

# Updated Interim Guidance for the Diagnosis, Evaluation and Management of Infants with Possible Congenital Zika Virus Infection

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# DISCLOSURES

- I have no financial disclosures.

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# UPDATED GUIDANCE

Centers for Disease Control and Prevention  
**MMWR**

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## Update: Interim Guidance for the Diagnosis, Evaluation, and Management of Infants with Possible Congenital Zika Virus Infection — United States, October 2017

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Source: Adebajo T, Godfred-Cato S, Viens L, et al. Update: Interim Guidance for the Diagnosis, Evaluation, and Management of Infants with Possible Congenital Zika Virus Infection — United States, October 2017. *MMWR Morb Mortal Wkly Rep* 2017;66:1089–1099. DOI: <http://dx.doi.org/10.15585/mmwr.mm6641a1>.

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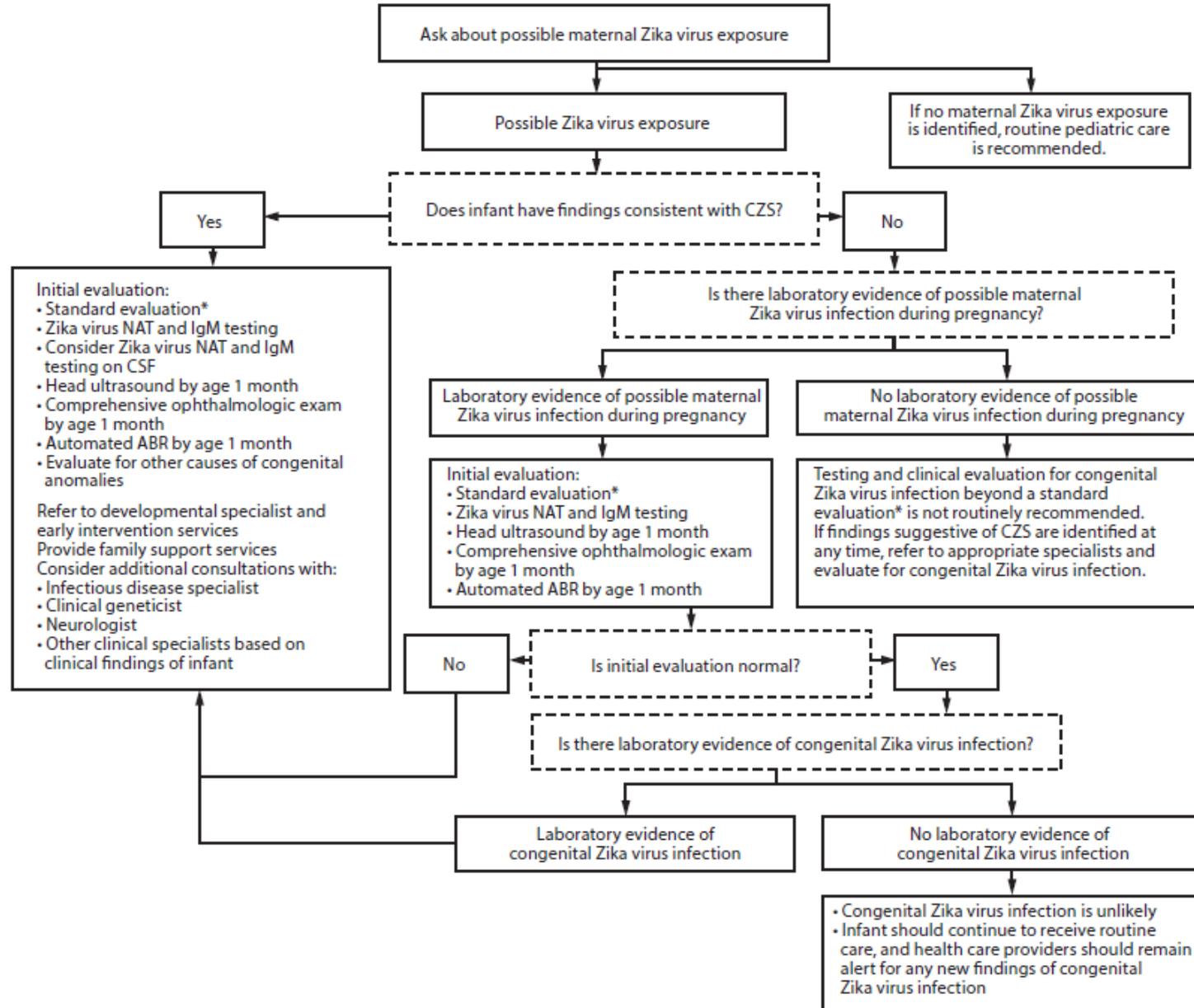


