Biovigilance Working Group Discussion Review

ACBSA
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CDC
Centers for Disease Control and Prevention

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- The findings and conclusions in this presentation have not been formally disseminated by the Centers for Disease Control and Prevention and should not be construed to represent any agency determination or policy.

Advisory Committee on Blood Safety and Availability, May 9, 2006

Developing a Blood Safety and Availability Strategic Plan

- Transform the Healthcare System
- Modernize Medicare and Medicaid
- Advance Medical Research
- Secure the Homeland

Advisory Committee on Blood Safety and Availability, May 9, 2006

- "Biovigilance" Discussion group
  - Judy Angelbeck
  - Glenn Pierce
  - Bill Duffell
  - Glenn Ramsey
  - Mike Libby
  - Ruth Solomon
  - Janet Ishimoto
  - Bob Wise
  - Matt Kuehnert

Bio-vigilance Focus Elements for the HHS ACBSA Strategic Plan

- Transform the healthcare system
  - Surveillance of adverse events related to blood donations and transfusions
  - Error prevention in blood collection centers, transfusion services, and clinical transfusion settings

Bio-vigilance
Definitions

"Bio" – Comprehensive interpretation of biologic products

Blood/plasma derivatives, immunoglobulins, albumin…

Organs (e.g., kidney, liver, lung, heart…)

Other Tissues (e.g., musculoskeletal, heart valves, skin, eyes, dura, stem cells…)

Xenotransplants

Genes

Recombinant products

Parts of devices/ drugs/vaccines

Synthetics

Bio-vigilance
Definitions

"Vigilance" – numerous facets for discussion

- Donor surveillance
  - deferral and lab testing
- Recipient surveillance
  - adverse events
- Emerging Infectious Disease (EID) monitoring
- Product quality assurance (QA)
- Availability/Use Assessment

Bio-vigilance
Definitions

- Adverse event system parameters
  - Infectious vs non-infectious
  - Severity
  - Characterization (e.g., root cause)
  - Intervention
- Focus on outcomes
- Also include errors, which may not result in an adverse event or poor outcome

Biovigilance
Reporting - current systems and gaps

- Blood, organs, and tissues all have systems for adverse event reporting, but most are passive, with multiple pathways
- Blood has regulatory pathway extending into hospital (i.e., blood bank), but does not ensure participation of clinician or recipient
- Only organs require outcome reporting
- Tissue regulations extend only to “hospital door”

Biovigilance
Surveillance Needs Require Two Models

- Comprehensive reporting model
  - For common, well-defined events and outcomes
  - Active surveillance approach
  - Selected site methodology (not yet developed)
- Sentinel model
  - For uncommon, unusual events and outcomes
  - Passive surveillance approach
  - Uniform national methodology using existing reporting
- For either model, need to determine intervention threshold (and what action should be)

synergy with preparedness group

Surveillance Events

Unusual Event	Denominator	Common Event
Sentinel Events (e.g., fatal clusters) Epi-Aid Investigation Laboratory Protocols	"Universal" Data Outcome-driven	Routine Events Benchmarking National surveillance template

Biovigilance
Developing an EID Model – the "third rail"

- EIDs pose a unique problem
  - not detected in donors
  - no recipient adverse outcomes
  - need "hypothesis algorithm" based on potential risk
    - Transmissible between humans
    - Asymptomatic bloodborne state
  - repositories should reflect current donors

