

Overview of Division of Emerging and Transfusion Transmitted Diseases (DETTD)

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Laboratory of Emerging Pathogens
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Update at 115th Meeting of the Blood Product
Advisory Committee
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Division of Emerging and Transfusion Transmitted Diseases organizational Chart



- Personnel in the immediate office of the Director include:
 - Hira Nakhasi, PhD. Director; J. Peyton Hobson, PhD., Deputy Director; Anne Eder, MD, PhD., Associate Deputy Director for Policy and Medicine; Sayah Nedjar, PhD., Associate Director for Managed Review.
- There are 3 research/review laboratories that include Laboratory of Bacterial and TSE agents (LBTSE); Laboratory of Molecular Virology (LMV); Laboratory of Emerging Pathogens (LEP) and one Product Review branch (PRB)
- The chief of PRB is David Leiby, PhD. There are 11 full time reviewers in that branch
- The chief of LBTSE is David Asher, MD and there are two Principal investigators including him
- The chief of LMV is Indira Hewlett, PhD and there are three Principal investigators including her
- The Chief of LEP is Sanjai Kumar, PhD and there are six Principal investigators including him

DETTD Mission

- **Plans and conducts research:**
 - Development, pathogenesis and proof-of-concept for detection assays for blood borne pathogens
 - Viral (HIV , HTLV, Hepatitis (HBV, HCV, HEV,HAV), Arboviruses (WNV, Dengue virus, CHIKV, ZIKV)
 - **Parasitic (Leishmania, Malaria, Chagas, Babesia)**
 - Bacterial
 - Biodefense agents (preparedness for Pan Flu, Ebola virus)
 - Transmissible Spongiform Encephalopathy agents or “prions”
 - Development of biomarkers for vaccine safety of blood-borne parasitic agents (**CBER priority**)
- **Proactively ensuring the safety of the blood supply through:**
 - Regulation of tests for blood screening and diagnostic
 - Evaluation of new technologies for rapid and multiplex screening of the blood supply
 - Develop policies in the form of guidances for users of blood screening and diagnostic products.

DETTD Mission-cont.

- **Reference materials for lot release testing:**
 - Develop and validate reference materials for lot release testing of test kits
 - Collaborate and develop International Standards for infectious agents assays
- **Investigational testing**
 - Inspections
 - Consultation
- **scientific and technical advice to other Agencies and Government components e.g. CDC, DOD, DHHS etc.**
- **Outreach:**
 - Blood Product Advisory Committee
 - DHHS Advisory Committee on Blood Organ and Tissue Safety Availability
 - Liaison to committees of blood establishments and device manufacturer
 - World Health Organization Collaborating Center for IVDs

Blood Safety and Availability: Impact on the US Public Health

- ~14 Millions of units are transfused annually
 - Risk of transmission through transfusion has significantly reduced with the introduction of tests:
 - Currently approved tests (NAT or serological):
 - HIV1/2/O, HTLVII/II, HCV, HBV, WNV, *T. cruzi*, Syphilis, CMV
 - In addition, blood is also screened using Investigational Assays for:
 - ZIKV NAT assay (nation wide)
 - Babesia using Investigation NAT and serological assays (in high risk areas)

Challenges for Blood Safety and Availability



- Re-emerging pathogens:
 - E.g. HIV variants, Dengue virus (DV), Chikungunya virus (CHIKv), Syphilis etc.
- Emerging pathogens:
 - Babesia, West Nile virus (WNV), ZIKV, Biodefense agents (Pan Flu, Ebola virus), Tick-borne pathogens, TSE agents
- Neglected Tropical Disease pathogens:
 - Parasitic- *Leishmania*, Malaria, *T. cruzi*
 - Arboviruses-DV, CHIKv, Yellow Fever virus
- Lack of assays to detect some of the pathogens
- Lack of assays to detect the blood borne pathogens in a multiplex format
- Lack of confirmatory assays
- Potential impact of travel-based deferrals on adequacy of the blood supply
- Pathogenesis of blood borne pathogens



Mission Relevant regulatory Research

- Studies on pathogenesis and standards development of HIV and other retroviruses and its impact on blood safety
- Studies on pathogenesis and standards development of WNV, DV and Zika virus infections and its impact on blood safety
- Studies on hepatitis viruses and development of standards for hepatitis virus assays
- Evaluation of advance detection technologies for reducing the risk of transfusion transmission of infectious agents
- Studies on evaluation of tests for detecting transmissible spongiform encephalopathies to ensure safety of blood and other biologics

Mission Relevant regulatory Research- cont.

- Safety of blood and blood products from the risk of transfusion transmitted malaria and *Babesia* and to ensure safety and efficacy of malarial vaccines.
- Reducing the risk of Leishmaniasis through vaccination- *Target Product profile for Leishmania vaccines.*
- Studies on diagnosis and vaccine efficacy of Ebola virus and its impact on blood safety.
- Developing methods to improve blood safety by reducing the risk of transmission of *Trypanosoma cruzi* parasites by blood transfusion

Select Examples of Significant Mission Relevant Research publications in DETTD

- CD47 regulates the phagocytic clearance and replication of the *Plasmodium yoelii* malaria parasite.
- Expression, Purification, and Biological Characterization of *Babesia microti* Apical Membrane Antigen 1.
- Role of pro-inflammatory cytokine IL-17 in *Leishmania* pathogenesis and in protective immunity by *Leishmania* vaccines.
- Live Attenuated *Leishmania donovani* Centrin Knock Out Parasites Generate Non-inferior Protective Immune Response in Aged Mice against Visceral Leishmaniasis.
- Aptamer-based detection of disease biomarkers in mouse models for Chagas drug discovery.

Select Examples of Significant Mission Relevant Research publications in DETTD- cont.

- Novel Time-Resolved Fluorescence Europium Nanoparticle Immunoassay for Detection of Human Immunodeficiency Virus-1 Group O Viruses Using Microplate and Microchip Platforms.
- Development of a microarray-based assay for rapid monitoring of genetic variants of West Nile virus circulating in the United States
- Comparison of multiplex PCR hybridization-based and single-plex real-time PCR-based assays for detection of low prevalence pathogens in spiked samples.
- Blood reference materials from macaques infected with variant Creutzfeldt-Jakob disease agent.



Development and evaluation of reference reagents and standards for assay development

- Babesia antibody
- Babesia RNA
- DV RNA
- CHIKv RNA
- ZIKV RNA
- vCJD
- *Plasmodium* antibody
- HIV-1 genotype RNA
- HIV-2 RNA
- HIV-Ag
- *T. cruzi* antibody

Research and Regulatory Output for

FY'16

- 11 Principle Investigators:
 - Support Staff- 52 FTEs
 - Contract Fellows- 23
- Research Publications- 44
- Review applications- 429
 - BLAs, PMAs, BLA and PMA suppl., INDS and IDEs, Presubmissions, Guidances for Industry



Thank You

