

# Fact Sheet-Zika MAC-ELISA Results

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## Fact Sheet for Health Care Providers: Interpreting Zika MAC-ELISA Results

February 26, 2016

### Dear Health Care Provider:

The U.S Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) to authorize the use of the Centers for Disease Control and Prevention's (CDC) Zika IgM antibody capture ELISA (Zika MAC-ELISA) for the *in vitro* qualitative detection of human IgM antibodies to Zika virus. It is intended for use in sera or cerebrospinal fluid (CSF) when submitted with a patient-matched serum sample from individuals meeting CDC Zika clinical and epidemiological criteria for testing in qualified laboratories designated by the CDC. The test is intended for use as part of CDC's algorithm for Zika testing.

FDA issued this EUA based on data submitted by CDC to FDA, and on the U.S. Secretary of Health and Human Services' (HHS) declaration that circumstances exist to justify the emergency use of *in vitro* diagnostic tests for the detection of Zika virus and Zika virus infection. This EUA will terminate when the HHS Secretary's declaration terminates, unless FDA revokes it sooner.

The information in this Fact Sheet is to inform you of the significant known and potential risks and benefits of the emergency use of the Zika MAC-ELISA. For more information on this EUA, please see FDA's website at <http://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm>.

### Why is this test needed at this time?

As of February 20, 2016, active Zika virus transmission is occurring in 29 countries and territories in the Americas. Among cases identified in 2015-16, it is believed that most transmission has occurred through mosquito bites and from mother to fetus. Sexual transmission has also been documented.

At this time, there are no FDA approved/cleared tests available that can detect Zika virus in clinical specimens in the United States. Therefore, CDC has developed this test to detect evidence of Zika virus infections in human sera and CSF. Current information on Zika virus infection for health care providers, including case definitions, is available at <http://www.cdc.gov/zika/hc-providers/index.html>. All information and guidelines, including those on Zika virus laboratory testing, may change as more data is gathered on this virus. Please check CDC's Zika Virus website regularly for the most current information (<http://www.cdc.gov/zika/index.html>).

If Zika virus infection is suspected based on current CDC clinical and/or epidemiological criteria, the Zika MAC-ELISA may be ordered. Please contact your state or local health department to facilitate testing. Anti-Zika IgM is typically detectable starting near day 4 post onset of symptoms and is reliably detectable for approximately 12 weeks following infection.

The results should be used in conjunction with clinical signs and symptoms, epidemiological information, and travel history to diagnose recent Zika virus infection. This test is authorized for use with serum, and with CSF (when submitted with a patient-matched serum sample).

As of February 20, 2016, serum is the priority specimen for collection and testing. Specimens should be collected with appropriate infection control precautions and according to the manufacturer's instructions for the specimen collection device. Sera should be collected in serum separator tubes and centrifuged after collection to reduce the likelihood of hemolysis.

### **What are the symptoms of Zika virus infection?**

Most patients with Zika virus infection exhibit no symptoms. Symptomatic patients typically experience a mild illness characterized by fever, rash, joint pain, and/or conjunctivitis. The incubation period is unclear, but likely to be several days. Symptoms generally resolve on their own within a week.

Some reports from Brazil, a country with a large number of Zika virus cases, indicate a possible association between Zika virus infection in pregnant women and increased incidence of microcephaly (a birth defect characterized by small head size and impaired cranial and neural development in neonates) as well as other poor pregnancy outcomes. Only limited information is available regarding the association between Zika virus infection and microcephaly. The likelihood of a connection between the Zika virus infection and microcephaly, and if there is a connection, the point at which Zika virus infection may impact fetal development during pregnancy, are unknown.

There are also reports from Brazil of a possible association between Zika virus infection and increased incidence of Guillain-Barré syndrome.

As of February 20, 2016, there have been more than 90 confirmed cases of Zika virus infection in the United States. Most, but not all of these individuals have a recent travel history to areas with ongoing transmission. Public health officials have determined that Zika virus poses a potential public health emergency.

### **What does it mean if the specimen tests positive for recent Zika virus infection?**

A positive test for Zika virus from the Zika MAC-ELISA indicates that anti-Zika IgM antibodies were detected in the sera or CSF of the patient. Confirmation of Zika MAC-ELISA positive or equivocal results requires additional testing by CDC or by qualified laboratories designated by CDC and in consultation with CDC, using the CDC-issued algorithm.

