

# ZIKA VIRUS TESTING GUIDANCE, UPDATED 7/20/2016

## Section 1: Which patients should be offered testing?

### SUMMARY OF CATEGORIES OF PATIENTS WHO SHOULD BE TESTED FOR ZIKA

- 1) Pregnant women who traveled to a Zika-affected area (see link to current list in Footnote 1 below). Must have been pregnant during travel or became pregnant within 8 weeks after travel.
  - If the woman had a Zika-like illness (fever, rash, arthralgia, or conjunctivitis) during travel or within 2 weeks after travel, or developed pregnancy complications (miscarriage, abnormal fetal ultrasound, etc.) or Guillain-Barré Syndrome (GBS), **test if** illness occurred within the last 3 months
  - If the woman did not develop a Zika-like illness, **test if** she returned from travel 2-12 weeks ago
  - **CONSULT THE PENNSYLVANIA DEPARTMENT OF HEALTH (DOH)** at 877-PA-HEALTH if fetal problem has been noted (e.g. abnormal ultrasound, fetal loss, etc.)<sup>2</sup>
- 2) Pregnant women who have a sex partner who traveled to a Zika-affected area<sup>1</sup>, and EITHER the pregnant woman or her partner developed a Zika-like illness (fever, rash, arthralgia, or conjunctivitis), pregnancy complications, or Guillain-Barré Syndrome (or her partner has tested positive for Zika).
  - If the partner was acutely ill, illness must have occurred during travel or within 2 weeks after travel; **test if** the woman was or became pregnant during the 6 month period after her partner's symptoms resolved
  - If the partner did NOT have a Zika-like illness, **test if** the woman was or became pregnant during the 8 week period after her partner's last day of travel, and also became ill within 10 weeks of partner's travel
  - **CONSULT DOH** (877-PA-HEALTH) if fetal problem has been noted (e.g. abnormal ultrasound, fetal loss, etc.)<sup>2</sup>
- 3) Men or non-pregnant women who traveled to a Zika-affected area<sup>1</sup>, and developed a Zika-like illness (fever, rash, arthralgia, or conjunctivitis) during travel or within 2 weeks after travel, or have been diagnosed with Guillain-Barré Syndrome.
  - **Test if** illness occurred within the last 3 months; antibodies to Zika virus are not reliably detected after this time period
- 4) Men or non-pregnant women who had a sex partner **-or-** a household member who traveled to a Zika-affected area<sup>1</sup>, and BOTH the patient and the traveler developed a Zika-like illness (fever, rash, arthralgia, or conjunctivitis) or Guillain-Barré Syndrome (or the traveler has tested positive for Zika).
  - If the traveler was acutely ill, illness must have occurred during travel or within 2 weeks after travel
  - **Test if** the patient's illness developed within the last 3 months, and within 6 months after traveler's illness if traveler was a sex partner, or within 45 days after traveler's illness if traveler was a household member
  - Note: If a household contact of a traveler tests positive for Zika, it may indicate local mosquito transmission.
- 5) **CONSULT DOH** (877-PA-HEALTH) regarding testing of infants and children.