synergy with research agenda group

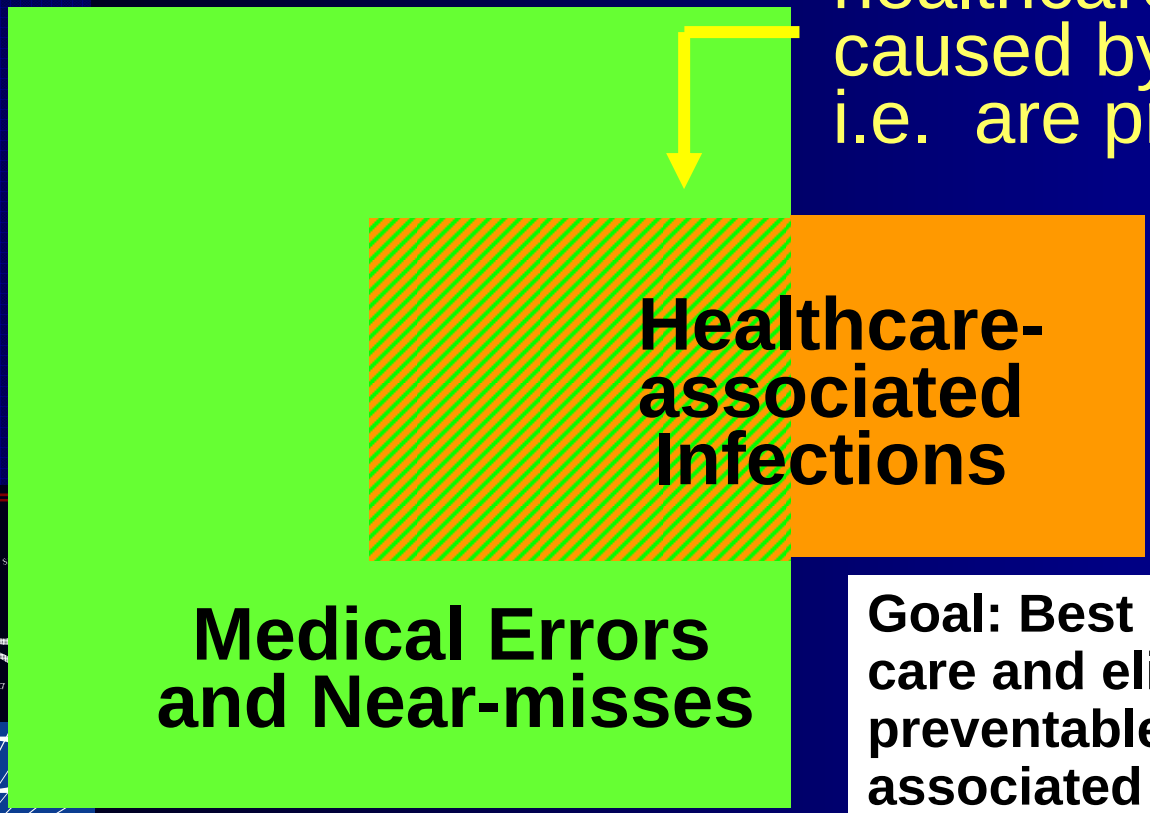
Product Quality Assurance: Error Prevention Should be Integrated into Biovigilance

- Errors need to be defined
  - Manufacturing vs “Bedside”
  - May result in adverse recipient outcome
  - However, some may not affect a patient, but still should be tracked
- Error investigation should not be punitive, but need to result in intervention (product QA)
- Error prevention is the “efferent” or “feedback” arm of biovigilance

synergy with policy group and transfusion practices group

Patient Safety:
Medical Errors and Adverse Events

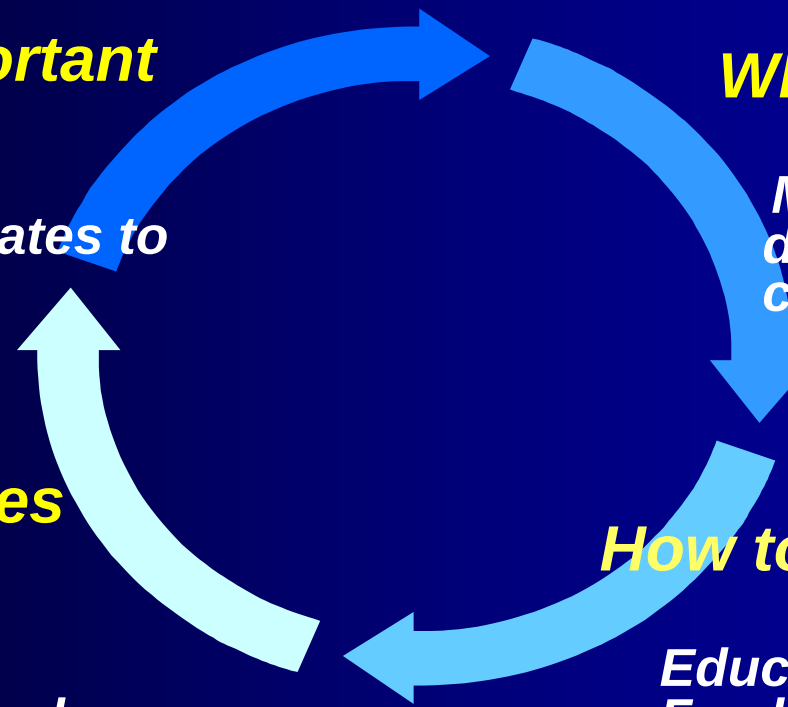
What proportion of healthcare infections are caused by errors...
i.e. are preventable?



Goal: Best quality of patient care and elimination of preventable hospital-associated infections

Quality Promotion / Adverse Outcome Prevention

Cycle for Success



Is there an important problem?

Compare local rates to benchmarks

Why? What?

Multi-disciplinary committees

How to affect change?

Education
Feedback
Decision support

Do the changes work?