# OVERVIEW OF CHANGES

- Guidance defines three groups of infants:
  1. Infants with birth defects consistent with CZS born to mothers with possible Zika virus exposure during pregnancy (regardless of mother's Zika virus test results)
  2. Infants without birth defects consistent with CZS born to mothers with lab evidence of possible Zika virus infection during pregnancy
  3. Infants without birth defects consistent with CZS born to mothers with possible Zika virus exposure during pregnancy but with no lab evidence of infection
- Updated information on interpreting lab testing results
- Updated recommendations for vision and hearing screening
- Some previously suggested screenings no longer recommended



**FIGURE: RECOMMENDATIONS FOR THE EVALUATION OF INFANTS WITH POSSIBLE CONGENITAL ZIKA VIRUS INFECTION BASED ON INFANT CLINICAL FINDINGS, MATERNAL TESTING RESULTS, AND INFANT TESTING RESULTS**



# STANDARD EVALUATION FOR ALL INFANTS WITH POSSIBLE ZIKA EXPOSURE DURING PREGNANCY

Should occur at birth and at each well-visit:

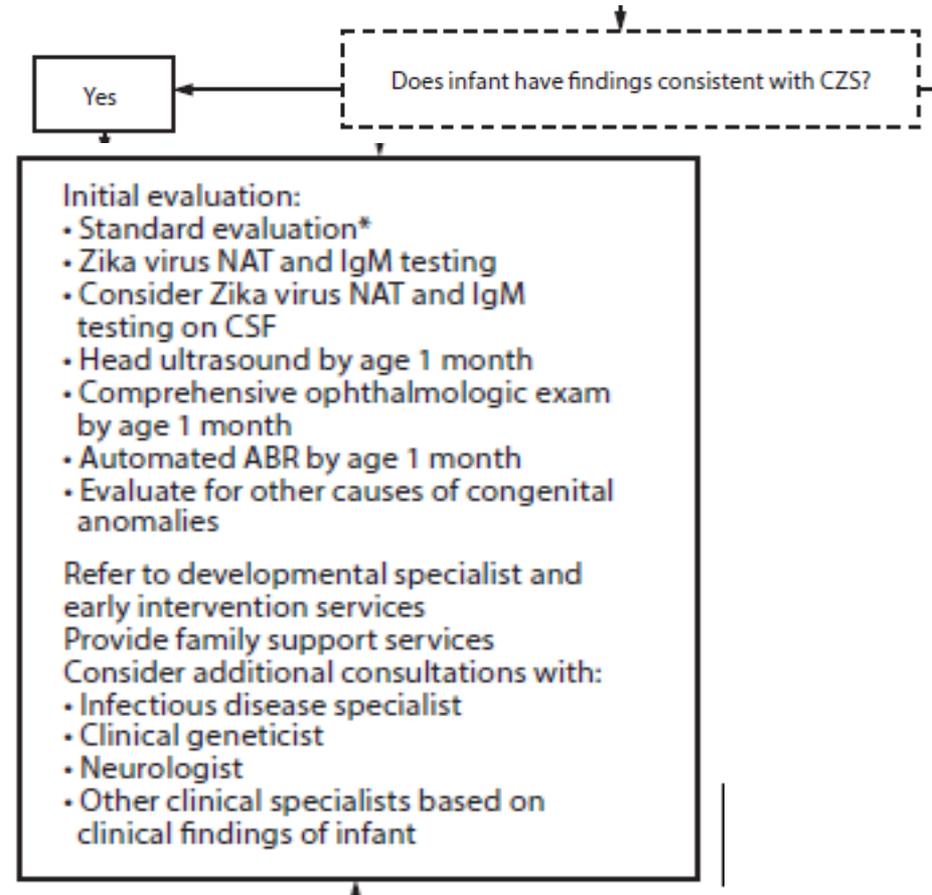
- Comprehensive physical exam, including growth parameters
- Developmental monitoring and screening
- Vision screening
- Newborn hearing screen at birth, preferably with automated auditory brainstem response



