

JOHNS HOPKINS BLOOMBERG SCHOOL OF PUBLIC HEALTH

**RESEARCH SUBJECT INFORMED CONSENT DOCUMENT
RSV-SERONEGATIVE INFANTS AND CHILDREN**

TITLE: A Phase I Study of the Safety and Immunogenicity of a Single Dose of the Live Recombinant RSV D46cpΔM2-2 Vero Grown Virus Vaccine (Lot RSV #008A), Delivered as Nose Drops to RSV-Seropositive Children 12 to 59 Months of Age and RSV-Seronegative Infants and Children 6 to 24 Months of Age

PROTOCOL NO.: CIR 308
WIRB Protocol #20151950

PROTOCOL VERSION: 2.0, January 29, 2016
SPONSOR: NIAID/NIH

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**STUDY-RELATED
PHONE NUMBER(S):** Ruth A. Karron, MD
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**STUDY
COORDINATOR(S):** Suzanne Woods, CRNP-P
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SUMMARY

- You are being asked to allow your child to be in a research study.
- This consent document is to help you decide if you want your child to join in the research study.
- Please read this consent document carefully and take as much time as you need.
- You should not join this research study until all of your questions are answered.
- You can choose not to have your child join the study.
- The decision to join or not join the research study will not cause your child to lose any medical benefits.
- If you decide not to have your child take part in this study, your child's primary healthcare provider will continue to care for your child.
- If you allow your child to join, you may have your child quit at any time.
- There will be no penalty if you decide to have your child quit the study.
- During the study, we will tell you if we learn any new information that might affect whether you wish to have your child continue to be in the study.
- The goal of a research study is to learn things to help others in the future.
- This study involves an experimental (investigational) nose drop vaccine that is being tested to prevent respiratory syncytial virus (RSV) illness in infants and children.
- An investigational vaccine is one that has **not** been approved by the U.S. Food & Drug Administration (FDA).
- Throughout the consent, the experimental (investigational) nose drop vaccine is referred to as "study vaccine".
- In this study, your child may receive a salt-water placebo instead of the study vaccine.
- A placebo has no beneficial effect. A placebo is used in research as a study control. A study control group serves as a comparison group when the vaccine results are tested. Part of your child's medical records may become part of the research record.
- The study sponsor, government agencies, and other groups associated with this study may review or copy your child's research records. There will be a risk that your child's research records may be given to others without your permission.
- The Data and Safety Monitoring Board (DSMB) is an independent committee that monitors the safety of the research.
- If the study results become public, your child's identifiable information will not be used.

PURPOSE OF THE STUDY

Scientists at the National Institutes of Health (NIH) are working with doctors at the Center for Immunization Research (CIR). They are developing a vaccine to prevent RSV illness in infants and children. This investigational RSV vaccine is given as nose drops. The vaccine contains a live, weakened form of the virus.

The purpose of this study is to look at the safety (side effects) of an experimental RSV vaccine. In addition, scientists will look at the antibody response (germ fighters) to the vaccine in healthy children. This research study is testing an experimental vaccine. The FDA has not licensed this vaccine. We have tested a very similar vaccine in adults and young children. There will be up to 60 infants and children taking part in this study.

Your child was chosen and you are being asked to allow your child to be in this research study because your child is between 6 and 24 months of age.

RSV is a virus (germ) that can cause breathing problems in children. Symptoms of infection with the virus may include:

- fever
- runny nose
- cough
- severe lung infections
- wheezing
- sore throat
- ear infection
- croup (barky cough with hoarseness)
- pneumonia (infection of the lungs)

At this time, there is no approved vaccine to prevent RSV illness.

PROCEDURES

Your child cannot take part in this study if they:

- have been previously diagnosed with wheezing
- live in a house with people with weak immune systems
- live with or are in a daycare room with babies younger than 6 months of age for the first 28 days after your child receives vaccine or placebo

Your child must wait 2 to 4 weeks after receiving routine vaccines before receiving the study vaccine or placebo.

