Prior Authorization Review Panel

CHC-MCO Policy Submission

A separate copy of this form must accompany each policy submitted for review.
Policies submitted without this form will not be considered for review.

Plan: PA Health & Wellness	**Submission Date: 11/1/2020**
Policy Number: PA.CP.MP.111	**Effective Date: 1/2018** **Revision Date: 10/2020**
Policy Name: Zika Virus Testing	**HC Approval Date:**

Type of Submission – Check all that apply:

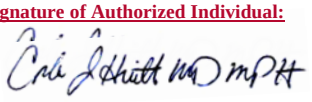
- ☐ **New Policy**
- ☐ **Revised Policy***
- ✓ **Retiring Policy** – *This option indicates the retirement of an active policy. If there is no indicated replacement, then "NONE" will be listed as the New/Replacement Policy.*
- ☐ **Annual Review – No Revisions**
- ☐ **Statewide PDL** - *Select this box when submitting policies for Statewide PDL implementation and when submitting policies for drug classes included on the Statewide PDL.*

***All revisions to the policy must be highlighted using track changes throughout the document.**

Please provide any changes or clarifying information for the policy below:

~~**Policy retired; Zika testing guidelines from CDC included in CP.CPC.03 Preventive Health and Clinical Practice Guidelines**~~

Policy retired; Zika testing guidelines from CDC included in CP.CPC.03 Preventive Health and Clinical Practice Guidelines

Name of Authorized Individual (Please type or print):	**Signature of Authorized Individual:**
Carla Huitt, MD MPH	

~~**Prior Authorization Review Panel**~~

~~CHC MCO Policy Submission~~

~~A separate copy of this form must accompany each policy submitted for review.~~
~~Policies submitted without this form will not be considered for review.~~

~~Plan: PA Health & Wellness~~	~~Submission Date:~~ 08/01/2018
~~Policy Number: PA.CP.MP. 111~~	~~Effective Date: 08/01/2018~~ ~~Revision Date: 07/2018~~
~~Policy Name: Zika Virus Testing~~	~~HC Approval Date: 08/14/18~~

~~Type of Submission – Check all that apply:~~

~~☒ New Policy~~
~~☐ Revised Policy*~~
~~☐ Annual Review – No Revisions~~
~~☐ Attestation of HC PARP Policy – *This option should only be used during Readiness Review for Community HealthChoices. The policy must be identical to the PARP approved policy for the HealthChoices Program, with the exception of revisions/clarifications adding the term "Community HealthChoices" to the policy.*~~

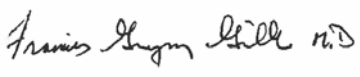
~~*All revisions to the policy must be highlighted using track changes throughout the document.~~

~~Please provide any changes or clarifying information for the policy below:~~

~~Policy Developed~~

~~References reviewed and updated. Coding reviewed.~~

~~CLEAN COPY ATTACHED. 12/04/2018 ALR~~

~~Name of Authorized Individual (Please type or print):~~ ~~Francis G. Grillo, MD~~	~~Signature of Authorized Individual:~~ 

Clinical Policy: Diagnostic Testing for Zika Virus

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Description
Zika virus is a flavivirus whose infection causes Zika virus disease. The virus is primarily transmitted by the bite of infected *Aedes* species mosquitoes. However, Zika virus can be sexually transmitted from an infected man to his sexual partners. While Zika virus infection is usually asymptomatic or causes mild illness, a causal relationship exists between prenatal Zika virus and microcephaly in the infant, as well as other serious brain anomalies. Diagnostic tests to evaluate for Zika virus infection include molecular and serologic testing. This policy describes the medical necessity requirements for these diagnostic tests.

***Note:** All references to possible exposure includes living in, traveling to, or having unprotected sex with someone who lives in or traveled to an area with risk of Zika.

Policy/Criteria

I. It is the policy of PA Health & Wellness® (PHW) that nucleic acid testing (NAT) using FDA Emergency Use Authorized tests, such as real time reverse transcriptase-polymerase chain reaction (rRT-PCR) testing, to evaluate for Zika virus infection, is **medically necessary** for any of the following:
- A. Symptomatic non-pregnant individuals with possible Zika virus exposure*, if < 14 days from symptom onset;
- B. Pregnant women with clinical symptoms consistent with Zika virus disease, with possible Zika exposure[2,4,6];
- C. Asymptomatic pregnant women with ongoing possible Zika virus exposure. Testing at least once per trimester should be considered if living in, or frequently traveling to, areas with active Zika virus transmission, unless a previous rRT-PCR test has been positive;[15]
- D. Asymptomatic pregnant women with a positive or equivocal MAC-ELISA test for Zika IgM, 2-12 weeks following potential Zika exposure. Testing should be conducted on all appropriate specimen types available;[13]
- E. Asymptomatic pregnant women who have recent possible Zika virus exposure (i.e., through travel or sexual exposure) but without ongoing possible exposure, if certain jurisdictions recommend testing for epidemiologic considerations such as seasonality;
- F. Amniocentesis specimens if amniocentesis is conducted for reasons other than Zika testing;
- G. Pregnant women who have recent possible Zika virus exposure and who have a fetus with prenatal ultrasound findings consistent with congenital Zika virus syndrome;
- H. Infants with birth defects consistent with congenital Zika syndrome, born to women with possible Zika exposure, ideally within 2 days of birth*;[9]
- I. Infants without birth defects consistent with congenital Zika syndrome, born to women with positive or inconclusive Zika virus testing, ideally within 2 days of birth
- J. Repeat testing if first result is inconclusive or equivocal.[4,9]