## KEY CHANGES BY GROUP

### INFANTS WITH BIRTH DEFECTS CONSISTENT WITH CZS BORN TO MOTHERS WITH POSSIBLE ZIKA VIRUS EXPOSURE DURING PREGNANCY

- Monitor for an expanded list of potential problems including difficulty breathing or swallowing and hydrocephaly after birth
- Follow-up care no longer guided by Zika virus testing results



## KEY CHANGES BY GROUP:

### INFANTS WITH BIRTH DEFECTS CONSISTENT WITH CZS BORN TO MOTHERS WITH POSSIBLE ZIKA VIRUS EXPOSURE DURING PREGNANCY

- Coordinated care by a multidisciplinary team and an established medical home is recommended
- Consider consultation with following specialists:
  - Infectious disease specialist for evaluation of other congenital infections
  - Neurologist by age 1 month
  - Ophthalmologist by age 1 month
  - Clinical geneticist
  - Early intervention and developmental specialists
  - Family and supportive services
- Possible consultations based on clinical findings of infant:
  - Endocrinologist
  - Lactation specialist, nutritionist, gastroenterologist, or speech or occupational therapist
  - Orthopedist, physiatrist, or physical therapist
  - Pulmonologist or otolaryngologist for concerns about aspiration



## KEY CHANGES BY GROUP:

### INFANTS WITH BIRTH DEFECTS CONSISTENT WITH CZS BORN TO MOTHERS WITH POSSIBLE ZIKA VIRUS EXPOSURE DURING PREGNANCY

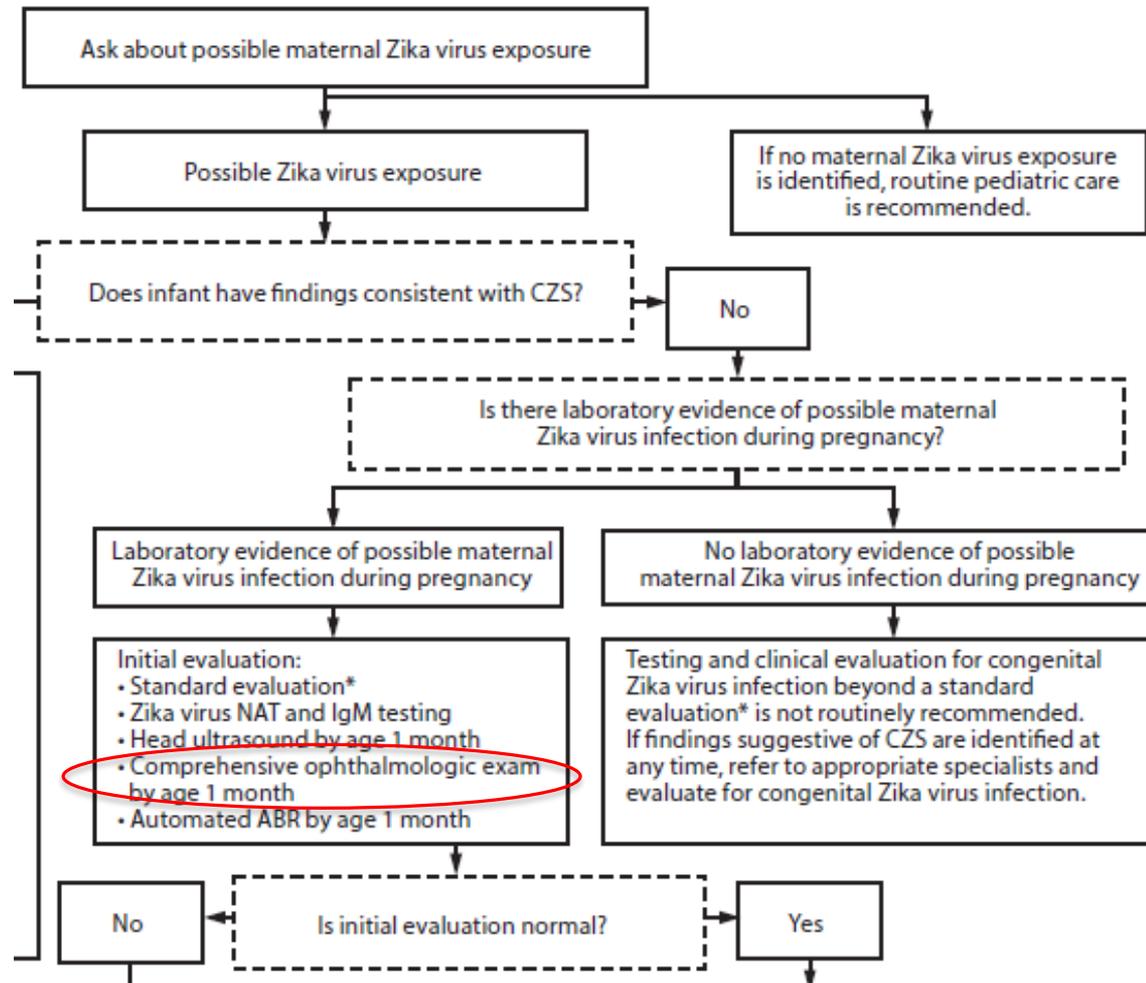
- Infants in this group no longer need:
  - Thyroid testing unless clinical symptoms indicate an issue
  - Diagnostic ABR test at 4-6 months if they passed newborn screening using automated ABR