#### FOOTNOTES:

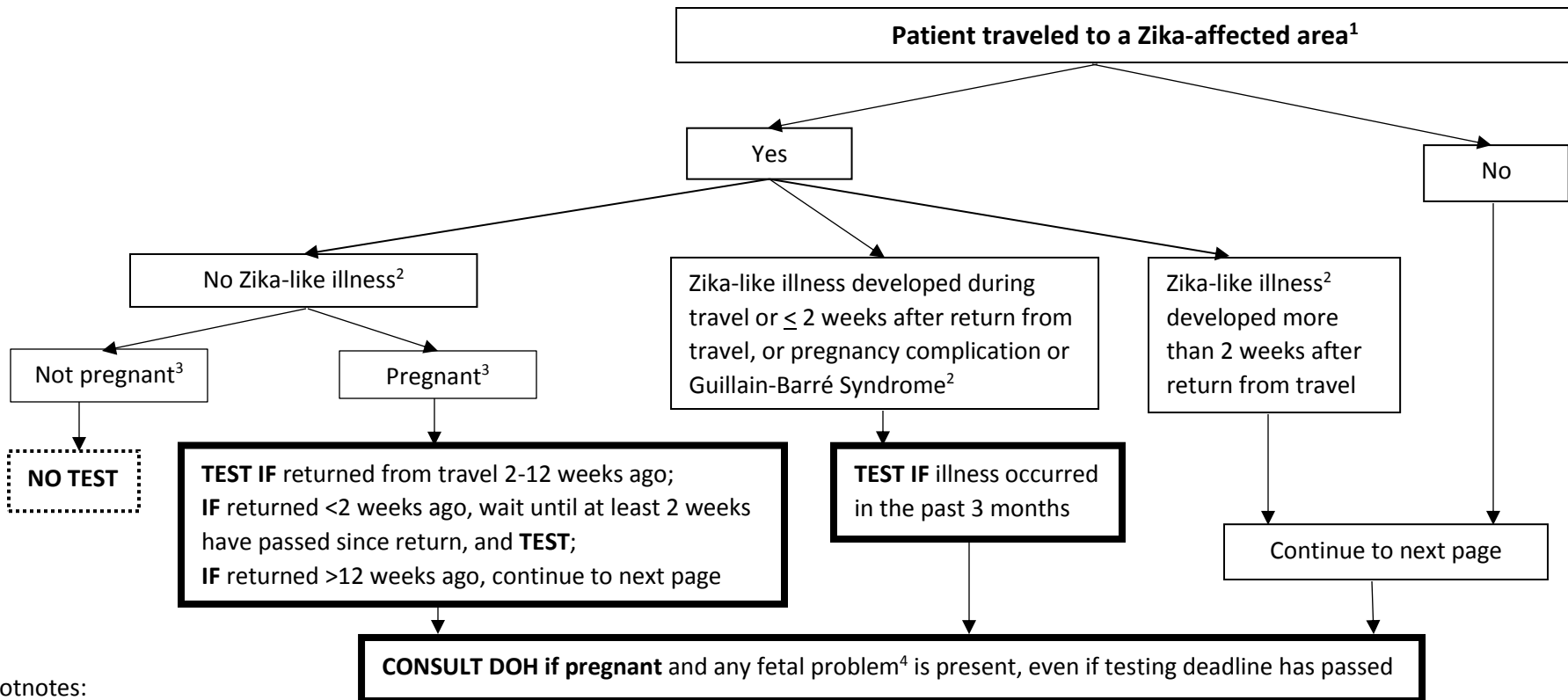
1. The current list of Zika-affected countries is at <http://wwwnc.cdc.gov/travel/page/zika-travel-information>. If patient's travel destination was near but not in a listed country, testing may still be indicated. Please call your local health department or DOH (877-PA-HEALTH) for consultation. Dengue and chikungunya virus testing is also recommended as there is considerable overlap of symptoms and affected countries for all three viruses.

2. Also see <http://www.cdc.gov/mmwr/volumes/65/wr/mm6512e2.htm> (Interim Guidelines for Health Care Providers Caring for Pregnant Women and Women of Reproductive Age with Possible Zika Virus Exposure).

**Detailed testing flow chart follows on the next two pages**

# ZIKA VIRUS TESTING GUIDANCE, UPDATED 7/20/2016

## Section 1: Which patients should be offered testing: Detailed testing flow chart



Footnotes:

<sup>1</sup>See <http://wwwnc.cdc.gov/travel/page/zika-travel-information>. **Please note:** if patient's travel destination not listed, but in same area as affected countries, testing may still be indicated. Please consult DOH (877-PA-HEALTH) if there are questions about whether patient travel is considered relevant or not.

