The Johns Hopkins Medical Institutions
(The Johns Hopkins Hospital
The Johns Hopkins Bayview Medical Center, etc.)

APPROVED
AS MODIFIED
Nov 29, 2017
WIRB®

RESEARCH SUBJECT INFORMATION AND CONSENT FORM	
TITLE:	Evaluation of the Efficacy of the live attenuated tetravalent dengue vaccine against DENV-2 and DENV-3 Challenge

This consent form contains important information to help you decide whether to participate in a research study.

The study staff will explain this study to you. Ask questions about anything that is not clear at any time. You may take home an unsigned copy of this consent form to think about and discuss with family or friends.

- **Being in a study is voluntary – <u>your choice</u>.**
- **If you join this study, you can still <u>stop at any time</u>.**
- **<u>No</u> one can <u>promise</u> that a study will help you.**
- **Do not join this study unless all of your <u>questions</u> are <u>answered</u>.**

After reading and discussing the information in this consent form, you should know:

- Why this research study is being done;
- What will happen during the study;
- Any possible benefits to you;
- The possible risks to you;
- Other options you could choose instead of being in this study;
- How your personal health information will be treated during the study and after the study is over;
- Whether being in this study could involve any cost to you; and
- What to do if you have problems or questions about this study.

<u>Please read this consent form carefully.</u>

The Johns Hopkins Medical Institutions
(The Johns Hopkins Hospital
The Johns Hopkins Bayview Medical Center, etc.)

APPROVED
AS MODIFIED
Nov 29, 2017
WIRB®

RESEARCH SUBJECT INFORMATION AND CONSENT FORM

TITLE:	EVALUATION of the EFFICACY OF THE LIVE ATTENUATED TETRAVALENT DENGUE VACCINE AGAINST DENV-2 AND DENV-3 CHALLENGE
PROTOCOL NO.:	CIR 323 WIRB® Protocol #20172389
SPONSOR:	OCRPRO/NIAID/NIH
INVESTIGATOR:	Anna P. Durbin, MD Rm. 251 624 N. Broadway Baltimore, Maryland 21205 United States
SITE(S):	Center for Immunization Research Johns Hopkins Bloomberg School of Public Health 624 N. Broadway Baltimore, Maryland 21205 United States
STUDY-RELATED PHONE NUMBER(S):	Anna P. Durbin, MD 410-614-4736 (office) 410-283-6522 (24-hour pager) 410-340-6852 (cell phone)

This consent form may contain words that you do not understand. Please ask the study doctor or the study staff to explain any words or information that you do not clearly understand. You may take home an unsigned copy of this consent form to think about it or discuss it with family or friends before making your decision.

STUDY PURPOSE

The purpose of this research study is to test the ability of a candidate dengue virus vaccine called TV003 to prevent people from getting infected with one dengue challenge virus called rDEN2Δ30-7169 or another dengue challenge virus called rDEN3Δ30. Vaccines are given to try to prevent infection or disease. Immunogenicity means we are trying to find out how well the vaccine TV003 can cause a response in your immune system and if that response will protect you from getting infected with dengue later on.

BACKGROUND INFORMATION

The manufacture of the study vaccine includes use of a genetically modified virus. Please ask the study doctor any questions you have about this.

The Johns Hopkins Medical Institutions
(The Johns Hopkins Hospital
The Johns Hopkins Bayview Medical Center, etc.)

APPROVED
AS MODIFIED
Nov 29, 2017
WIRB®

Infection with a dengue virus can make people very sick and sometimes people will die from it. Every year, lots of people (about 100 million) get sick from dengue. Some people will get a severe (very bad) dengue infection. Some of these people will have severe bleeding under the skin and inside the body. This is called dengue hemorrhagic fever or DHF. Some people will have a very low blood pressure and go into shock. This is called dengue shock syndrome or DSS.

Dengue virus is spread to people by mosquitoes. This virus is found in warm places like the Caribbean, South America, Central America, Asia, Africa, and parts of Australia. The virus is not found very often in the United States. From 1977 to 2004, a total of 3,806 suspected cases of dengue were reported in the United States. Almost all of these cases came into the United States from other countries. It has been seen 6 times in the last 25 years in south Texas. It may have come from dengue outbreaks in northern Mexico and in Hawaii. In 2009 and 2010, there were 28 cases of dengue contracted in the Florida Keys. In 2013, 16 cases of dengue were reported in Florida.