II. It is the policy of PHW that Zika IgM capture enzyme linked immunosorbent assay (MAC-ELISA) and subsequent plaque-reduction neutralization (PRNT)** testing for IgM nonnegative samples is **medically necessary** to evaluate for Zika virus infection for any of the following:
- A. Symptomatic non-pregnant individuals with possible Zika virus exposure, if < 14 days from symptom onset and rRT-PCR is negative, or if ≥ 14 days after symptom onset;

B. Symptomatic pregnant women with possible Zika virus exposure, within 4 days – 12 weeks of symptom onset*;[6, 7]
C. Asymptomatic pregnant women who may have had Zika virus transmission through travel or sexual contact, within 2 – 12 weeks of possible exposure**,** if certain jurisdictions recommend testing for epidemiologic considerations such as seasonality, even if rRT-PCR testing conducted within two weeks of exposure was negative;-[2, 4,6, 7, 11]
D. Pregnant women who have recent possible Zika virus exposure and who have a fetus with prenatal ultrasound findings consistent with congenital Zika virus syndrome;
E. Infants with birth defects consistent with congenital Zika syndrome, born to women with possible exposure to Zika virus, ideally within 2 days of birth*;[9]
F. Infants without birth defects consistent with congenital Zika syndrome, born to women with positive or inconclusive Zika virus testing, ideally within 2 days of birth;
G. Repeat testing is first result is inconclusive or equivocal.[4,9]

**Note: PRNT is not routinely recommended for testing any specimens in Puerto Rico.

III. It is the policy of PHW that PRNT testing is medically necessary to evaluate for Zika virus infection for any of the following:
A. Infants whose initial sample is IgM nonnegative and rRT-PCR results were negative, if PRNT was not performed on the mother's sample;
B. Infants ≥ 18 months old, whose initial (neonatal) sample was anti-Zika IgM nonnegative, with Zika-specific neutralizing antibodies detected by previous PRNT in either the mother's or infant's sample.[13]
C. Infants ≥ 18 months old, whose initial (neonatal) sample was negative by both MAC-ELISA and rRT-PCR,[13] or who was not tested at birth, and both (1 and 2):
    1. Infant's mother had laboratory evidence of possible Zika virus infection during pregnancy;
    2. The infant has clinical findings suggestive of congenital Zika virus syndrome, including any of the following:[13]
        a. Microcephaly;
        b. Abnormal neuroimaging findings such as intracranial calcifications, decreased brain parenchymal volume, ventriculomegaly and extra-axial fluid, abnormal gyral patterns, or hypoplasia of brain structures;
        c. Neurologic abnormalities such as congenital limb contractures, dysphagia, sensorineural hearing loss, epilepsy, abnormal tone or movement, including marked hypertonia and extrapyramidal movement;
        d. Ocular abnormalities such as microphthalmia, coloboma, intraocular calcifications, optic nerve hypoplasia and atrophy, macular disc scarring, or cortical visual impairment
D. IgM testing for Zika virus is ambiguous (e.g. inconclusive, equivocal, and indeterminate), and retesting has not resolved the ambiguity.[4]

IV. It is the policy of PHW that evaluation, including rRT-PCR, histopathologic examination, and immunohistochemical staining of placental and fetal tissue specimens, is **medically necessary** for any of the following:

A. Testing of placental tissue after live birth in symptomatic pregnant women and women with infants with possible Zika virus–associated birth defects, without a definitive diagnosis of laboratory-confirmed Zika virus infection during pregnancy;
B. Testing of placental tissue after live birth in asymptomatic pregnant women who have recent possible Zika virus exposure and a fetus or infant with possible Zika virus–associated birth defects;
C. The evaluation of fetal loss and stillbirth if the woman had recent possible Zika virus exposure.[10]

V. It is the policy of health plans affiliated with PHW that diagnostic tests to evaluate for Zika virus infection are considered **experimental/investigational** under any of the following circumstances:
A. Testing for non-pregnant asymptomatic individuals;
B. Preconception screening.