Monitor progress toward improvement

Biovigilance
Availability and Use Surveillance

- A system is needed to track
  - Products transfused/transplanted
  - Products requested but not received (“unmet needs”) and secondary consequences (e.g., cancelled surgery)
- An intervention portfolio is needed to respond to inequities, and to increase product availability
  - Increase donation
  - Explore other sources (e.g., xenotransplant, synthetics)
- Organ Network (OPTN) can be viewed as model, BASIS and rare blood registries are start

synergy with donor pool group

Biovigilance: Developing a Model

Participation by Healthcare/Recipients is Critical

- Central reporting of biologic product adverse events, errors, and outcomes would be ideal (e.g., blood bank for hospitals, UDC for hemophilia population)

- Incentives to ensure compliance
  - Accreditation
  - Reimbursement
  - Simplify process to end user so that reporting is simple and clear, then educate

  One suggestion was quality performance parameters tied to reimbursement

  synergy with reimbursement group

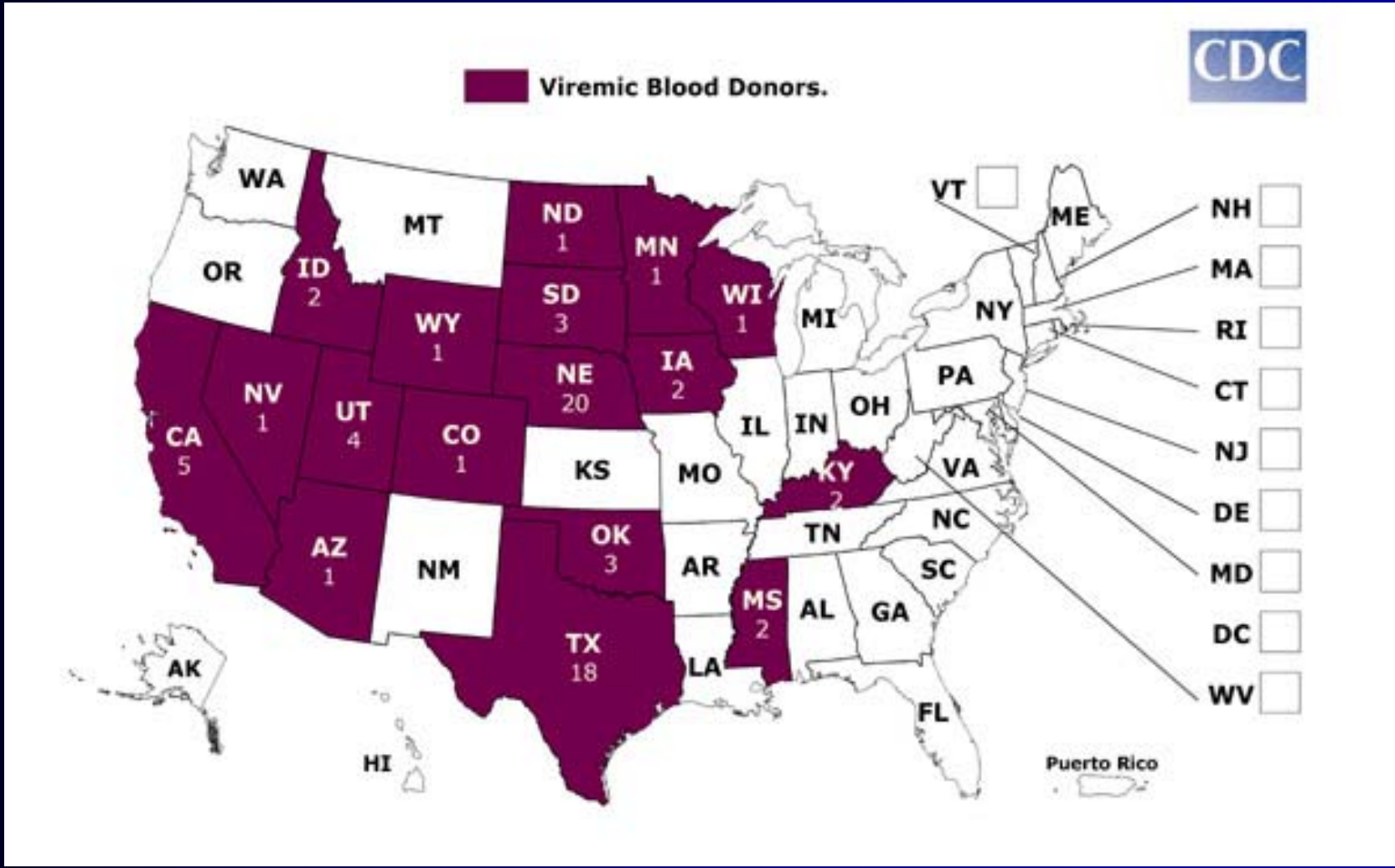
Biovigilance
For interventions, synergy needed

- Comprehensive tracking of all biologic products, including available data on
  - Source
  - Processing
  - Release criteria
  - End user (healthcare personnel, recipient)
    - Recipient data expected to be most challenging, particularly for outpatient or battlefield settings
    - New accreditation may be necessary
- Tracking will prevent errors, improve product QA, and enhance biovigilance