False positive serological results are possible (see next paragraph). Laboratory test results should always be considered in the context of clinical observations and epidemiologic information in making a final diagnosis and patient management decisions. Any positive test result for Zika virus infection should be reported to your local and state health departments. In the United States and its territories, positive results must be reported to CDC. For guidelines on Zika virus, please refer to <http://www.cdc.gov/zika/hc-providers/index.html>.

Positive and equivocal results are not definitive for diagnosis of Zika virus infection. False positive results may occur in some patients with recent, closely-related flavivirus infections, such as dengue infections. In patients who have received yellow fever or Japanese encephalitis vaccination, cross-reactive antibodies in both the IgM and neutralizing antibody assays may make it difficult to identify which flavivirus is causing the patient's current illness. It is possible that the Zika MAC-ELISA may generate positive results in patients with a history of non-Zika flavivirus infections. In the event of a false positive result, risks to patients could include any or all of the following: the impaired ability to detect and receive appropriate medical care for the true infection causing the symptoms, in the case of pregnant women, an unnecessary increase in the monitoring of a woman's pregnancy, or other unintended adverse effects.

It should be emphasized that the identification of possible Zika virus infection in a pregnant woman does not provide any definitive information about the state of health of the fetus. Many questions remain about the association between Zika virus infection in a mother and the impact to the child, such as timing, likelihood, and relevance of symptomatic vs. asymptomatic infection. Detection of Zika virus infection in the mother does not mean there is definite harm to the child.

### **What does it mean if the specimen tests negative for recent Zika virus infection?**

A negative Zika MAC-ELISA result does not rule out Zika virus infection, particularly if testing is conducted less than 4 days after onset of symptoms (before IgM levels are expected to become detectable) or more than 12 weeks after the infection is thought to have occurred (as IgM levels are expected to drop). As with any test, providers must consider the patient's likelihood of exposure and the possibility of false laboratory results when making treatment or other patient management decisions. The possibility of a false negative result should especially be considered if the patient's recent exposures or clinical presentation are consistent with Zika virus infection and diagnostic tests for other causes of illness are negative. Conversely, a negative result in an asymptomatic patient with a lower likelihood of exposure (e.g., a short term traveler to an affected area) may suggest the patient is not infected.

Please refer to CDC guidance for Health Care Providers Caring for Pregnant Women and Women of Reproductive Age with Possible Zika Virus Exposure:

[http://www.cdc.gov/mmwr/volumes/65/wr/mm6505e2er.htm?s\\_cid=mm6505e2er.htm\\_w](http://www.cdc.gov/mmwr/volumes/65/wr/mm6505e2er.htm?s_cid=mm6505e2er.htm_w)

It is also important to note that Zika virus infection is not the sole suspected cause of microcephaly in neonates.

### **Reporting Adverse Events**

You should report adverse events, including problems with test performance or results, to MedWatch at [www.fda.gov/medwatch](http://www.fda.gov/medwatch), by submitting a MedWatch Form 3500 (available at [http://www.fda.gov/medwatch/safety/FDA-3500\\_fillable.pdf](http://www.fda.gov/medwatch/safety/FDA-3500_fillable.pdf)) or by calling 1-800-FDA-1088.

Centers for Disease Control and Prevention  
Zika MAC-ELISA Emergency Use Authorization

**Pregnant patients should receive the Fact Sheet for Pregnant Women: Understanding Results from the Zika MAC-ELISA. All other patients should receive the Fact Sheet for Patients: Understanding Results from the Zika MAC-ELISA.**

Contact Information for the Manufacturer:  
CDC Emergency Operations Center (EOC)  
1600 Clifton Road  
Atlanta, Georgia, USA, 30329  
Office phone: **CDC EOC (770-488-7100)**

Any significant new findings observed during the course of the emergency use of the Zika-MAC ELISA will be made available at <http://www.cdc.gov/zika/index.html>.

## **Fact Sheet for Patients: Understanding Results from the Zika MAC-ELISA**

**February 26, 2016**

**Dear Patient:**

**If you are pregnant, please ask your doctor for the Fact Sheet for Pregnant Women.**

You are being given this Fact Sheet because your blood or cerebrospinal fluid (CSF) was tested for evidence of Zika virus infection. This testing is being done because you have symptoms of Zika virus infection and/or you live in or have traveled to areas with ongoing Zika virus transmission. The test being used for your specimen(s) is called the Zika MAC-ELISA, which is a laboratory test designed to help detect Zika virus infection in humans.

