Guide to Interpretation of Zika Laboratory Results for Imported Cases
(To be used in conjunction with clinical and epidemiological criteria)

**PCR results**

- Negative or equivocal for all samples
- PCR positive for at least one sample

**Serology results**

- Serum or CSF sample collected > 4 days after symptom onset
- Zika IgM negative
- Zika IgM positive

*What were the dengue IgM results?*

- Positive
- Negative or equivocal

**Suspect flavivirus case**

- Did PRNT** testing indicate a 4-fold or greater difference in neutralizing antibody titers between Zika virus and dengue virus or other flaviviruses endemic to the region where exposure occurred?
  - < 4-fold difference
  - ≥ 4-fold difference

- Suspect flavivirus case
- Confirmed case

*Not a case unless PCR testing is positive (see above). Resample if sample was collected ≤ 4 days of symptom onset.*

- Probable case

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*A seroconversion from negative for Zika IgM in an acute sample to positive for Zika IgM in a convalescent sample would meet confirmed case criteria if dengue IgM is negative for both samples.

**PRNT testing will not be routinely performed for imported Zika cases. PRNT testing may be performed on samples from PUIs with a severe outcome, pregnant women, and suspect local cases.

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Dashed line indicates how results would be interpreted if PRNT is performed.

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Guide to Interpretation of Zika Laboratory Results for Symptomatic Pregnant Women or Suspect Local Cases
(To be used in conjunction with clinical and epidemiological criteria)

**PCR results**

- **Negative or equivocal for all samples**
  - Was the serum sample collected ≤ 4 days after symptom onset?
    - Yes → Not a case
    - No → See serology results

- **PCR positive for at least one sample**
  - More than one sample PCR positive?
    - Yes → Suspect case unless serology results meet probable or confirmed criteria.
    - No → See serology results

**Serology results**

- **Serum or CSF sample collected > 4 days after symptom onset**
  - Zika IgM negative → Not a case unless 2 samples are PCR positive (see above). Resample if sample was collected ≤ 4 days of symptom onset.
  - Zika IgM positive → What were the dengue IgM results?
    - Positive → Suspect flavivirus case
    - Negative or equivocal → Probable case

- **One sample PCR positive**
  - Did PRNT* testing indicate a 4-fold or greater difference in neutralizing antibody titers between Zika virus and dengue virus or other flaviviruses endemic to the region where exposure occurred?
    - < 4-fold difference → Suspect flavivirus case
    - ≥ 4-fold difference → Probable case

*PRNT testing will be approved on a case by case basis and may require a second serum sample.
- - - - Dashed line indicates how results would be interpreted if PRNT is performed.
**Guide to Interpretation of Zika Laboratory Results for Pregnant Women Not Meeting Clinical Criteria**  
*(To be used in conjunction with epidemiological criteria)*

PCRs is recommended for pregnant women with one of the following four symptoms: fever, rash, conjunctivitis, and arthralgia in the 21 days before sample collection.

**START**

- **Serology results:**
  - **Serum sample collected within 2-12 weeks of travel return date**
  - **Zika IgM negative** → Not a case*
  - **Zika IgM positive** → What were the dengue IgM results?
    - Positive → Suspect flavivirus case
    - Negative or equivocal → Suspect Zika case

Did PRNT** testing indicate a 4-fold or greater difference in neutralizing antibody titers between Zika virus and Dengue virus or other flaviviruses endemic to the region where exposure occurred?

- < 4-fold difference → Suspect flavivirus case
- ≥ 4-fold difference → Suspect Zika case

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*It is unknown how long Zika IgM can be detected for, but it is considered to be at least 2-12 weeks. Testing of samples collected after 12 weeks is permitted, however, a negative IgM result does not definitively prove that the person wasn’t exposed to Zika virus. A positive result would be indicative of exposure in concurrence with other testing (see above).

**PRNT testing will be approved on a case by case basis. PRNT may provide more conclusive results and will also be recommended for suspect Zika cases, although it won’t change the case status at this time.*
Differentiating between Zika and dengue infections in patients with positive flavivirus labs:

- Dengue and Zika clinical differentiation:
  - Conjunctivitis is more common with Zika infections than dengue.
  - Thrombocytopenia and leukopenia are more common and severe in cases of dengue fever compared to Zika fever.
  - Zika is not known to cause severe syndromes that can be seen with dengue (dengue hemorrhagic fever, dengue shock syndrome).

- Dengue and Zika lab differentiation:
  - Zika IgM titers are usually positive in dengue fever patients. Dengue IgM titers may or may not be positive in Zika fever patients. IgM ELISA results from BPHL are not quantitative and the values derived from this assay cannot be compared between illnesses.
  - Co-infections with these two viruses will be difficult to identify unless PCR results are positive for both viruses. In general, only one case should be created if the person is PCR positive for one virus and not the other.

- When should you create a dengue case:
  - Sample tested PCR positive for dengue virus.
  - The clinician ordered dengue testing, did not request Zika testing, and dengue IgM or PCR was positive.
  - The clinician ordered Zika testing and Zika IgM was negative, while dengue IgM was positive.
  - PRNT testing indicates a ≥4 fold difference in antibody titers for dengue in comparison to the Zika antibody titer (PRNT testing will not be routinely performed).