Partners Are Essential

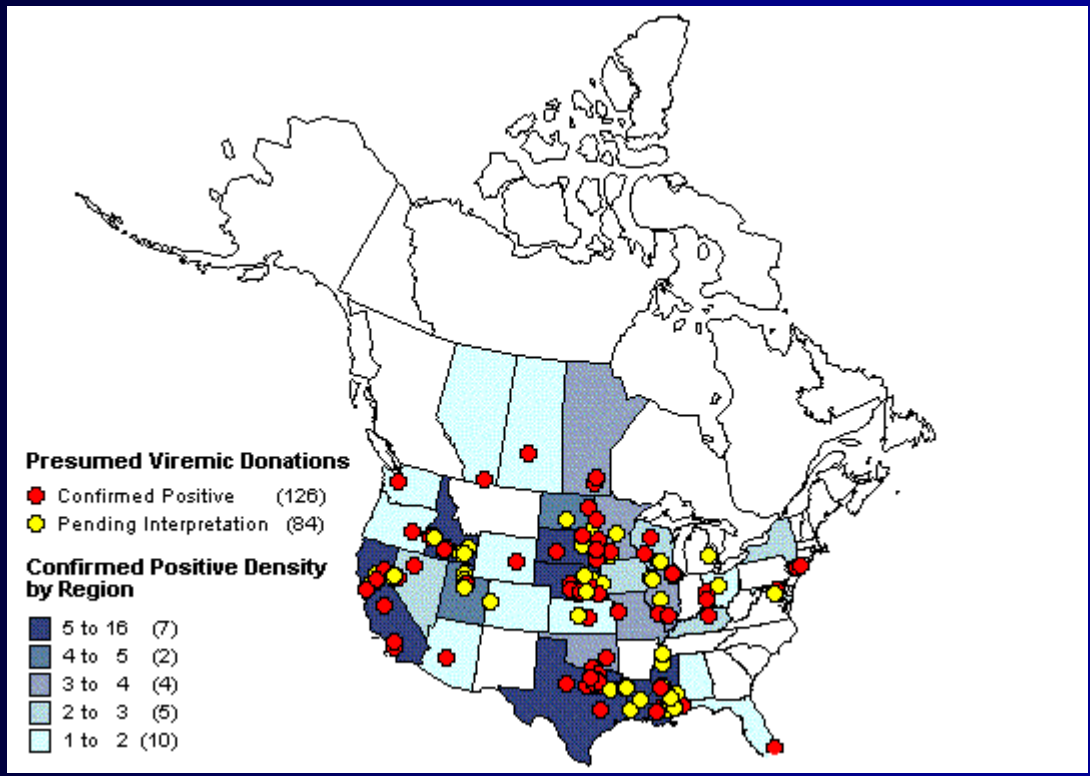
- Federal gov't
- State gov't
- Industry
- Trade orgs
- Patient advocacy/consumer orgs
- Accrediting orgs
- Healthcare orgs
- Clinical orgs
- IT companies
- Media
- Community