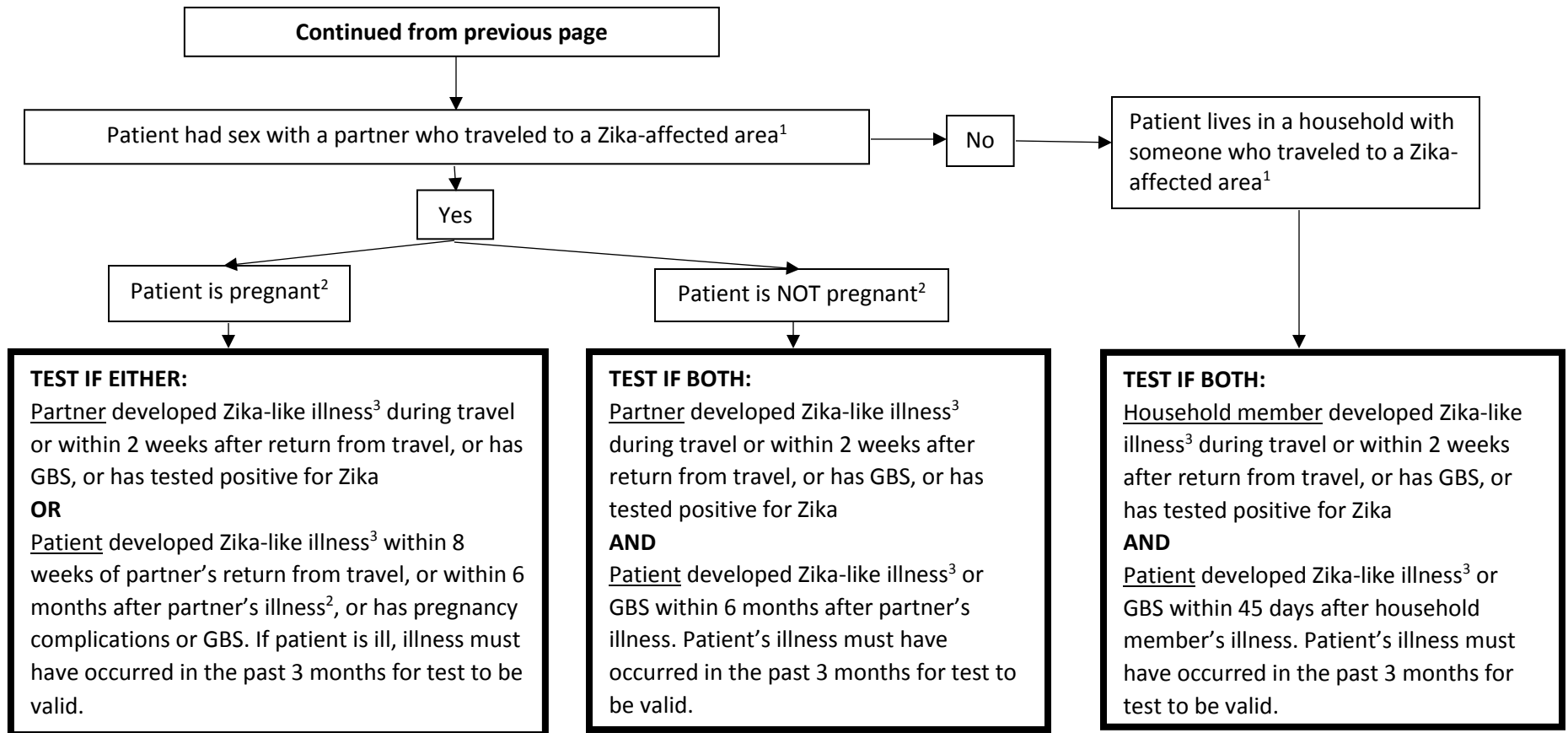
<sup>2</sup>Zika-like illness is defined as having **1 or more** of the following: fever, maculopapular rash, arthralgia, or conjunctivitis, with onset within 2 weeks of exposure. Pregnancy complications (such as miscarriage or abnormal fetal ultrasound) and Guillain-Barré Syndrome (GBS) are also associated with Zika infection. Dengue and chikungunya virus testing is also recommended as there is considerable overlap with symptoms and affected countries for all three viruses.

<sup>3</sup>Include women who were pregnant during travel and women who became pregnant up to 8 weeks after the last day of travel. **Pregnant women are considered asymptomatic if they do not meet the definition of symptomatic (defined below).**

<sup>4</sup>If pregnancy complications are present, **or if the patient is an infant or child**, consult with local health department or DOH by calling 877-PA-HEALTH. Also see <http://www.cdc.gov/mmwr/volumes/65/wr/mm6512e2.htm> (Interim Guidelines for Health Care Providers Caring for Pregnant Women and Women of Reproductive Age with Possible Zika Virus Exposure).

# ZIKA VIRUS TESTING GUIDANCE, UPDATED 7/20/2016

## Section 1: Which patients should be offered testing: Detailed testing flow chart, continued



### Footnotes:

<sup>1</sup>See <http://wwwnc.cdc.gov/travel/page/zika-travel-information>. **Please note:** if patient's travel destination not listed, but in same area as affected countries, testing may still be indicated. Please consult DOH (877-PA-HEALTH) if there are questions about whether patient travel is considered relevant or not.

<sup>2</sup>For women whose partner was asymptomatic, include those who became pregnant within 8 weeks of their partner's last day of travel. If partner was symptomatic, include those who became pregnant up to 6 months after partner's symptoms resolved.

<sup>3</sup> Zika-like illness is defined as having **1 or more** of the following: fever, maculopapular rash, arthralgia, or conjunctivitis, with onset within 2 weeks of exposure. Pregnancy complications (such as miscarriage or abnormal fetal ultrasound) and Guillain-Barré Syndrome are also associated with Zika infection. Dengue and chikungunya virus testing is also recommended as there is considerable overlap with symptoms and affected countries for all three viruses.