## KEY CHANGES BY GROUP:

### INFANTS WITHOUT CLINICAL FINDINGS CONSISTENT WITH ZIKA BORN TO MOTHERS WITH LAB EVIDENCE OF EXPOSURE DURING PREGNANCY

- Infants should receive a comprehensive eye exam by an ophthalmologist by age 1 month (same as infants with indications of Zika)



**KEY CHANGES BY GROUP:  
INFANTS WITHOUT CLINICAL FINDINGS CONSISTENT WITH ZIKA BORN  
TO MOTHERS WITH EXPOSURE TO ZIKA BUT WITHOUT LAB EVIDENCE  
OF EXPOSURE DURING PREGNANCY**

- Includes infants born to mothers who:
  - Were never tested during pregnancy
  - Tested negative but still had possible exposure to Zika
- These infants require no testing or clinical evaluation beyond standard evaluation and routine preventative care
- Laboratory testing of these infants not routinely recommended
- If at any time findings consistent with CZS are made, appropriate referrals and evaluation should follow



# TESTING RECOMMENDATIONS FOR CONGENITAL ZIKA VIRUS INFECTION

- Testing is recommended for:
  - Infants with clinical findings consistent with CZS and
  - Infants without clinical findings consistent with CZS who were born to mothers with lab evidence of possible Zika virus exposure during pregnancy
- Concurrent Zika virus RNA nucleic acid testing (NAT) of serum and urine and Zika virus IgM testing of serum should be performed within a few days after birth, if possible



# INTERPRETING TEST RESULTS FOR CONGENITAL ZIKA VIRUS INFECTION

## Infant test result (serum, urine or cerebrospinal fluid)

NAT	IgM	Interpretation
Positive	Any result	Confirmed congenital Zika virus infection(1)
Negative	Nonnegative*	Probable congenital Zika virus infection(2)(4)
Negative	Negative	Congenital Zika virus infection unlikely(3)(4)

\*Nonnegative serology terminology varies by assay and might include “positive,” “equivocal,” “presumptive positive,” or “possible positive”

- (1) Distinguishing between congenital and postnatal infection is difficult in infants who live in areas with ongoing Zika virus transmission and who are not tested soon after birth. If timing of infection cannot be determined, evaluate infants as if they have congenital Zika virus infection.
- (2) If Zika virus plaque reduction neutralization test is negative, this suggests infant’s IgM test is a false positive.
- (3) Congenital Zika virus infection is unlikely if specimens are collected within first few days after birth and clinical evaluation is normal, but providers should remain alert for any new findings.
- (4) Lab results should be interpreted in context of timing of infection during pregnancy, maternal serology results, clinical findings consistent with CZS, and any confirmatory testing with plaque reduction neutralization testing.