This Fact Sheet contains information to help you understand the risks and benefits of using of the Zika MAC-ELISA. If possible, you may want to discuss with your health care providers the risks and benefits described in this Fact Sheet.

### **What is Zika virus Infection?**

Zika virus infection is caused by the Zika virus and is most often spread to people through mosquito bites. Spread from mother to fetus and through sex has also been documented. Since 2015, a large number of Zika virus infection cases have been reported in several South and Central American countries. Cases have also been reported in the United States among persons who have traveled recently to these countries.

Most people who are infected with Zika virus do not have any symptoms. Those that do usually have mild illness with symptoms that may include fever, rash, joint pain, or redness of the eyes. These symptoms often resolve on their own within a week.

There have been reports from Brazil of a possible link between Zika virus infection and an illness that can cause temporary paralysis (Guillain-Barré syndrome). There have also been reports of birth defects and other poor pregnancy outcomes in pregnant women with Zika virus infection.

### **What is the Zika MAC-ELISA?**

The Zika MAC-ELISA is a laboratory test to detect proteins the human body makes to fight a Zika virus infection. These proteins, called antibodies, appear in the blood starting 4-5 days after the start of illness and last for up to 12 weeks. In some people, they are present for longer than 12 weeks.

The Zika MAC-ELISA has not been cleared or approved by the U.S. Food and Drug Administration (FDA). However, FDA has authorized the emergency use of this test under an Emergency Use Authorization (EUA).

### **Why was my sample tested using the Zika MAC-ELISA?**

Your blood or CSF sample(s) are being tested because you have symptoms that resemble Zika virus infection or because you live in or have traveled recently to a place where Zika virus infection is known to occur. The sample(s) collected from you will be tested using the Zika MAC-ELISA to help determine whether you may have been recently infected with Zika virus. The test results, along with other information, could help your doctors make decisions about how to take care of you.

### **What are the known risks and benefits of the CDC Zika MAC-ELISA?**

Besides possible discomfort during sample collection, there is a risk that the test result will be incorrect (see next paragraphs for more information). The benefit of having this test is that the results of this test, along with other information, can help your health care provider make decisions about how to take care of you.

### **If this test is positive for Zika virus, does it mean that I have Zika virus infection?**

If you have a positive result with the Zika MAC-ELISA, it is likely that you recently were infected with the Zika virus. There is a chance that this test can give a positive result that is wrong; this is called a false positive result. There are some other very closely related viruses (such as dengue virus) that can cause the human body to produce antibodies that may cause the test to be positive.

If your result from this test is positive or equivocal (unclear), you should ask your healthcare provider or health department if additional testing has or will be carried out to rule out a false positive result. It is important that you work with your health care provider or health department to help you understand the next steps you should take.

### **If this test is negative, does it mean that I do not have Zika virus infection?**

If you have a negative test, it does not necessarily mean that you have not been infected with Zika virus. If your sample was collected just after you became ill, it is possible that your body had not yet had enough time to make antibodies for the test to measure. If the sample was collected more than 12 weeks after your illness, it is possible that your body has already fought off the virus and the amount of antibodies is so low that they cannot be measured. Your health care provider will help you to interpret your test results and work with you to continue to monitor your health.

### **What is an Emergency Use Authorization (EUA)?**

An EUA is a tool that FDA can use to allow the use of certain medical products for emergencies based on scientific data. The U.S. Secretary of Health and Human Services (HHS) has declared that circumstances exist to allow the emergency use of authorized diagnostic tests for Zika virus infection, such as the Zika MAC-ELISA.

At this time, there are no FDA approved/cleared alternative tests available that detect Zika virus infection. FDA has authorized the emergency use of the Zika MAC-ELISA to test for antibodies to Zika virus in blood and CSF. Use of this test is authorized only for the duration of the potential emergency, unless it is terminated or revoked by FDA sooner.

**How can I learn more?**

Information about Zika virus and any significant new findings observed during the course of the emergency use of the Zika MAC-ELISA will be made available at:  
<http://www.cdc.gov/zika/index.html>

Please also contact your health care provider if you have any questions.