There are 4 types of dengue virus (types 1, 2, 3, and 4). Infection with one of these types protects you against only that one dengue virus type. Therefore, people can have more than one type of dengue infection.

The more serious forms of the infection (DHF and DSS, described above) occur more often in people who were previously infected with one dengue virus, but then later become infected by another, different dengue virus.

We want to test a vaccine called TetraVax-DV TV003 (we call it TV003) to see if it can protect you from getting infected with a dengue virus called rDEN2Δ30-7169 or another dengue virus called rDEN3Δ30. TV003 is considered experimental and has not been approved by the U.S. Food and Drug Administration (FDA). This vaccine was developed by scientists at the National Institutes of Health (NIH). TV003 is made up of 4 dengue vaccine viruses:

- rDENlΔ30 (a dengue 1 vaccine)
- rDEN2/4Δ30(ME) (a dengue 2 vaccine)
- rDEN3Δ30/31 -7164 (a dengue 3 vaccine)
- rDEN4Δ30 (a dengue 4 vaccine)

rDEN2Δ30-7169 and rDEN3Δ30 are live dengue 2 (DENV-2) and dengue 3 viruses (DENV-3), respectively. We will refer to rDEN2Δ30-7169 and rDEN3Δ30 as rDENV-2 and rDENV-3, respectively in this consent document. They are genetically-modified dengue viruses developed by scientists at the NIH and have not been approved by FDA. We want to study the effect of TV003, rDENV-2, and rDENV-3 on people who have no previous exposure to flaviviruses. Examples of flaviviruses include dengue viruses, West Nile virus, yellow fever virus, and Zika virus. We also want to see if people who get TV003 are protected against becoming infected with rDEN2 or rDENV-3 when that virus is given one month later.

A total of 60 subjects will be enrolled in this study. Of these, 40 adult subjects will receive the TV003 vaccine and 20 will receive the placebo in the first vaccination (see Treatment

Assignments table below). A placebo is a substance that looks like the vaccine but does not have any vaccine product in it; this placebo is like salt water. You will have approximately a 66% chance of getting the vaccine and approximately a 33% chance of getting the placebo. Before the end of the study, you will be told in writing if you were given the vaccine or a placebo. **One month after vaccination, 30 subjects will receive** rDENV-2 and 30 subjects will receive rDENV-3.

All of the vaccine viruses used to make TV003 were made from live dengue viruses that were made weaker by removing certain parts of the virus. We want to combine the 4 dengue vaccine viruses to see if they are safe in healthy adults when given together as TV003 in a single dose. This is called a tetravalent vaccine.

We also want to see if TV003 can make good germ fighters (antibodies) against all 4 dengue virus types. rDENV-2 and rDENV-3 were made from live dengue viruses. They have been used as challenge viruses in controlled human infection models for dengue to see how well the vaccine works. We also want to see if rDENV-2 and rDENV-3 are safe in people and if they can make good antibodies against dengue virus type 2 or 3, respectively.

One month after you receive the TV003 vaccine or placebo, you will receive a dose of rDENV-2 or rDENV-3. All subjects will get rDENV-2 or rDENV-3 at one month to help us learn different things. The things we want to learn are: 1) If giving TV003 first can prevent subjects who receive the vaccine, followed by a “challenge” dose of rDENV-2 or rDENV-3, from getting a rDENV-2 or rDENV-3 infection and rash. 2) For those subjects who got a placebo first, we want to further test the safety of rDENV-2 and rDENV-3 and see if they make good germ fighters to dengue virus type 2 or 3, respectively. This will help learn more about how our body protects us against dengue.

All of the vaccines used to make the TV003 mixture have already been tested individually in research participants. These vaccines were given alone in 10 different studies at the Center for Immunization Research and showed no serious side effects. Two of these vaccines have been tested in subjects who had already gotten a different dengue vaccine at the Center for Immunization Research. There were no serious side effects. The TV003 mixture has already been given to more than 160 people.

The most common side effect in subjects who got TV003 was a mild rash. Approximately 62% of the people who received TV003 had a mild rash. A mild rash was the only noticeable side effect that occurred more frequently in those who received TV003 than in those who received placebo. Nobody who got TV003 had a fever or a dengue-like illness.

rDENV-2, one of the viruses that may be given at one month, has previously been given to more than 50 people at the Center for Immunization Research. rDENV-3, the other virus that may be given at one month, has previously been given to about 30 people at the Center for Immunization Research. Neither of these viruses caused dengue-like illness in any subject. The most common side effect was a rash that occurred in 80% (8 out of 10) of subjects who got the rDENV-2 or rDENV-3. The rash was mildly itchy in about 25% of subjects who got a rash.

