

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?**