## **Fact Sheet for Pregnant Women: Understanding Results from the Zika MAC-ELISA**

**February 26, 2016**

### **Dear Madam:**

You are being given this Fact Sheet because your blood or cerebrospinal fluid (CSF) was tested for evidence of Zika virus infection. This testing is being done because you have symptoms of Zika virus infection and/or you live in or have traveled to areas with ongoing Zika virus transmission. The test being used for your specimen(s) is called the Zika MAC-ELISA, which is a laboratory test designed to help detect Zika virus infection in humans.

This Fact Sheet contains information to help you understand the risks and benefits of using the Zika MAC-ELISA. If possible, you may want to discuss with your health care providers the risks and benefits described in this Fact Sheet.

### **What is Zika virus Infection?**

Zika virus infection is caused by the Zika virus and most often spread to people through mosquito bites. Spread from mother to fetus and through sex has also been documented. Since 2015, a large number of Zika virus infection cases have been reported in several South and Central American countries. Cases have also been reported in the United States among persons who have traveled recently to these countries.

Most people who are infected with Zika virus do not have any symptoms. Those that do usually have mild illness with symptoms that may include fever, rash, joint pain, or redness of the eyes. These symptoms often resolve on their own within a week.

There have been reports from Brazil of a possible link between Zika virus infection and an illness that can cause temporary paralysis (Guillain-Barré syndrome). There have also been reports of birth defects and other poor pregnancy outcomes in pregnant women with Zika virus infection. The connection between Zika virus infection and birth defects is not well understood. Zika virus infection in a mother does not definitely mean a poor pregnancy outcome will occur. However, pregnant women who have had a Zika virus infection should be monitored more closely by their health care providers throughout their pregnancy.

### **What is the Zika MAC-ELISA?**

The Zika MAC-ELISA is a laboratory test to detect proteins the human body makes to fight a Zika virus infection. These proteins, called antibodies, appear in the blood starting 4-5 days after the start of illness and last for up to 12 weeks. In some people, they are present for longer than 12 weeks.

The Zika MAC-ELISA has not been cleared or approved by the U.S. Food and Drug Administration (FDA). However, FDA has authorized the emergency use of this test under an Emergency Use Authorization (EUA).

### **Why was my sample tested using the Zika MAC-ELISA?**

Your blood or CSF sample(s) are being tested because you have symptoms that resemble Zika virus infection and/or because you live in or have traveled recently to places where Zika virus infection is known to occur. The sample(s) collected from you will be tested using the Zika MAC-ELISA to help determine whether you may have been recently infected with Zika virus. The test results, along with other information, could help your doctor make decisions about how to take care of you and better monitor your pregnancy.

### **What are the known risks and benefits of the CDC Zika MAC-ELISA?**

Besides possible discomfort during sample collection, there is still a risk that the test result will be incorrect (see next paragraphs for more information). The benefit of having this test is that the results of this test, along with other information, can help your health care provider make decisions about how to take care of you and your baby.

### **If this test is positive for Zika virus, does it mean that I have Zika virus infection?**

If you have a positive result with the Zika MAC-ELISA, it is likely that you recently were infected with the Zika virus. There is a chance that this test can give a positive result that is wrong; this is called a false positive result. There are some other very closely related viruses (such as dengue virus) that can cause the human body to produce antibodies that may cause the test to be positive.

If your result from this test is positive or equivocal (unclear), you should ask your health care provider or health department if additional testing has or will be carried out to rule out a false positive result. It is important that you work with your health care provider or health department to help you understand the next steps you should take. They will also work closely with you to monitor the health and development of your child.

### **If this test is positive for Zika virus, does it mean that my child will have a birth defect?**

No, not necessarily. First, the link between Zika virus infection and poor pregnancy outcomes, such as birth defects, is not well understood. Having Zika virus infection does not necessarily mean harm to the child. Second, this test can give positive results when the patient has a history of infection with some other viruses (see above). While the results of this test are not conclusive, a positive or equivocal test result may lead your doctors to conduct additional testing or to follow your pregnancy more closely.

### **If this test is negative, does it mean that I do not have Zika virus infection?**

If you have a negative test, it does not necessarily mean that you have not been infected with Zika virus. If your sample was collected just after you became ill, it is possible that your body had not yet had enough time to make antibodies for the test to measure. If the sample was collected more than 12 weeks after your illness, it is possible that your body has already fought off the virus and the amount of antibodies is so low that they cannot be measured. Your health care provider will help you to interpret your test results and work with you to continue to monitor your health and the health of your baby.

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