2006 West Nile Virus Viremic Blood Donor Activity in the United States (Reported to CDC as of August 15, 2006)

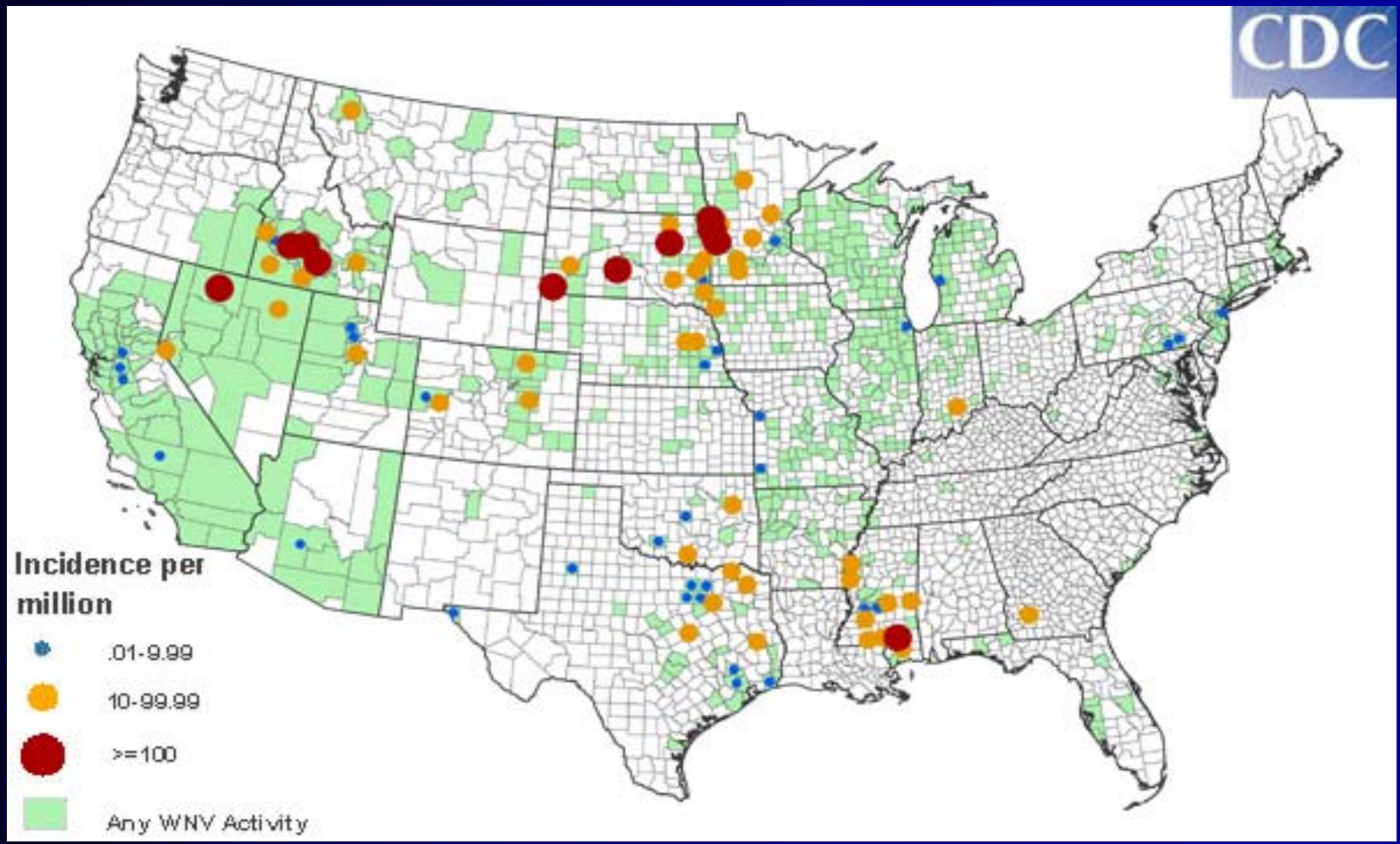


AABB West Nile Virus Biovigilance Network

The West Nile Virus (WNV) Biovigilance Network collates data on blood donors with suspected WNV infection in the United States and Canada. Data are collected from blood donor screening performed by nucleic acid testing (NAT). The data are reported to the AABB site by facilities responsible for testing virtually all blood donations in the United States and Canada. The reports provided here illustrate the geographic and temporal distribution of WNV infection as reflected by presumed viremic blood donors (PVDs) during the 2006 peak season.



2006 West Nile Virus Human Neuroinvasive Disease Incidence in the United States (Reported to CDC as of August 15, 2006)



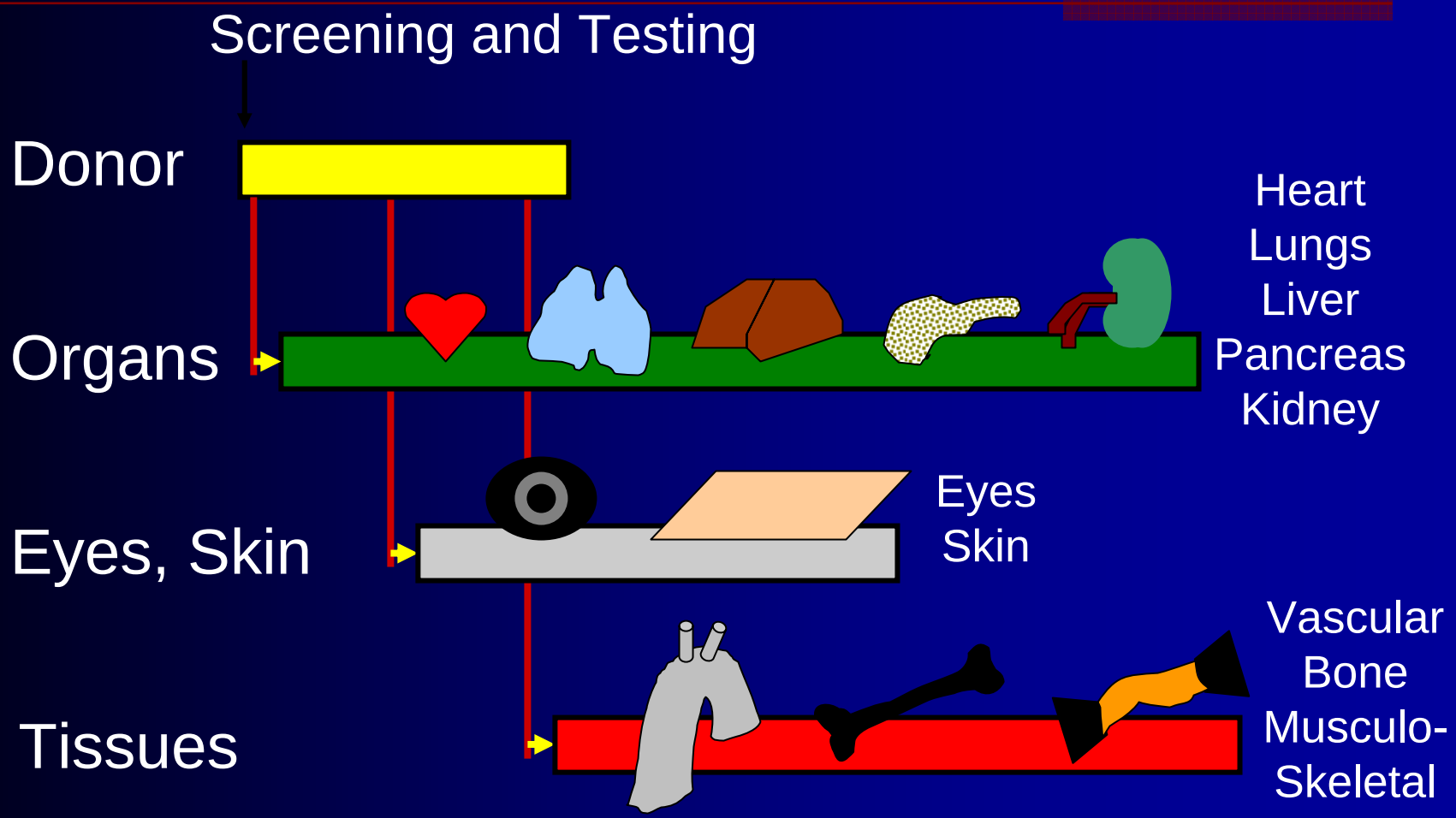
Organ Transplant-Transmitted Infections: Availability and Safety Issues

