Epidemiology and Vector Control Summary
Blood Supply Safety Summary
Vaccine Summary
Potential Role of Vaccines in Pregnancy

- **Pregnant women as a target:** Prevention of microcephaly is a primary goal, but several expressed concern about use of vaccines in pregnancy:
  - Need for demonstrated safety in non-pregnant adults before testing in pregnant women
  - Potential need for sterilizing immunity
  - Rapidity of immune response
  - Limits approaches – e.g., live-attenuated

- Several invoked **rubella** approach (target broad population in order to protect)
Preclinical development issues

- **Strain selection** – data showing excellent cross-reactivity

- **Immune correlates** – have one for JE and recently for dengue (both neutralizing Ab titers)

- **Harmonized assays** – e.g., reporter virus particles for neutralization

- **Animal models** – good model for viremia curves in NHPs; gap for pathogenesis
Clinical development issues

- **Potential trial pathways:** traditional vs. Phase 2/2b vs. human challenge/Phase 2

- Key questions about **efficacy endpoints**, particularly given current diagnostics – Urine PCR 3x/month suggested

- Need to locate trials well for high incidence

- Potential role of **human challenge**
  - Could provide immune correlate (at least immune profile)
  - Could offer demonstration of sterilizing immunity
  - Efficacy in small N
  - Questions about GBS, other neurologic sequelae, sexual transmission and prevention of pregnancy
Other questions and critical gaps

- Potential role of prior flavivirus exposure
- Pathogenesis and risk of Guillain-Barré syndrome
- Critical gaps for vaccine developers:
  - Viral samples from endemic settings
  - Sera from endemic settings, particularly to define likely neutralizing Ab target
  - Standardized assays
  - Well characterized animal models
  - More information on viral structure and contact points for neutralizing antibodies
  - Diagnostics
Therapeutics Summary
Use of drugs in pregnancy

- Outlined specific considerations for drugs in pregnancy
  - Impact of pregnancy physiology
  - Specific preclinical information needed (special tox, placental transfer)
  - Ethical considerations

- Potential use cases – chemoprophylaxis vs. treatment after infection

- Approved drugs vs. novel drugs (including monoclonals)
Other issues/critical gaps

- Kinetics of viral infection and disease; implications for therapeutic window
- Replication sites in humans
- Potential use of monoclonals – early stage but could be long-lasting; concerns about cost and placental transfer
- Animal models – including microcephaly, accurate placental transfer
Diagnostics Summary
Diagnostic Needs

- Sensitive and specific molecular assays.
  - Good pipeline

- Sensitive and specific serologic assays that can discriminate antibody response to Zika virus from other flaviviruses
  - Serologic assays that can be used for risk stratification in pregnant women in endemic regions.
  - More studies to determine best antigen(s) to use.

- Sensitive and specific rapid tests that can be used at point-of-care

- Assays to discriminate vaccine response from natural infection

- Access to well-characterized clinical specimens (acute and convalescent) for assay validation, regulatory approval.
  - Serial bleeds after PCR positive to validate serologic assays.
Clinical specimens

- Need access to well-characterized clinical specimens (acute and convalescent) for assay validation, regulatory approval.
  
  - Critical to have convalescent serum (serial bleeds) from PCR positive cases to validate serologic assays.
  
  - Assess reliability of detecting Zika specific IgM/IgG response in primary and secondary infection.
Diagnostic Testing - Research Needs

- Studies to determine the duration of Zika virus shedding in various specimen types (urine, saliva, semen, amniotic fluid, CSF).

- Best antigen(s) for serology tests
  - functional characterization studies of antibodies and their binding epitopes cross-reacting between Zika and other flaviviruses.
  - novel diagnostic assays and antigens capable of distinguishing the antibody response to related flaviviruses.

- Improved, highly specific, high-throughput quantitative assays to measure antibody-mediated neutralization and enhancement of Zika virus infection.
Other critical gaps/conclusions?

What should HHS do in the immediate and longer term to accelerate research and development of countermeasures?