAD)
- ❑ Transfusion associated graft vs. host disease (TA-GVHD)
- ❑ Transfusion-related acute lung injury (TRALI)
- ❑ Infection

# Hemovigilance Module

## Process Incidents

### ❑ Transfusion Service

- Product Check-In
- Sample Receipt
- Sample Testing
- Product Storage
- Available for Issue
- Product Selection
- Product Manipulation
- Product Issue



### ❑ Clinical Service

- Product/Test Request
- Sample Collection
- Sample Handling
- Request for Pick-up
- Product Administration



# Biovigilance Challenges

- Hurdles
  - Nature of the myriad US healthcare system settings
  - IT infrastructure
  - Voluntary and regulatory reporting systems developed before concepts of interoperability, thus leading to a fragmented federal reporting system to overlay Hemovigilance/Biovigilance
  - Lack of common definitions and common data elements
  - Lack of a national blood policy
  - Sustained funding