The Johns Hopkins Medical Institutions
(The Johns Hopkins Hospital
The Johns Hopkins Bayview Medical Center, etc.)

APPROVED
AS MODIFIED
Nov 29, 2017
WIRB®

If you enroll in this study, you will receive the vaccine TV003 or the placebo when the study starts. The vaccine or placebo will be given as a shot under the skin in your upper arm. You will be randomly assigned to either the vaccine or placebo group and neither you nor the staff will know which you received.

One month later, you will receive either rDENV-2 or rDENV-3 as a shot under the skin in your upper arm. You will be randomly assigned to receive either the rDENV-2 or rDENV-3 and neither you nor the staff will know which you received. Approximately 3 months after you receive rDENV-2 or rDENV-3, you will be told if you got TV003 or if you got placebo at your first shot and you will be told if you received rDENV-2 or rDENV-3. This information is available to the study doctor at any time if needed in an emergency. The table below describes what vaccine you will get at each vaccination visit.

Treatment Assignments

# subjects	Vaccination #1 (Day 0)	Challenge (Day 28)
40	TV003	rDENV-2 or rDENV-3
20	Placebo	rDENV-2 or rDENV-3

STUDY PROCEDURES

Entering the Study
There may be reasons why you cannot take part in this study. The staff will discuss these with you. Before entering the study, you will have blood and urine tests to see if you are in good health. This is called the "screening visit."

To find out about your health, you will have:

- A complete medical history
- A physical examination
- Several laboratory tests, including a complete blood count (CBC)
  - A blood clotting test (PT/PTT)
  - Blood chemistries (including tests of your kidneys, liver, and muscle)
  - Pregnancy test (women only)
  - A urinalysis
  - HIV test (a test for the virus that causes AIDS)
  - Hepatitis B test (a test for a virus that hurts the liver)
  - Hepatitis C test (a test for a virus that hurts the liver)
  - Blood tests to see if you have ever had or have ever been exposed to dengue virus or other similar viruses

You will be told of any abnormal results that may require follow up by your private physician. Based on the results of these screening tests, you may be invited to participate in the study.

The Johns Hopkins Medical Institutions
(The Johns Hopkins Hospital
The Johns Hopkins Bayview Medical Center, etc.)

APPROVED
AS MODIFIED
Nov 29, 2017
WIRB®

If your tests show that you have HIV, the study doctor must notify the local health department. A separate HIV testing education form explains how positive results are reported to the local health department. Counseling will also be made available to you to discuss your positive HIV test.

If your tests show that you have hepatitis B or hepatitis C virus, the study doctor must notify the health department. The health department will be notified in writing of the following information: laboratory test date, type of test, result of test, your name, age, sex, and address.

Women

Women who are pregnant or breast-feeding will not be able to take part in the study. The effects of the vaccine on the unborn fetus and breast-feeding infant are not known. All women who can become pregnant must agree to use very good birth control during this study (reliable methods include: hormonal birth control, condoms with spermicide, diaphragm with spermicide, surgical sterilization, intrauterine device, intrauterine coil, and abstinence [no sexual intercourse]). Discuss with the study doctor what birth control you may use while in the study. A pregnancy test will be done during the screening visit and on the day of vaccination. This test must be negative for the staff to give you the vaccine. A pregnancy test will also be done on several visits after you receive the vaccine.

If you become pregnant during the study, tell the staff right away. We may ask you to continue to come in for regular study visits and/or ask you to agree to let us keep checking on you until the end of your pregnancy. We will ask you to sign a medical information release form so that we can learn about your pregnancy and, if applicable, your baby's health at birth.

Length of Study

You will take part in this study for about 7 months. In the unlikely event that a Serious Adverse Event was not resolved at the end of the study, you may be followed somewhat longer, typically until it is resolved or stabilized.

It is very important for you to come to all of your study visits. If you are unable to return to the center for study visits, you may be asked to have blood drawn at a local Quest Lab so that we can follow you for safety. It is very important that you understand the requirements of the study before you decide to sign this consent form and join the study.

Study Visits

Inoculation Days (Study Day 0 and Study Day 28):

On the day you get the inoculation, your visit will last about 2 to 3 hours. You will have your blood drawn and receive a physical examination. If you are a female of child bearing potential, we will do a pregnancy test. We will make sure the test is negative before we give you the vaccine or challenge virus; a positive test will exclude you from getting inoculated. Ways to prevent pregnancy will be discussed with you.