In addition, after receiving the study vaccine or placebo, your child must:

- wait 2 weeks to receive killed vaccines
- wait 4 weeks to receive live vaccines
- not take part in any other experimental vaccine or drug studies for 8 weeks

We will ask you to review and sign this study consent prior to your child's participation and ask you to complete a comprehension assessment to see how well you understand the study.

TOPICAL ANESTHETIC CREAM

Before each blood draw, we will offer to put anesthetic skin cream (numbing cream) in several places where the blood may be taken to help decrease the pain. An information sheet on this numbing cream will be offered.

SCREENING VISIT

If the screening was not already done under a separate screening informed consent, then the screening visit is to find out if your child may enter the study. This visit may take place at your home or an agreed upon location. This visit will take about one hour and may include:

- reviewing and signing the study consent document and medical record release form
- completing a comprehension assessment
- obtaining your child's medical history
- offering numbing cream to decrease pain for the blood draw
- collecting about 1 teaspoon of blood to test for antibodies against RSV
- a physical exam

If the physical exam results are not normal, then the study staff will tell you and refer your child for follow-up care with your child's primary medical provider.

ENROLLMENT VISIT

If your child is eligible, then the enrollment visit must take place at your child's primary medical practice or at one of the CIR sites where emergency equipment is available. We will give your child either one dose of study vaccine or one dose of placebo by nose drops. Placebo is a salt water nose drop without the study vaccine. Study doctors will compare results from children who receive placebo to the results of children who receive the study vaccine. Whether your child receives the study vaccine or placebo will be decided by chance (like tossing dice). Your child will have a 2 out of 3 chance of being given the study vaccine and a 1 out of 3 chance of being given the placebo. Neither you nor the study doctors or study nurses will know whether your child received the study vaccine or placebo until the study ends. However, this information is available to the study doctor if needed in an emergency.

Your child's enrollment visit will take about 1 hour and may include:

- physical assessment including your child's temperature, heart rate, and breathing rate or a physical exam. If a physical exam is performed at the screening visit, then a physical assessment will be completed at the enrollment visit;
- a blood draw if not enough blood was collected at the screening visit
- a nasal rinse using about 2 tablespoons of salt water to check for other viruses and to check for antibodies in the nose
- lying on their back while receiving one dose of the study vaccine or placebo given by nose drops using a small syringe without a needle

- continuing to lie down for 1 minute after receiving study vaccine or placebo
- staying in the clinic for 30 minutes after the study vaccine or placebo is given

You will also be getting:

- a thermometer and a temperature card to record your child's temperature daily for 29 days (including enrollment day), and at any other time you are concerned about a fever.
- contact telephone numbers and information about when to call a study nurse or study provider. Study staff will be available 24 hours a day during the first 28 days after enrollment and during the winter RSV-surveillance season. During all other times, the study staff can answer your questions during regular business hours.

IN-PERSON STUDY VISIT DAYS

After your child is enrolled, the study staff will contact you daily for 4 weeks. There will be about 8 visits and a follow-up visit approximately 8 weeks after receiving vaccine or placebo.

Your child will have in-person study visits on days 3, 5, 7, 10, 12, 14, 17, and 28 (each \pm 1 day). These visits will take place at your home or an agreed upon location. Each visit will take about 30 minutes and will include:

- updating your child's health history since the last visit
- a physical assessment including temperature, heart rate, and breathing rate
- rinsing the nose with salt water to check for study vaccine and other viruses

Your child will have a follow-up study visit about 56 days after enrollment and will include:

- collecting about 1 teaspoon of blood to test for antibodies against RSV
- applying numbing cream before the blood draw to decrease pain (if requested)
- a salt water nasal rinse to check for study vaccine and antibodies in the nose

NON-VISIT STUDY DAYS

After your child is enrolled, the study staff will be in contact with you for 20 non-visit day reports. On study days 1- 27 (each \pm 1 day) when an in-person study visit is not completed, you will be reporting the daily temperature measurement and any illness symptoms.