- 25,000 organ transplants annually
- Nearing 100,000 patients on transplant list
- Transplant transmitted infections rare… but often fatal
  - HIV, 1985
  - Hepatitis C, 2000
  - Chagas Disease, 2001
  - West Nile Virus (WNV), GA 2002, NY/PA 2005
  - Lymphocytic Choriomeningitis Virus (LCMV), WI 2003, MA/RI 2005
  - Rabies, 2004

Increasing Use of Allografts: Technological advances and safety challenges

- >1,000,000 allografts implanted annually
  - Majority musculoskeletal
  - Some but not all tissues can be sterilized
- Investigations of tissue-transmitted infxn
  - *Candida albicans*
  - Hepatitis C virus
  - Group A Streptococcus
  - *Clostridium sordellii*
  - Clostridial endophthalmitis

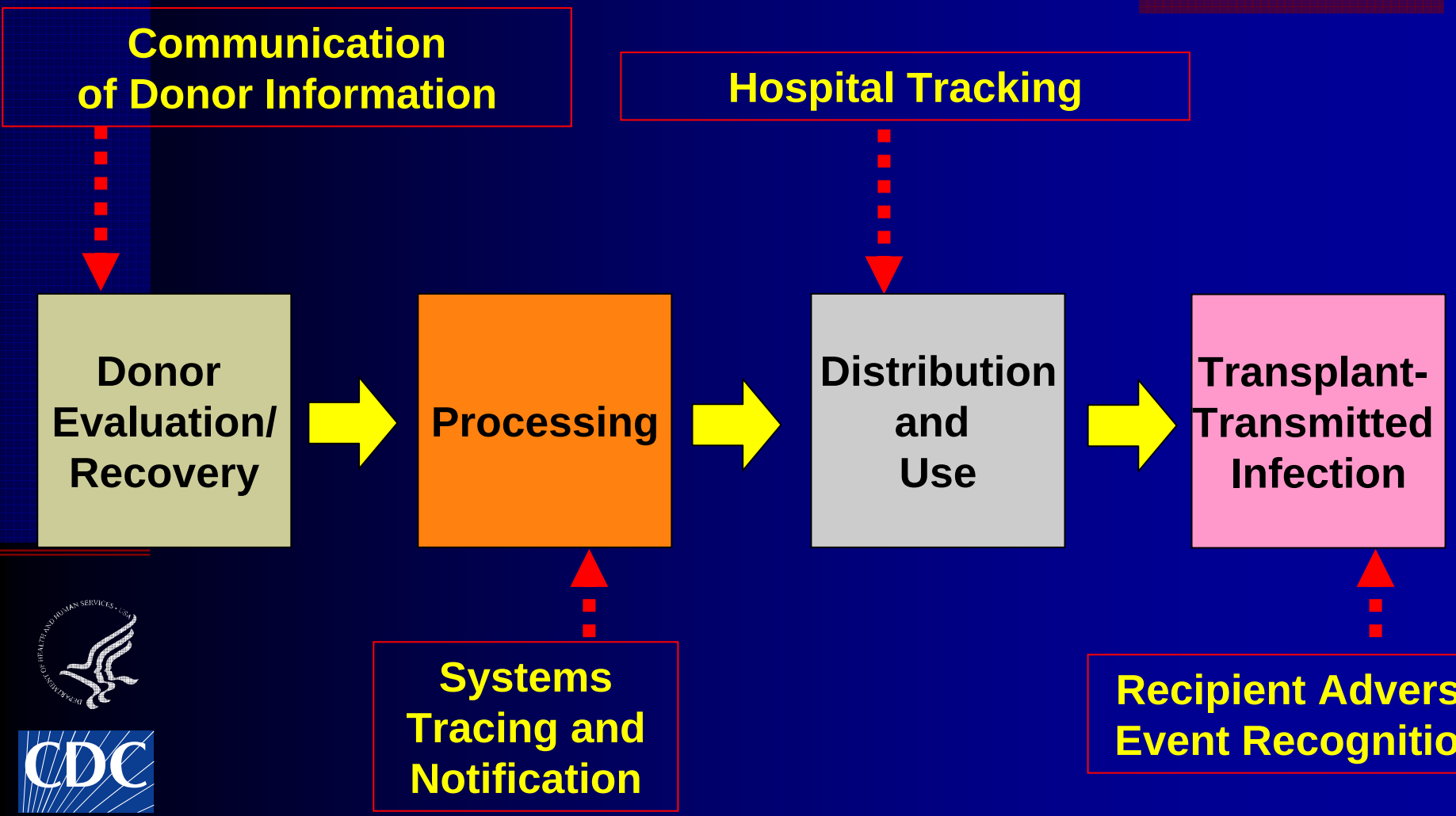
Organ and Tissue Recovery: A Complex Process