You will be asked to stay at least 30 minutes after each inoculation to check if you feel sick or have any side effects. We will give you a thermometer and a card to record your temperatures. You will be told how to take your temperature and how to record it.

The Johns Hopkins Medical Institutions
(The Johns Hopkins Hospital
The Johns Hopkins Bayview Medical Center, etc.)

APPROVED
AS MODIFIED
Nov 29, 2017
WIRB®

Follow-up Visits:
You will be asked to come to the clinic on the days shown in the following table.

STUDY VISITS VACCINATION #1 (TV003 OR Placebo)

Study Day	0	4	6	8	10	12	14	16	21
Vaccinate	X								
Physical exam	X	X	X	X	X	X	X	X	X
Medical History	X								
Vital signs	X	X	X	X	X	X	X	X	X
Pregnancy Test	X								X
Temperature review		X	X	X	X	X	X	X	X
Blood Draw	X	X	X	X	X	X	X	X	X
Oral Fluid Collection	X						X		

STUDY VISITS FOLLOWING CHALLENGE WITH rDEN2Δ30-7169 or rDEN3Δ30

Study Day	28	32	34	36	38	40	42	44	49	56	84	118	208
Challenge	X												
Physical exam	X	X	X	X	X	X	X	X	X	X	X	X	X
Medical History	X												
Vital signs	X	X	X	X	X	X	X	X	X	X	X	X	X
Pregnancy Test	X									X	X	X	X
Temperature review		X	X	X	X	X	X	X	X				
Blood Draw	X	X	X	X	X	X	X	X	X	X	X	X	X
Oral Fluid Collection	X						X			X	X	X	X

Each follow-up visit will take about 30 minutes. At each visit we will perform some or all of the following:

- Ask you questions about how you are feeling
- Do a pregnancy test (for women)
- Review your temperatures
- Draw your blood
- Give you a physical examination

You will have blood drawn at each study visit. Each time we will take less than 5 tablespoons of blood. The total amount of blood to be taken from you during the 7-month study is a little more than 2 pints. We will not take more blood than the Red Cross recommends over the 2-month period after both inoculations.

The blood we draw at your visits will be tested to:

- Check on your health after vaccination
- Look for vaccine virus in your blood
- See if your body has made antibodies (germ fighters) against the vaccine virus
- Test markers on your white blood cells and genes and look for proteins in your blood that may be important for your body to fight dengue infection

The Johns Hopkins Medical Institutions
(The Johns Hopkins Hospital
The Johns Hopkins Bayview Medical Center, etc.)

APPROVED
AS MODIFIED
Nov 29, 2017
WIRB®

While you are in the study we will ask you to:

- Take your temperature (check for a fever) 3 times a day, every day, for 16 days after each inoculation. We will ask you to write down these temperatures and bring them to your visits.
- Contact the staff or study doctor before taking medication or receiving any vaccines. This includes medicines that you buy without a prescription like herbal or over-the-counter medicines, and medicines that affect the immune system, such as prednisone.
- Wait to get routine licensed vaccines, like the flu shot (or nasal spray flu vaccine), until after study Day 56 (about 4 weeks after challenge). This may put you at more risk for illness such as the flu. We will ask you to tell us if you do get a licensed vaccine during the study.
- Not join another clinical study. You may not receive any other experimental drugs or vaccines while you are in this study.
- Not donate any blood products.
- Avoid drinking large amounts of alcohol.
- Tell the staff if you receive any blood products.

We may take photographs of your skin or the injection site where you get the vaccine. These pictures will help us follow the skin rash and any other changes that may occur during the study. Your face or any other identifying marks will not be in the picture. You can refuse to have a photograph taken.

In addition:

- It is important that you tell the staff if you become sick or feel bad. We may ask you to come to the clinic so that we can check on you.
- A study doctor will be available at all times to check on you and treat you during the study.
- If you become ill during the study, additional tests (for example blood tests, nasal wash, or x-rays) may be done. You will not be charged for these tests. Any risks associated with these tests will be explained to you before they are performed. You may refuse to have these tests done if you do not want them.
- We can be reached 24 hours a day, if needed, during the study.
- Because dengue virus is spread by mosquitoes, we ask that you avoid mosquitoes for at least 3 weeks after you have been vaccinated and/or challenged.
- We will contact you to remind you of study visits and to check on you if you miss a study visit. We may contact you by one or more of the following means:
    - Telephone call
    - Text message
    - Electronic media (Twitter, Facebook, etc.)
    - Email message
    - Card mailed by US Postal Service
    - Ask one of the people you provided as a contact to remind you to come to the clinic

The Johns Hopkins Medical Institutions
(The Johns Hopkins Hospital
The Johns Hopkins Bayview Medical Center, etc.)