ILLNESS-VISIT STUDY DAY(S)

If your child has a fever, respiratory symptoms, or ear infection, then an illness visit may be scheduled. This visit will take place at your home or an agreed upon location. Each visit will take about 30 minutes and will include:

- updating your child's illness history
- a physical assessment including temperature, heart rate, and breathing rate
- a salt water nasal rinse to check for study vaccine and other viruses

Your child may catch other germs that may cause illness during or after the study.

RSV-SURVEILLANCE SEASON

Your child's health will be monitored weekly for illness from November 1 to March 31. If your child needs medical care for a fever, respiratory symptoms or an ear infection, we will do an illness visit with a physical assessment and a salt water nasal rinse.

A blood sample will be collected in the month of October before RSV-surveillance season. Another blood sample will be collected in the month of April after the RSV-surveillance season. You may choose to have your child receive numbing cream before the blood draws to decrease pain. These samples are collected to check for antibody responses to wild-type RSV infection.

RISKS AND DISCOMFORTS

RISKS OF THE STUDY VACCINE

- If the study vaccine is not weakened enough, then it may cause a runny nose, sore throat, cough, or other signs of a cold. It is also possible to cause a sinus infection, croup, ear infection, fever, wheezing or pneumonia.
- There is no specific medicine to treat RSV illness. If any symptoms occur, then your child will receive prompt medical care.
- The study vaccine virus could spread from your child to other people and may make them sick.
- The study vaccine could cause a severe allergic reaction. A severe reaction can cause hives, throat swelling, rapid heart rate, weakness, difficulty breathing, and death. These reactions are rare.
- There may be other side effects or risks of the study vaccine that we do not know of yet. If we learn about any new side effects or risks while you are in the study we will let you know and you can decide if you want to continue in the study.

RISKS OF NASAL RINSE

A nasal rinse may cause brief discomfort like the feeling of getting ocean (salt) water in the nose and may rarely cause a nosebleed.

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RISKS BLOOD DRAWING

Blood drawing can cause discomfort, bleeding, bruising, or a small risk of infection at the place where the blood is taken. Sometimes, blood drawing can cause older children to feel lightheaded or to faint. It can take more than one try to get blood from a child.

RISKS OF THE NUMBING CREAM (ANESTHETIC)

Possible side effects of the numbing cream include temporary skin discoloration on the places where the cream is placed. Skin rash, hives (an itchy rash), and rarely dizziness or sleepiness are reported.

BENEFITS

- If your child receives the study vaccine, then it is possible that he or she may be protected against one type of RSV illness that is in the community. RSV illness protection should not be expected.
- If your child receives placebo, there is no direct benefit of protection against RSV.
- Your child taking part in the study may help find a vaccine that works to prevent severe RSV illness. Such a vaccine may be of future benefit to babies and children in this country and the rest of the world.

COSTS

The sponsor, the National Institute of Allergy and Infectious Diseases (NIAID) of the NIH, covers the costs of the study. There will be no costs to you or your health insurance for your child to take part in this study.

You may have unexpected expenses from allowing your child to be in the study. These expenses are discussed in the section “In Case of Injury”.

PAYMENT FOR YOUR CHILD’S PARTICIPATION

You will receive the first check, gift card, or both at the scheduled follow-up visit about 56 days after enrollment. This payment will include:

- \$25 for each completed study visit
- \$5 for each completed non-visit contact
- \$25 for each illness visit

You will receive the final payment at the post-RSV-surveillance season visit in April for the RSV-surveillance season. This payment will include:

- \$25 for the pre-RSV surveillance season visit
- \$5 for each weekly report to study staff
- \$25 for the post-RSV surveillance season visit
- \$25 for each illness visit
- \$25 bonus if all study and RSV-surveillance season visits and contacts are completed

If you decide to take your child out of the study early, then you will only be paid for the study days that your child completed.

