DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Centers for Disease Control
and Prevention (CDC)

Memorandum

Att. E 3

Date July 28, 2017

From Jerrell Little
IRB-B Administrator
Human Research Protection Office

Subject IRB Approval of Amendment to CDC Protocol 7005, "Determining the Prevalence and Duration of Persistent Zika Virus RNA in Pregnant Women and Congenitally exposed Infants in Puerto Rico in 2017-2018" (Expedited)

To Margaret Honein, PhD, MPH
NCCBBBD/DCDD

CDC's IRB-B has reviewed and approved your request to amend protocol 7005, "Determining the Prevalence and Duration of Persistent Zika Virus RNA in Pregnant Women and Congenitally exposed Infants in Puerto Rico in 2017-2018". These changes included the following:

Protocol Changes

1. A CDC Dengue Branch study co-investigator has been removed. Three study co-investigators from UPR were added to the study. These UPR co-investigators will play a key role in the recruitment of study participants (p. 9).

2. We added text in the background section of the study summary and body of the protocol related to IgM testing (p. 10,14)

3. We modified study objectives to include IgM detection in blood (p. 10,15)

4. The specimen collection schedule has been modified in light of emerging evidence that pregnant women may have intermittent viral shedding. Under the study methods, we modified, the frequency and time points for sample collection of pregnant women if they were to test ZIKV negative in two consecutive tests: 1) deleted text about no longer collecting samples after a pregnant woman has tested ZIKV negative in two consecutive tests; 2) substituted text to reflect that pregnant woman who test negative by rRT-PCR on two subsequent collection dates will be followed monthly through 3 months post-delivery and blood and urine samples will be collected monthly and tested for ZIKV until 1 month post-delivery (p. 11,17,43).

5. Under the study methods, we modified, the frequency of infant visits (no change in specimen collection). All infants will continue to have study visits until six months of age. Once infants

test ZIKV negative in two consecutive tests they will continue to have monthly study visits in which only study forms will be completed or until six months of age. (p. 11,18,24,33,44)

6. We deleted text in the study methodology related to reporting of cases to the Zika Active Pregnancy Surveillance System (ZAPSS), as women should already be reported to ZAPSS since eligibility criteria for the study is a positive ZIKV PCR test (p. 12).

7. We added a study hypothesis for persistent detection of ZIKV RNA in pregnant women and its association with adverse pregnancy outcomes, regardless of the presence of IgM (p. 16)

8. We changed the term “study sites” to “University of Puerto Rico” (p. 17, 19, 20, 22, 23)

9. We added two new study definitions; 1) duration of ZIKV IgM persistence (pregnant women); 2) Duration of ZIKV IgM persistence (live-born infants) (p. 19)

10. We have re-worded the study period to reflect that sample collection, laboratory testing and patient follow-up will continue for another 9 months until all pregnant women have been followed through 3 months post-delivery and their congenitally exposed infants have been followed through 6 months of age. (p. 20)

11. We updated Table 9.3.1 “Proposed Timelines for Study” to reflect new start dates based on local IRB approvals (p. 20)

12. We have added text under for the infant cohort to reflect that infants born to women enrolled in the pregnancy cohort will be enrolled when the pregnant woman and the infant’s father sign the infant informed consent form, which can be done at any time following the enrollment of the pregnant woman but must be done prior to delivery (p. 24, 27,47)

13. We deleted text which explained the process of infant follow-up if they were to be followed by a pediatrician outside of the University of Puerto Rico, and per UPR requirements added text on conducting infant follow-up at the University of Puerto Rico only (p. 20, 33)

14. We deleted text on specific sample collection and storage practices as these are not relevant in the body of the protocol (p. 33,34,35)

15. We have changed the amount of urine that will be collected from pregnant woman on table 9.8.3.1 from a 5 mL maximum to a 60 mL maximum. This is a correction to the actual maximum amount that can be collected. The standard urine cup that will be used collects 120 mL total, and should be filled no more than half-way (i.e. 60 mL and not 5mL) (p. 36)

16. We updated Table 9.8.7.1 “List of study objectives with their respective outcomes” to align to modified objectives (p. 38)

17. We shortened the text on study identifier’s as most of the text was not needed in the body of the protocol (p. 40)

18. Appendix 2 and Appendix 3 were replaced with a new simplified Appendix 2 “Summary of Study Visits” (p. 51)

19. We updated appendix 5 “List of study objective with related outcomes and statistical tests” to become appendix 4, and updated appendix 4 to reflect the modifications made to the study objectives (p. 56)