Background
Zika virus is a flavivirus that was originally discovered from a sentinel rhesus monkey in the Zika Forest in Uganda during a study of yellow fever in 1947.[1] Since its discovery, few cases of the infection had been reported until outbreaks in the State of Yap, Federated States of Micronesia, and French Polynesia in 2007 and 2013, respectively.[1] Zika virus was first identified in the Americas in March 2015 in Brazil.[1] A summary of the 2016 Zika virus epidemic reported 5,168 cases of noncongenital Zika virus disease, with diagnoses in 49 states and the District of Columbia, although 48% were reported from three states: Florida, New York, and California.[14] 95% of cases occurred in travelers returning from areas with Zika virus transmission, 4% of cases were locally transmitted, and 1% were acquired through sexual transmission, laboratory transmission, or an unknown route (1 person).[14] Compared to the first 8 months of 2016, the first 8 months of 2017 had significantly fewer reported cases of Zika virus - 4,205 vs. 331.

Among recent cases, Zika virus is primarily transmitted by the bite of infected *Aedes* species mosquitoes – most commonly through *Ae. aegypti* and possibly through *Ae. albopictus* mosquitoes.[3] Documented sexual transmission of the Zika virus has occurred from infected males to their sexual partners,[4] and from females to male sexual partners.[14] At the present time, testing for risk for sexual transmission of Zika virus is of uncertain value unless either partner is symptomatic, and the couple is wishing to conceive, because of the limited understanding of the shedding of the virus in the male genitourinary tract.[4]

The virus can also be transmitted from mother to fetus during any trimester of pregnancy.[3] Although most persons infected with Zika virus are asymptomatic, the most common symptoms of Zika virus disease are fever, rash, joint pain, and conjunctivitis; these symptoms usually last for up to one week.[2] No antiviral medication is available, and supportive care is recommended. A causal relationship exists between prenatal Zika virus infection and congenital microcephaly, as well as other serious brain and eye anomalies.[5] Preliminary research has found that the risk of congenital birth defects is greatest with Zika virus infection in the first and second trimesters.[12]

Furthermore, a temporal and geographical observation has been made between Zika virus infection and Guillain-Barre syndrome.[1] Continued investigations attempt to understand the link between Zika virus infection and Guillain-Barre syndrome.

The U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization to allow the use of CDC's diagnostic tools to assess Zika virus infection. The diagnostic tests for evaluating for Zika virus infection include NAT and serologic testing. Most tests that have received FDA emergency use authorization are rRT-PCR tests for the *in vitro* detection of Zika virus nucleic acids. The CDC's Trioplex rRT-PCR assesses Zika, dengue, and chikungunya viruses simultaneously. According to "Revised diagnostic testing for Zika, dengue, and chikungunya viruses in US Public Health Laboratories," viral RNA can be identified in serum during the first 7 days of these illnesses,[7] and additional information from the CDC states that urine samples can be collected less than 14 days after the onset of symptoms for rRT-PCR testing.[8]

Serologic testing includes the Zika IgM MAC-ELISA and PRNT tests for the respective detection of viral specific IgM and neutralizing antibodies to Zika virus. While virus specific IgM antibodies may be detectable ≥ 4 days after onset of illness, serum collected within 7 days of illness onset may not have detectable levels of these antibodies.[7] IgM antibodies to Zika virus remain present for approximately 2-12 weeks, although there are reports of prolonged IgM responses with Zika virus infection, as with other flaviviruses.[13] Furthermore, Zika antibodies may be detectable in pregnant women months after infection with the virus, making it difficult to determine whether they were infected before or after conception.[13] Importantly, an IgM positive result from the MAC-ELISA cannot differentiate between the presence of Zika and dengue viruses, and thus is indicative of the presence of a flavivirus.[7] Therefore, PRNT assays can be used to discriminate between cross reacting antibodies in cases that are positive for IgM.[7]

Laboratory evidence of maternal Zika virus infection includes (1) Zika virus RNA detected by RT-PCR in any clinical specimen or (2) positive Zika virus IgM with confirmatory neutralizing antibody tiers that are ≥4 fold higher than dengue virus neutralizing antibody titers in serum by PRNT.[10] Testing is inconclusive if Zika virus neutralizing antibody tiers are < 4 fold higher than dengue virus neutralizing antibody titers.[10]

Reviews, Revisions, and Approvals	Date	Approval Date
Policy developed.	05/18	
References reviewed and updated. Coding reviewed.	10/19	
Policy retired; Zika testing guidelines from CDC included in CP.CPC.03 Preventive Health and Clinical Practice Guidelines	10/2020	

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