Issues to be Addressed

• Emerging Viruses and Product Safety
  – Presentation slides contributed by Thomas R. Kreil, Ph.D., Associate Professor of Virology, Pathogen Safety Steering Committee, Chairman

• Emerging Viruses/Donor Management

• Patient Notification System
MERS-CoV

Virology

- Middle East respiratory syndrome coronavirus (MERS-CoV)
  - Lipid-enveloped, large (~100 nm) diameter
  - Source of human infection: Camels, rare human-to-human
  - Virus reservoir: bats (?)

Epidemiology

- April 2012 – July 23, 2014: 837 laboratory-confirmed cases, at least 291 related deaths
- USA: 2 imported cases (for now)

Virus Safety Margins

Virus **reduction capacity** has been confirmed by an FDA study*, using the closely related SARS coronavirus

- Heat treatment
- Solvent/detergent (S/D)
- UV-C irradiation

* Transfusion [2006] 46: 1770

**Blood Components**

Evaluation of inactivation methods for severe acute respiratory syndrome coronavirus in noncellular blood products

Miriam E.R. Darnell and Deborah R. Taylor
Virology
- Filovirus (filamentous shape)
- Lipid-enveloped, large
- Virus reservoir: bush meat (?)
- Human infection: quite effective human-to-human (bodily fluids)

Epidemiology
- As of August 31: 3,685 cases, 1,841 deaths (~50% lethality)
- Primarily: Guinea, Liberia, Sierra Leone

Virus safety margins

Virus reduction capacity can generally be assumed for lipid enveloped (LE) virus, as all LE viruses tested were shown to be inactivated, e.g. for S/D:

- Bovine Viral Diarrhea
- Vesicular stomatitis
- Pseudorabies
- West Nile
- Coronavirus
- Sindbis
- Vaccinia
- Equine arthritis

Robustness of solvent/detergent treatment of plasma derivatives: a data collection from Plasma Protein Therapeutics Association member companies

* Transfusion [2009] 49: 1931; Robustness of solvent/detergent treatment of plasma derivatives: a data collection from Plasma Protein Therapeutics Association member companies
Chikungunya Virus (CHIKV)

Virology
• Discovered in 1953, Africa
  – Makonde: "that which bends up"
• Acute onset of fever, severe polyarthralgia
• Mosquito-borne arbovirus: Lipid-enveloped, medium sized (~50 nm) diameter

Epidemiology
• French Overseas, 2005/2006: La Reunion ~ 250,000 cases
• India, 2006/07: ~ 1,25 mio cases
CHIKV: Emergence …

→ Crippling virus set to conquer Western Hemisphere *

The Americas
Emergence since late 2013; as of September 5, 2014

• 31 countries or territories, Carribean, Central-, South- or North America
  – 651,344 suspected
  – 9,182 confirmed

• USA
  – 926 travel-associated
  – 8 locally-acquired (Florida)

http://www.cdc.gov/chikungunya
Virus Safety Margins

Virus reduction capacity of plasma product manufacturing processes has been confirmed

- Pasteurization for human serum albumin
- Vapor heating for Factor VIII inhibitor bypassing activity (FEIBA)
- Solvent/detergent (S/D) treatment for IVIG
- Incubation at low pH for IVIG

TRANSFUSION COMPLICATIONS

Chikungunya virus and the safety of plasma products


Leydold S … Kreil TR; Transfusion [2012] 52:2122
Donor Management

• What is donor management in emerging viruses:
  – Addition of behavior/exposure questions to health history
  – Class or geographic exclusions
  – Addition of screening measures (eg., skin or throat exam)

• When is donor management considered:
  – Agent is transmissible by blood
  – Results in disease/morbidity/chronicity
  – Asymptomatic viremia
  – For plasma therapies—not cleared in manufacturing (West Nile Virus model)
Donor Management

- Only healthy people can donate

<table>
<thead>
<tr>
<th>Are you</th>
<th>Yes</th>
<th>No</th>
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<tbody>
<tr>
<td>1. Feeling healthy and well today?</td>
<td></td>
<td></td>
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<tr>
<td>2. Currently taking an antibiotic or other medication for infection?</td>
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<td>3. Currently taking any other medications?</td>
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- Temperature, blood pressure and pulse normal at each donation
• 1998 – U.S.
• FDA was considering promulgating a regulation
• 2002 - Canada

Industry provided funding
  – Member companies (initial investment, annual fees & activity fees)
  – Non-Member companies (annual fees & activity fees)
Importance

• Direct to Patient

• Withdrawals and Recalls
  – Patients
    • Instantaneous notifications
    • Role in safety
    • Confidence in therapy
  – Providers
    • Notifications
    • Assist in patient care
Collaboration

- Patient Notification Working Group (PNWG)
  - Patients, FDA & Industry
  - Annual calls to discuss registrants statistics
  - Raise awareness about PNS
  - Enhancements
    - Spanish language
    - Optimizing for Mobile technology
    - Application of “QR” codes
Notifications

- PPTA informed of “Event” notification
- Manufacturer PNS contact
  - 1 per company
  - Interaction between Stericycle & their company
  - Direct negotiations with FDA on notification language
- Primary Method of Notification
  - E-mail
  - Phone
  - Fax
- Second Notification
  - Follow up with U.S. mail
Thank you!!!