APPROVED
AS MODIFIED
Nov 29, 2017
WIRB®

RISKS AND DISCOMFORTS

TV003 is an experimental vaccine that is made up of live but weakened viruses. rDENV-2 and rDENV-3 are live dengue viruses. We do not know all the risks that may occur. We do know some risks that have happened in other dengue vaccine studies and we know some of the side effects that have happened during our testing of the dengue vaccines in this study. We have given some of the vaccines contained in TV003 to people who have never received a dengue vaccine and we did not see any increase in side effects. We also know the effects of the TV003 vaccine, the rDENV-2 challenge virus, and the rDENV-3 challenge virus when they were given to subjects in previous studies. The effects of the vaccines and the challenge viruses on the unborn child and breast-feeding infant are not known so you should not become pregnant or breast-feed during this study.

Common side effects of TV003: A common side effect seen in previous studies of TV003 was a temporary rash over the upper body, stomach, and arms. The rash did not hurt and it lasted about 1 week. This rash occurred in 56 of 84 subjects (67%) who received TV003. About 7% of subjects who received TV003 had a brief drop in their white blood cell count (blood cells that fight infection) to below the normal value. All of these cell counts returned to normal within a few days. About 5% of subjects who received TV003 had an increase in the level of a liver enzyme called ALT in the blood. The liver test in these subjects returned to normal before the end of the study.

Common side effects of rDENV-2 and rDENV-3: In previous studies, approximately 90% of people who received rDENV-2 and about 90% of people who received rDENV-3 developed temporary rash. The rash involved the arms, back, chest, stomach, and legs and was itchy in about 50% of people who developed a rash. Almost 18% of people who received rDENV-2 had a brief drop in their white blood cell count below the normal level. All of these cell counts returned to normal within a few days. About 8% of people who received rDENV-2 had a mild increase in liver ALT that returned to normal in a few days. Subjects who received rDENV-3 did not have increase in their ALT level. About 20% had a decrease in their white blood cell count.

Dengue fever has not occurred in any subject who has received TV003, rDENV-2, or rDENV-3. Dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS) have not occurred in any subject who received TV003, rDENV-2, rDENV-3, or any other experimental dengue vaccine.

The risks for TV003, rDENV-2, and rDENV-3 are listed below.

Immediate risks from vaccination

- You may have pain, redness, tenderness, itching, and/or swelling where we give you the shot.
- You may have a fever, headache, eye pain, bruising, bleeding problems, muscle or joint aches, upset stomach, or not feel like eating.
- You may get a low white blood cell count, low platelet (particles that help the blood to clot) count, and abnormal blood chemistries.
- You may get a skin rash. This rash may be itchy.

- You could have an allergic reaction (a rash, hives, or trouble breathing) right after vaccination. Some allergic reactions can be life-threatening. We will watch you for at least 30 minutes after you are vaccinated to check for signs of an allergic reaction and will treat you immediately for any sign of an allergic reaction.

Delayed risks from vaccination
If you receive these vaccines, your risk of developing DHF or DSS following a second infection with dengue virus may be increased if you do not develop antibodies to all 4 types of dengue and you travel to an area where dengue virus occurs. We will tell you if you received TV003 or placebo before you complete the study. Subjects who develop DHF/DSS can become very sick and should be treated in a hospital. We do not know how long this risk will last, but it may be for the rest of your life.

The countries currently reporting dengue are listed in the BACKGROUND INFORMATION section of this consent. This list may change over time. An up-to-date map can be found on the Centers for Disease Control internet website http://www.healthmap.org/dengue/index.php. You can also find out if dengue virus is present in the specific country you plan to travel to by contacting Dr. Durbin at 410-340-6852 or by contacting the local health department in the country where you plan to travel.

Subjects who develop DHF/DSS can become very sick and should be treated in a hospital. Because we do not know how long you will be at risk for DHF/DSS, we advise you not to travel to areas where there are dengue viruses (listed in the BACKGROUND INFORMATION section of this consent form). If, in the future, you must travel to a place where dengue viruses are active, you should protect yourself from mosquito bites.