2005 CDC/HRSA/FDA Organ and Tissue Safety Workshop Priorities

1. Better communication network within and between organ and tissue community
2. Unique donor ID linking organs and tissues
3. Clear mechanisms for adverse event reporting by healthcare facilities
4. Strong(er) information dissemination to broad array of clinicians, health professionals and patients
5. Notification algorithm for trace-back and trace-forward tracking

Critical Points for Intervention in Preventing Transplant-Transmitted Infection: Priority Focus Areas



DEPARTMENT OF HEALTH AND HUMAN SERVICES
Centers for Disease Control and Prevention
Sentinel Network for Detecting Emerging Infections Among Allograft Donors and Recipients
Announcement Type: New
Funding Opportunity Number: AA081

The objective of the network will be to detect and prevent emerging infectious diseases through:

- Improved communication among those in the tissue community, healthcare facilities, and public health officials

- Improved identification and tracking of tissues to facilitate interventions following recognition of infections among recipients

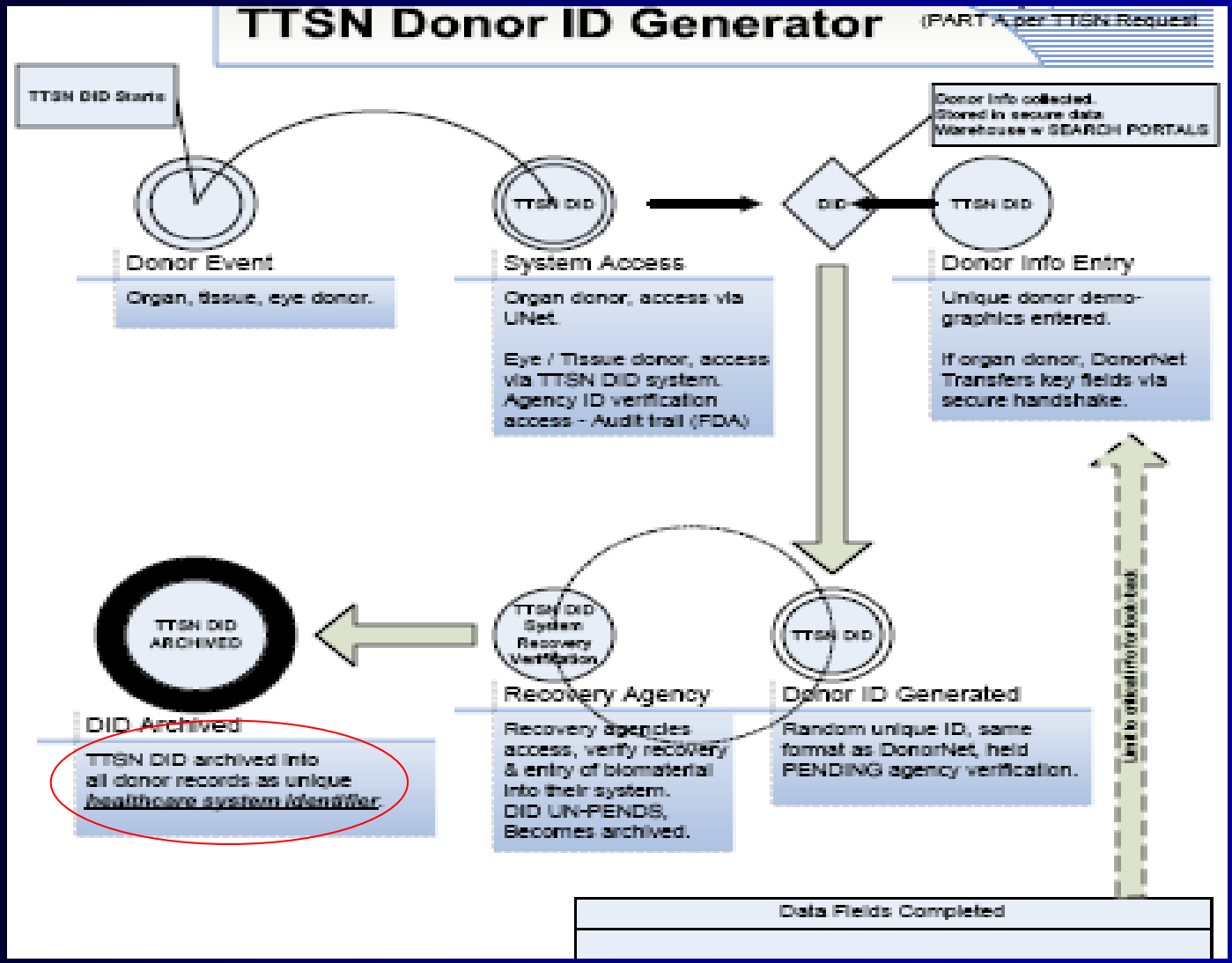
- Improved pathologic and microbiologic capabilities on donor specimen samples through shared resources and collaborations