# ZIKA VIRUS TESTING GUIDANCE, UPDATED 7/20/2016

## Section 2: Which specimens should be collected, and which tests should be ordered?

**TABLE 1. General guidance regarding specimen type(s) and recommended testing for patients with suspected Zika virus infections**

Has patient had a Zika-like illness <sup>1</sup> ?	How many days have passed since the patient's symptom onset date?	Specimen Type(s)	Recommended Test	Where to Obtain Testing
No, but patient is <u>pregnant</u> and was potentially exposed to Zika	No symptoms, but in order to find antibodies to Zika, sample must be collected 2-12 weeks after patient's last possible day of exposure (e.g. last day of travel)	Serum	Antibody (Zika and dengue IgM ELISA with reflex to plaque reduction neutralization test [PRNT])	Only available via DOH. Call 877-PA-HEALTH to arrange testing
Yes, patient has/had a Zika-like illness <sup>1</sup>	≥4 days and ≤ 12 weeks	Serum	Antibody (Zika and dengue IgM ELISA with reflex to plaque reduction neutralization test [PRNT])	Only available via DOH. Call 877-PA-HEALTH to arrange testing
Yes, patient has/had a Zika-like illness <sup>1</sup>	<14 days	Serum, paired <u>with</u> urine	Molecular (real-time reverse transcriptase polymerase chain reaction [rRT-PCR])	Commercially available via LabCorp and ViraCor
Yes, patient has/had a Zika-like illness <sup>1</sup>	<7 days	Serum	Molecular (real-time reverse transcriptase polymerase chain reaction [rRT-PCR])	Commercially available via Quest, LabCorp and ViraCor. Also available via DOH; call 877-PA-HEALTH to arrange testing.

**Footnote for Section 3:**

<sup>1</sup>Zika-like illness is defined as having **1 or more** of the following: fever, maculopapular rash, arthralgia, conjunctivitis, **with onset occurring during or within 2 weeks** after travel to an area with Zika virus transmission, or complications of pregnancy or Guillain-Barré Syndrome. Dengue and chikungunya virus testing is also recommended as the symptoms are very similar to Zika and most countries with Zika also have dengue and chikungunya.

# ZIKA VIRUS TESTING GUIDANCE, UPDATED 7/20/2016

## Section 3: How are test results interpreted?

**TABLE 1. Interpretation of results of molecular testing for suspected Zika virus infection.**

Zika virus RNA (rRT-PCR)	Interpretation
Detected	Current Zika virus infection
Not Detected	No evidence of current Zika virus infection

### Notes for Section 3, table 1:

**Abbreviations:** rRT-PCR = Real-time reverse transcriptase polymerase chain reaction

- rRT-PCR (molecular) testing should be performed for patients possibly exposed to Zika virus who have recent symptoms consistent with Zika virus infection.
- Providers who request molecular testing for Zika virus infection from a commercial testing laboratory are advised to retain and store in a refrigerator (2-8°C) an aliquot of the patient's serum for possible additional Zika testing. If the rRT-PCR is negative and the specimen was collected  $\geq 4$  days after onset of symptoms, forward the aliquot to DOH for Zika antibody testing. If the rRT-PCR is negative and the specimen was collected  $\leq 4$  days after onset of symptoms, antibodies may not have had time to appear. Therefore, another serum specimen should be collected within 12 weeks of symptom onset and submitted to DOH for Zika antibody testing.
- For specimens that are rRT-PCR negative from the commercial laboratory and no stored serum specimen is available, another serum specimen should be collected within 12 weeks of symptom onset for Zika IgM ELISA testing.
- Appropriate samples for molecular testing are serum samples collected  $< 7$  days and urine samples collected  $< 14$  days after symptom onset. Urine must always be collected and sent with a patient-matched serum specimen.

# ZIKA VIRUS TESTING GUIDANCE, UPDATED 7/20/2016

## Section 3: How are test results interpreted?

**TABLE 2. Interpretation of results of antibody testing for suspected Zika virus infection**

(See notes on following page)