# TESTING RECOMMENDATIONS FOR POSTNATAL ZIKA VIRUS INFECTION

- Guidance for testing and clinical management of infants and children with postnatal Zika virus infection is in line with recommendations for adults
  - Zika virus PCR and serologic testing is recommended during the first 2 weeks after symptom onset to diagnose postnatal Zika virus disease.
  - Serologic testing is recommended 2-12 weeks after symptom onset



# AAP CALL TO ACTION

- In the wake of recent hurricanes, pediatricians may see displaced families from areas with Zika outbreaks who need additional care
- CDC is urging providers to be vigilant for these women and children from Puerto Rico and the US Virgin Islands
- AAP News article, October 24, 2017:
  - <http://www.aappublications.org/news/2017/10/24/Zika102417>



# CDC RESOURCES

Health Care Providers Caring for Infants and Children.

<https://www.cdc.gov/zika/hc-providers/infants-children.html>

Pocket Guide: Evaluation for Infants with Possible Congenital Zika Infection.

<https://www.cdc.gov/zika/pdfs/pediatric-evaluation-follow-up-tool.pdf>

## Key Take Aways

### Updated Interim Guidance for the Diagnosis, Evaluation, and Management of Infants with Possible Congenital Zika Virus Infection

CDC updated its interim infant guidance to incorporate information from the recently published guidance for healthcare providers caring for pregnant women with possible Zika virus exposure, uncertainty regarding optimal laboratory testing for congenital Zika virus infection, and recognition of new findings in infants that might be related to Zika virus infection during pregnancy. CDC's updated interim guidance includes recommendations for the diagnosis, evaluation, and follow-up care of infants in three main groups.

#### Overview of changes

The updated recommendations emphasize the importance of pediatric healthcare providers assessing risk for congenital Zika virus infection, communicating closely with obstetrical providers, and remaining alert for any problems among infants without birth defects who were born to mothers with possible Zika virus exposure during pregnancy.

- To assist health care providers with clinical management decisions, the guidance defines three groups of infants:
  - Infants with birth defects consistent with congenital Zika syndrome born to mothers with possible Zika virus exposure during pregnancy (regardless of the mother's Zika virus test results).
  - Infants without birth defects consistent with congenital Zika syndrome born to mothers with laboratory evidence of possible Zika virus infection during pregnancy.
  - Infants without birth defects consistent with congenital Zika syndrome born to mothers with possible Zika virus exposure during pregnancy but without laboratory evidence of Zika virus infection during pregnancy.
- The new guidance provides updated information on interpreting laboratory testing results for infants.
- The updated guidance provides a review and clarification of the guidance for prenatal diagnosis (serial ultrasounds and amniocentesis).

The new guidance also provides updated information on infant follow-up care:

- Recommendations for vision and hearing screening have been updated.
- Some previously recommended screenings (e.g., thyroid screening, hearing screening at 4- to 6-months of age) are no longer recommended because of a lack of data on whether these screenings are needed.