The best way to protect yourself from mosquito bites is to:

- Wear long sleeved shirts and long pants
- Use a mosquito spray or cream that contains a chemical called DEET (20 - 30% DEET)
- Stay in places that have screens on the windows
- Use mosquito bed nets

When you enroll in the study, you will be given a card that tells you in detail how to avoid being bitten by mosquitoes on the day of vaccination.

If a licensed vaccine against all 4 dengue types becomes available in the future, you should talk with your doctor about whether or not you should receive such a vaccination before traveling to a dengue-endemic region. We do not know if your participation in this vaccine study will affect the ability of a future dengue vaccine to protect you against dengue infection.

There may be other side effects and risks that we don't know about yet. If we learn about any new side effects or risks while you are in the study, we will tell you and you can decide if you want to continue in the study.

The Johns Hopkins Medical Institutions
(The Johns Hopkins Hospital
The Johns Hopkins Bayview Medical Center, etc.)

APPROVED
AS MODIFIED
Nov 29, 2017
WIRB®

Blood drawing

- Blood drawing can cause pain, bruising, a lump called a hematoma, or infection at the place where blood is taken.
- Blood drawing can cause subjects to feel lightheaded or to faint.
- Bleeding may occur from the site of blood draw.
- There may be psychological or social risks that might result from taking part in the study, such as the first time testing for HIV.

Other risks

We will ask you to wait to get routine licensed vaccines like the flu shot (or nasal spray flu vaccine) until at least 8 weeks after you have joined the study. This may put you at more risk for illness such as the flu.

NEW FINDINGS

The study doctor or staff will share with you any new findings that may develop while you are participating in this study that might change your decision to be in this study. You may be asked to sign a revised consent form if this occurs.

BENEFITS

You will not receive any medical benefit from taking part in this study. If you receive the study vaccine you may develop antibodies against dengue virus infections. We hope that the information we gather from this study will lead to a dengue vaccine that could help many people around the world.

COSTS

There will be no costs to you for being in this study.

Ask your study doctor to discuss the costs of treating possible side effects. Otherwise, you might have unexpected expenses from being in this study.

PAYMENT FOR PARTICIPATION

You will be paid for your screening visit only if you are enrolled in the study. If you are an alternate on the day of vaccination and are not vaccinated, you will be paid $150.00 for your time. You will only be paid for the visits that you complete. You will be paid $80.00 for the screening visit and $80.00 for each completed follow-up visit. Because you must stay in the clinic for a longer amount of time on vaccination day, you will be paid $150.00 for each vaccination day visit.

After screening, there are 22 study visits, including the 2 vaccination days. You will also be paid a $250.00 bonus if you complete all study visits on time. The total amount you will be paid if you complete all visits is $2,230.00. To comply with federal law, this payment will be reported as income to the Internal Revenue Service (IRS).

If you choose to withdraw before the study is completed, you will only receive payment for the number of visits that you have completed.

The Johns Hopkins Medical Institutions
(The Johns Hopkins Hospital
The Johns Hopkins Bayview Medical Center, etc.)

APPROVED
AS MODIFIED
Nov 29, 2017
WIRB®

ALTERNATIVE TREATMENT
This is not a treatment study. You may choose not to be in this study.

CONFIDENTIALITY
The National Institutes of Health has given us a Certificate of Confidentiality for this study. This Certificate does not mean that the government approves or disapproves of this study. This Certificate adds special protection for research information that identifies you. It allows us, in some circumstances, to refuse to give out study information about you without your consent when it is sought in a legal action. Still, we may disclose identifying information about you if, for example, you need medical help. We may also give out information about you if the government it audits us. The research team will also give information to local or state authorities:

- if they suspect abuse or neglect of a child or dependent adult;
- if certain communicable diseases are present; and
- if the team learns that you plan to harm someone. In this case, the team also may warn the person who is at risk

Information describing the study will be posted on a clinical trials registration website. This website can be accessed at: https://www.ClinicalTrials.gov/ Information from this study will be given to the sponsor. The sponsor is the organization responsible for financing and overseeing this study. The sponsor of this study is the National Institutes of Health (NIH), National Institute of Allergy and Infectious Diseases (NIAID), Office of Clinical Research Policy and Regulatory Operations (OCRPRO). "Sponsor" includes any persons or companies that are contracted by the sponsor to have access to the research information during and after the study. Information about side effects of TV003, rDEN2Δ30-7169, and rDEN3Δ30 will also be given to the US Food and Drug Administration (FDA). It may be given to governmental agencies in other countries where the study vaccine may be considered for approval. Medical records which identify you, including photographs, and the consent form signed by you *will be* looked at and/or copied for research or regulatory purposes by the sponsor, and *may be* looked at and/or copied for research or regulatory purposes by:

- The FDA
- Department of Health and Human Services (DHHS) agencies
- Governmental agencies to whom certain diseases must be reported
- Governmental agencies in other countries
- Johns Hopkins University
- The Johns Hopkins University Bloomberg School of Public Health
- The Western Institutional Review Board® (WIRB®)

Absolute confidentiality cannot be guaranteed because of the need to give information to these parties. The results of this research study may be presented at meetings or in publications. Your identity will not be disclosed in those presentations.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

The Johns Hopkins Medical Institutions
(The Johns Hopkins Hospital
The Johns Hopkins Bayview Medical Center, etc.)

APPROVED
AS MODIFIED
Nov 29, 2017
WIRB®

COMPENSATION FOR INJURY
A study doctor will be available at all times while you are in the study to check on you and treat you for any short-term medical care resulting from you taking part in this research study. The services at the Johns Hopkins Hospital or the Johns Hopkins Bayview Medical Center will be available to you in case of any such injury. This short-term medical care will be paid for through our contract with NIH. Short-term medical care will be given at a facility determined by JHU and NIH. No long-term medical care or financial compensation for research-related injuries will be offered by the Johns Hopkins University, Johns Hopkins Hospital, the NIH, or the federal government. At your request, your insurance company will be billed for payment of any such long-term treatment or hospitalization. It is up to you to check with your insurance company before you start this study to find out what your insurance company will pay for.

You do not lose any legal rights by being in this study.

VOLUNTARY PARTICIPATION AND WITHDRAWAL
Your participation in this study is voluntary. You may decide not to participate or you may leave the study at any time. If you decide to withdraw from the study soon after you are vaccinated, the study doctor may ask permission to follow you briefly for safety reasons. We may ask you to let us check on you or return for a follow-up and/or final study visit.

Your decision to withdraw or to not take part will not result in any penalty or loss of benefits to which you are entitled. If you decide to leave the study, the samples that have been collected will be used as described in this consent form. If you do not wish us to use these samples after you leave the study, you may request that we destroy them and they will be destroyed. You should ask the study doctor listed below any questions you may have about this research study. You may ask questions in the future if you do not understand something that is being done.

You may be withdrawn from the study at any time by the study doctor or the sponsor without your consent if:

- The study sponsor decides to stop or cancel the study for any reason;
- The study staff or the study sponsor decides to discontinue your participation for any reason;
- The staff or your study doctor feels that staying in the study is harmful to your health;
- You do not follow instructions from the staff or do not keep appointments;
- The Data and Safety Monitoring Board (a scientific review board that monitors clinical research studies) feels the study should be stopped;
- The FDA or WIRB® feel the study should be stopped;
- If new information becomes available regarding the safety of the vaccine;
- You do not consent to continue in the study after being told of changes in the research that may affect you; or
- For any other reason.

The Johns Hopkins Medical Institutions
(The Johns Hopkins Hospital
The Johns Hopkins Bayview Medical Center, etc.)

APPROVED
AS MODIFIED
Nov 29, 2017
WIRB®

STORAGE OF UNUSED SAMPLES

We will store any unused blood and urine samples once this study is finished. Your samples will be used only for research. We may use these samples to learn more about dengue and other diseases. The blood samples may be used for tests to detect:

- Immune responses to the test vaccine (immunology)
- Why the dengue virus causes severe disease in some people (pathogenicity)
- Genetic differences in responses to vaccines or dengue fever infection (samples will be used anonymously)

Your samples will not be sold. Your samples will not be used to make commercial products. We will label your stored samples with a code that only the study team can link to you. We will keep any information that can be traced back to you private to the extent permitted by law. In some cases, the Western Institutional Review Board® (WIRB®) will review new research proposals that would like to use your samples. WIRB is a group of people who perform independent review of research.

Reports about research with your samples will be kept with the study records only. There will be no direct benefit to you. From studying your samples, we may learn more about how to prevent, treat, or cure dengue virus diseases or other diseases. Results from research using your samples may be presented in publications and meetings but your name will not be used.

The research tests we perform are not like routine medical tests and may not relate directly to your medical care, so we may not put future test results in your medical record. However, if you wish, someone on the study team will discuss the test results with you. We will not share these test results with your private doctor unless you ask us to do so.