Informed Consent Form changes

Pregnant woman informed consent form

1. We have added Dr. Carmen Zorrilla as the investigating physician in charge of the study at UPR (p. 1)
2. We have added the full name of the University of Puerto Rico (p.1)
3. We have deleted unnecessary text on how long the pregnant woman is expected to participate in the research study (p. 2)
4. We have re-worded what will happen during the enrollment visit to make it more comprehensible for the pregnant women reading the consent form (p. 2)
5. We have added text that specifies what type of information the questionnaire at the first study visit will collect (p. 2)
6. For better legibility of the informed consent by the pregnant woman we have deleted all measurements related to blood and urine collection given in milliliters (mL) and have replaced with teaspoons of blood and urine will be collected (p. 3,5).
7. We have corrected a previous error on the equivalent in teaspoons of 7.5 mL from 6 teaspoons to 1.5 teaspoons (p. 3,5)
8. We have deleted the word routine visits and added the word follow-up visits (p. 3)
9. We have deleted the section on laboratory visits (p. 4)
10. We have added a table that explains the summary of study visits (p. 4)
11. We have added a table that explains the laboratory sample volume and type (p. 5)
12. We have added required UPR IRB consent form text box on UPR IRB regulations (p.5)
13. We have modified the text for Post- delivery visits which explains follow-up visits for all women and follow-up visits for women who continue to be positive (p. 5)
14. We have deleted excessive language on medical records (p. 6)
15. We have added required UPR IRB consent form language on what will happen if the pregnant woman gets injured as a result of this study (p. 7)
16. We have added required UPR IRB consent form language regarding additional information on confidentiality (p. 8)
17. We have deleted the section on “will it cost me anything to be part of this research study” (p. 10)

18. We have moved the section " what are my privacy rights", "will I be paid to take part of this study" to be below the section on "additional information on confidentiality" (p. 10)
19. We have updated the study contact information to be that of the study staff in the UPR clinic (p. 10)
20. We have removed signature lines for "sample storage and future testing" and "contacting research subjects for future studies" and have just kept the initial boxes (p. 13, 14)
21. We have added the UPR IRB consent form signature page (p. 15)

Infant informed consent form

1. We have added the full name of the University of Puerto Rico (p.1)
2. We have deleted unnecessary text on how long the infant is expected to participate in the research study (p. 2)
3. We have added text on what type of information will be collected from the infant at delivery (p.3)
4. We have deleted the word enrollment visit and added the word study visit (p. 2)
5. We have added a table that explains the summary of study visits (p. 3)
6. We have added a table that explains the laboratory sample volume and type (p. 3)
7. We have deleted the sections "first study visit" and "routine study visits" (p. 4)
8. We have deleted two bullet points that were part of the possible risks related to this study (p. 5)
9. We have re-positioned the bullet points for the privacy of infant information (p. 6)
10. We have added required UPR IRB consent form language regarding additional information on confidentiality (p. 6)
11. We have added required UPR IRB consent form language on what will happen if the infant gets injured as a result of this study (p. 8)
12. We have deleted the section on "will it cost me anything to have my infant be part of this research study" (p. 8)
13. We have moved the section " what are my privacy rights" to be below the section on "additional information on confidentiality" (p. 8)
14. We have updated the study contact information to be that of the study staff in the UPR clinic (p. 9)
15. We have added a section on Birth and Neonatal Sample Sharing Authorization (p. 11)
16. We have removed signature lines for "sample storage and "future testing" and have just kept the initial boxes (p. 12)
17. We have added the UPR IRB consent form signature page (p. 13)

The action was reviewed in accordance with the expedited review process outlined in [45 CFR 46.110(b)(1), under categories 1 and 2, minor changes to previously approved research during the period (of one year or less) for which approval is authorized].

Reminder: IRB approval of protocol #7005 will still expire on 4/18/2018.

Any problems of a serious nature must be brought to the immediate attention of the CDC IRB, and any proposed changes to the protocol should be submitted as an amendment to the protocol for CDC IRB approval before they are implemented.

If you have any questions, please contact your National Center Human Subjects Contact or the CDC Human Research Protection Office (404) 639-7570 or e-mail: huma@cdc.gov.

cc:
CGH Human Subjects