- Development of recommendations to improve the safety of organ and tissue transplantation

Formation of the Transplantation Transmission Sentinel Network

- Cooperative agreement awarded to United Network for Organ Sharing (UNOS)
- Collaborative effort between CDC, HRSA, FDA, UNOS, AOPO, AATB, and EBAA
- Objective will be to improve and coordinate detection of transmission through organ and tissue transplantation

Transplantation Transmission Sentinel Network – Task Part A

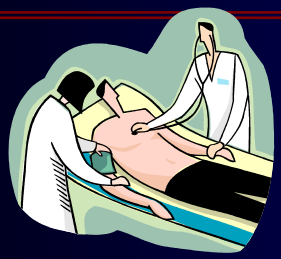


NEISS-CADES
National Electronic Injury Surveillance System – Cooperative Adverse Drug Event Surveillance

- Federal collaboration
  - CDC
  - Food and Drug Administration (FDA)
  - Consumer Product Safety Commission (CPSC)
- National Electronic Injury Surveillance System – All Injury Program (NEISS-AIP)
- Active surveillance of adverse drug events occurring in non-hospitalized patients

Courtesy, Jhung, Cohen, Budnitz, Pollack, CDC

NEISS-CADES Dataflow



Patient visits ED

Clinician charts ADE

NEISS coder abstracts data

CDC, CPSC, FDA review and analyze data

Disseminate findings

Courtesy, Jhung, Cohen, Budnitz, Pollack, CDC

Summary
Bio-vigilance (and error prevention) elements

- Donor surveillance
- Recipient surveillance (outcome focus)
- EID monitoring
- Product quality assurance
- Availability/use assessment
- Comprehensive tracking and adverse event/error reporting (source to recipient)
- Collaborative partner involvement and education essential; take best practices from all systems

My own suggestions

Now is the time to do this!

- Consider aligning strategic plan to Secretary's principles – "fragmentation to integration"
  - Health Information Technology Standards
    - Adverse incident reporting
    - E-prescribing (e.g., use)
    - Data exchange (e.g., tracking)
  - Safety Board for monitoring and response
    - Adapt for biologic product adverse events
    - Ensure compatibility with drugs and vaccine monitoring
- Public and private sectors in partnership

Bio-vigilance Working Group Recommendation Summary

1. Bio-vigilance should be comprehensive (e.g., blood, organs, other tissues), and include surveillance data collection and intervention thresholds.
2. Donor surveillance data should be collected and analyzed in a national scope.
3. Recipient surveillance data, focusing on transfusion/transplantation outcome, should be implemented in a national scope; reporting by the end user should be as simple and clear as possible, and there should be adequate incentives to ensure compliance.
4. Emerging Infectious Disease (EID) monitoring should be accomplished using a hypothesis generating algorithm for newly discovered threats, then assessed using virtual repositories or other suitable rapid investigative research methods if needed.
5. Comprehensive tracking of all biologic products that includes critical data elements is needed, from source to the end user.
6. A system to evaluate use and availability is needed to measure products used, products requested but not received, and intervention to respond to inequities.
7. Collaborative partner involvement and education is needed that includes federal government, industry, trade organizations, patient advocates and consumer organizations, accrediting organizations, healthcare organizations, clinical practice organizations, IT companies, media, and community, with the Secretary of HHS coordinating.