There are risks associated with a loss of confidentiality of your health information and genetic testing results. Information about genetic test results may affect your employment, insurance, or family relationships. The sponsor cannot be certain that your genetic test results could never be linked to you.

A federal law called the Genetic Information Nondiscrimination Act (GINA) provides some protection for your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information collected in this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information collected in this research when making a decision about your employment.

However, this federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

The Johns Hopkins Medical Institutions
(The Johns Hopkins Hospital
The Johns Hopkins Bayview Medical Center, etc.)

APPROVED
AS MODIFIED
Nov 29, 2017
WIRB®

If you do not want your unused samples used for future research, you should not join this study.

You can change your mind at any time about allowing your samples to be used for future research. If you do change your mind, call or write the study doctor or study nurse and let them know. Then your samples will no longer be made available for research. Your samples will be destroyed.

SOURCE OF FUNDING FOR THE STUDY/CONFLICT OF INTEREST

A conflict of interest occurs when a researcher or the University has a financial or other interest that might affect the researcher's judgment when conducting a research study. The National Institutes of Health (NIH) pays for the conduct of this study through the NIH Contract No. HHSN272200900010C "Operation of a Facility for the Study of Infectious Agents, Vaccines and Antimicrobials in Adult and Pediatric Human Subjects" with Johns Hopkins University. Funding for this research study will be provided by the Office of Clinical Research Policy and Regulatory Operations (OCRPRO)/Division of Clinical Research (DCR)/National Institute of Allergy and Infectious Diseases (NIAID)/National Institutes of Health (NIH). Dr. Durbin is a faculty member at Johns Hopkins University.

QUESTIONS

If you have any questions concerning your participation in this study, or if at any time you feel you have experienced a research-related injury or a reaction to the study vaccine, or if you have questions, concerns or complaints about the research, contact:

> Dr. Anna P. Durbin at 410-614-4736 (office), 410-283-6522 (24-hour pager), or 410-340-6852 (cell phone)

If you have questions about your rights as a research subject, or if you have questions, concerns or complaints about the research, you may contact:

> Western Institutional Review Board® (WIRB®)
> 1019 39th Avenue SE Suite 120
> Puyallup, Washington 98374-2115
> Telephone: 1-800-562-4789 or 360-252-2500
> E-mail: Help@wirb.com

WIRB is a group of people who perform independent review of research.

WIRB will not be able to answer some study-specific questions, such as questions about appointment times. However, you may contact WIRB if the research staff cannot be reached or if you wish to talk to someone other than the research staff.

Do not sign this consent form unless you have had a chance to ask questions and have received satisfactory answers to all of your questions.

If you agree to participate in this study, you will receive a signed and dated copy of this consent form for your records.

The Johns Hopkins Medical Institutions
(The Johns Hopkins Hospital
The Johns Hopkins Bayview Medical Center, etc.)

APPROVED
AS MODIFIED
Nov 29, 2017
WIRB®

CONSENT
I have read the information in this consent form. All of my questions about the study and my participation in it have been answered. I freely consent to participate in this research study.

I authorize the release of my medical records, including photos and the results of HIV and hepatitis testing, for research or regulatory purposes to the sponsor, FDA, DHHS agencies, governmental agencies in other countries, and WIRB®.

By signing this consent form, I have not given up any of my legal rights.

_____
Printed Name of Subject

CONSENT SIGNATURE

Signature of Subject	Time	Date
Signature of Person Conducting Informed Consent Discussion	Time	Date

Printed Name of Person Conducting
Informed Consent Discussion

The Johns Hopkins Medical Institutions
(The Johns Hopkins Hospital
The Johns Hopkins Bayview Medical Center, etc.)

APPROVED
AS MODIFIED
Nov 29, 2017
WIRB®

Attestation Statement

I confirm that the research study was thoroughly explained to the subject. I reviewed the consent form with the subject and answered the subject's questions. The subject appeared to have understood the information and was able to answer the following questions correctly:

1. What is the purpose of this study?
2. If you decide to be in the study, what will you be asked to do?
3. What is the possible benefit of participating in this study?
4. What are the possible risks of participating in this study?
5. If you decide not to participate in this study, what options do you have?
6. Will participating in this study cost you anything? If so, what will you have to pay for?
7. Do you have to be in this study?
8. If you decide to be in the study, can you leave the study when you want to?

Printed Name of Person Conducting the Informed Consent Discussion	Position
Signature of Person Conducting the Informed Consent Discussion	Date