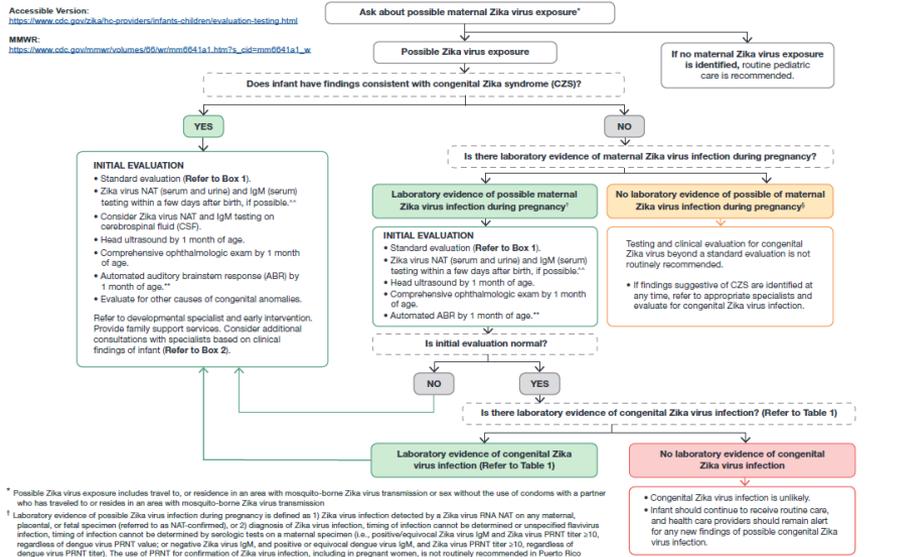



Centers for Disease Control and Prevention  
National Center on Birth Defects and Developmental Disabilities

## CDC's Response to Zika

### EVALUATION FOR INFANTS WITH POSSIBLE CONGENITAL ZIKA VIRUS INFECTION

Accessible Version: <https://www.cdc.gov/zika/hc-providers/infants-children/evaluation-testing.html>  
MMWR: [https://www.cdc.gov/mmwr/volumes/64/wr/mm6411a1.htm?\\_r=1&\\_c=mm6411a1\\_w](https://www.cdc.gov/mmwr/volumes/64/wr/mm6411a1.htm?_r=1&_c=mm6411a1_w)



**INITIAL EVALUATION**

- Standard evaluation (Refer to Box 1).
- Zika virus NAT (serum and urine) and IgM (serum) testing within a few days after birth, if possible.<sup>1,2</sup>
- Consider Zika virus NAT and IgM testing on cerebrospinal fluid (CSF).
- Head ultrasound by 1 month of age.
- Comprehensive ophthalmologic exam by 1 month of age.
- Automated auditory brainstem response (ABR) by 1 month of age.<sup>3</sup>
- Evaluate for other causes of congenital anomalies.

Refer to developmental specialist and early intervention. Provide family support services. Consider additional consultations with specialists based on clinical findings of infant (Refer to Box 2).

**INITIAL EVALUATION**

- Standard evaluation (Refer to Box 1).
- Zika virus NAT (serum and urine) and IgM (serum) testing within a few days after birth, if possible.<sup>1,2</sup>
- Head ultrasound by 1 month of age.
- Comprehensive ophthalmologic exam by 1 month of age.
- Automated ABR by 1 month of age.<sup>3</sup>

**Footnotes:**

<sup>1</sup> Possible Zika virus exposure includes travel to, or residence in an area with mosquito-borne Zika virus transmission or sex without the use of condoms with a partner who has traveled to or resides in an area with mosquito-borne Zika virus transmission.

<sup>2</sup> Laboratory evidence of possible Zika virus infection during pregnancy is defined as 1) Zika virus infection detected by a Zika virus RNA NAT on any maternal, placental, or fetal specimen (referred to as NAT-confirmed), or 2) diagnosis of Zika virus infection, timing of infection cannot be determined or unspecified flavivirus infection, timing of infection cannot be determined by serologic tests on a maternal specimen (i.e., positive/equivocal Zika virus IgM and Zika virus PRNT titer >10, regardless of dengue virus PRNT titer; or negative Zika virus IgM, and positive or equivocal dengue virus IgM, and Zika virus PRNT titer >10, regardless of dengue virus PRNT titer). The use of PRNT for confirmation of Zika virus infection, including in pregnant women, is not routinely recommended in Puerto Rico (<https://www.cdc.gov/zika/laboratory-testing-guidance.html>).

<sup>3</sup> This group includes women who were never tested during pregnancy as well as those whose test result was negative because of issues related to timing or sensitivity and specificity of the test. Because the latter issues are not readily discerned, all mothers with possible exposure to Zika virus during pregnancy who do not have laboratory evidence of possible Zika virus infection, including those who tested negative with currently available technologies, should be considered in this group.