	Zika IgM ELISA and dengue IgM ELISA	Zika PRNT	Dengue PRNT	Interpretation
<b>Preliminary Results</b>	Positive for Zika virus AND negative for dengue virus	pending	pending	Presumptive recent Zika virus infection
	Positive for dengue virus AND negative for Zika virus	pending	pending	Presumptive recent dengue virus infection
	Positive for Zika virus AND positive for dengue virus	pending	pending	Presumptive recent flavivirus virus infection
	Equivocal (either or both assays)	pending	pending	Equivocal results
	Inconclusive in one assay AND inconclusive or negative in the other	pending	pending	Inconclusive results
<b>FINAL RESULTS</b>	Positive or equivocal (either assay)	≥10	<10	Recent Zika virus infection
	Positive or equivocal (either assay)	<10	≥10	Recent dengue virus infection
	Positive or equivocal (either assay)	≥10	≥10	Recent flavivirus infection; due to cross-reactivity or possible co-infection, specific virus cannot be identified
	Inconclusive in one assay AND inconclusive or negative in the other	≥10	<10	Evidence of Zika virus infection; timing cannot be determined
	Inconclusive in one assay AND inconclusive or negative in the other	<10	≥10	Evidence of dengue virus infection; timing cannot be determined
	Inconclusive in one assay AND inconclusive or negative in the other	≥10	≥10	Evidence of flavivirus infection; specific virus and timing cannot be determined
	Any result (either or both assays)	<10	<10	No evidence of Zika virus or dengue virus infection
	Negative for Zika virus AND negative for dengue virus	N/A	N/A	No evidence of recent Zika virus or dengue virus infection

# ZIKA VIRUS TESTING GUIDANCE, UPDATED 7/20/2016

## Section 3: How are test results interpreted?

### Notes for Section 3, table 2:

**Abbreviations:** ELISA = enzyme-linked immunosorbent assay; IgM = immunoglobulin M antibodies; PRNT = plaque reduction neutralization test.

- For persons with suspected Zika virus disease, Zika virus real-time reverse transcription–polymerase chain reaction (rRT-PCR) should be performed on serum specimens collected <7 days after onset of symptoms, and on urine specimens collected <14 days after onset of symptoms.
- In the absence of rRT-PCR testing, negative IgM or neutralizing antibody testing in specimens collected <7 days after illness onset might reflect collection before development of detectable antibodies and does not rule out infection with the virus for which testing was conducted.
- Zika IgM positive result is reported as “presumptive positive” to denote the need to perform confirmatory PRNT.
- Report any positive or equivocal IgM Zika or dengue results to state or local health department.
- To resolve false-positive results that might be caused by cross-reactivity or nonspecific reactivity, presumptive positive Zika IgM results should be confirmed with PRNT titers against Zika, dengue, and other flaviviruses to which the person might have been exposed. In addition, equivocal and inconclusive results that are not resolved by retesting also should have PRNT titers performed to rule out a false-positive result.

Adapted from:

Rabe IB, Staples JE, Villanueva J, et al. Interim Guidance for Interpretation of Zika Virus Antibody Test Results. MMWR Morb Mortal Wkly Rep.

ePub: 3 June 2016. DOI: <http://www.cdc.gov/mmwr/volumes/65/wr/mm6521e1.htm>



## Zika Virus Laboratory Submission Form

Approved by:

Public Health Official Name/Date

**Patient Information:**

Last name:		First Name:		MI:
DOB:	Age:	Sex:(Circle one)		
____/____/____		Male	Female	
Street Address:				
City:		State:	Zip:	County:
Specimen Source:	Collection Date:	Patient ID:		

**Submitter Information:** Add additional submitters on back of the form

Name:				
Street Address:		City:	State:	Zip Code:
Telephone:		Fax:		

**Reason for Testing and Travel History:** All information must be completed or testing will NOT be performed

<input type="checkbox"/> Patient traveled to Zika-affected area	<input type="checkbox"/> Patient is symptomatic and did not travel to Zika-affected area, but had <b>sexual contact</b> with a person who did travel to affected area	<input type="checkbox"/> Patient is symptomatic and did not travel to Zika-affected area, but is a <b>household contact</b> of a person who did travel to affected area
<input type="checkbox"/> Other: Country (or countries):		
Travel Dates: _____/_____/_____ to _____/_____/_____		

**Clinical Information:** All information must be completed or testing will NOT be performed

Pregnancy Status (if female)	Yes	No	Gestational Age:		EDD:			
Has patient experienced any symptoms?	Yes	No	Date of Onset: _____/_____/_____					
Fever (≥38°C or 100°F)	Yes	No	Unknown		Arthralgia	Yes	No	Unknown
Conjunctivitis	Yes	No	Unknown		Rash	Yes	No	Unknown
Mosquito Bite	Yes	No	Unknown		Guillain-Barre syndrome	Yes	No	Unknown
Other: (List)								
Ever vaccinated for:		<input type="checkbox"/> Yellow fever <input type="checkbox"/> Japanese encephalitis <input type="checkbox"/> Tickborne encephalitis <input type="checkbox"/> Dengue fever						
Past history of Arbovirus infection (such as West Nile or dengue):								

Submit specimens on cold pack(s) directly to the address below. Call the laboratory if you have any questions.