During the study, you or your child may receive:

- age-appropriate treats, books, or small toys (value less than \$10)
- child safety seat educational materials
- referrals to certified car seat educators at community inspection stations
- certified lactation counseling services (if appropriate)
- bus tokens, taxi fare, or parking passes (as needed for study visits)

PARTICIPATION ALTERNATIVE

At this time, there are no licensed vaccines to protect against RSV illness. You may choose not to have your child take part in this study.

VOLUNTARY PARTICIPATION AND WITHDRAWAL

Your child joining this study is your choice. You may decide not to have your child join, or your child may leave the study at any time. You may decide not to allow your child to stay in the study after being told of changes in the research. Your choice will not result in any penalty or loss of benefits to which you and your child are entitled. If you decide to have your child leave the study early:

- we ask that you tell the study staff
- we ask that your child stays in the safety evaluation until the end of the study

The sponsor or study doctors have the right to take your child out of the study at any time for any reason including the following:

- it would be dangerous for your child to continue
- you do not follow study procedures as directed by the study doctors
- new information about the study vaccine safety is available
- it is in your child's best interest
- the FDA, study sponsor, or DSMB decide to end the study

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NEW FINDINGS

You will be told about any new information that might change your mind about having your child be in this study. You may be asked to sign a new consent document if this happens.

PRIVACY AND CONFIDENTIALITY

Your child's name and birthdate are not given to anyone unless required by law. All of the information you give us during this study will be put in locked file cabinets and on password-protected computer files. The only people who will have access to this information will be those who are involved in the study, including the researchers, laboratory, and other study staff.

Others who may see your child's information are the groups of people who make sure that the study is being done as it should:

- Johns Hopkins Bloomberg School of Public Health
- Western Institutional Review Board® (WIRB)
- NIAID
- DSMB
- legal counsel
- Office for Human Research Protections
- FDA
- Study sponsor and sponsor contractors

Maryland state law requires us to report certain diseases and information about child abuse.

Because of the need to give information to these parties, complete confidentiality cannot be promised; but these parties must keep your child's identity private. The information that identifies your child will not be given out to people who are not working on the study unless it is required by law or you give us permission.

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 have 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.

At the end of the study, what we learn from the research may be used in a medical journal or used for teaching. Your child's name and other details about your child's health will not be used so that your child cannot be identified.

After the study is finished, you may review or request a copy of your child's research record.

SOURCE OF FUNDING FOR THE STUDY

The Johns Hopkins Center for Immunization Research receives funding from the NIH to conduct this study.

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IN CASE OF INJURY

If you need to talk with someone about this research study, then call Dr. Ruth Karron at (410) 955-1622, Suzanne Woods, CRNP-P (443) 813-0697 (24 hours), or Johns Hopkins Office of Human Subjects Research at (888) 262-3242 or fax (410) 502-0584.

You should call if:

- you think you or your child has not been treated fairly
- your child has been hurt by joining the study
- you have any questions about the study

Either the study staff or Johns Hopkins Office of Human Subjects Research will answer your questions and help you find medical care for your child.

A study clinician can be reached during the study to treat your child for any short-term medical care resulting from participation in this research study. This short-term medical care will be provided through our contract with the NIH and will be at a facility determined by JHU and the NIH. The Johns Hopkins Hospital, JHU, the NIH, or the federal government will offer no long-term medical care or financial compensation for research-related injuries. You or your insurance company will be billed for payment of any such 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. Your health insurance company may not pay for these charges because your child is in a research study. Your child does not lose any legal rights by being in this study.

QUESTIONS

If you have any questions, concerns, or complaints about your child's participation in this study or any time you feel your child has a study-related injury or a reaction to the study vaccine, contact:

Dr. Ruth Karron at (410) 955-1624 or
Suzanne Woods, CRNP-P at (443) 813-0697 (24 hours)

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

Western Institutional Review Board® (WIRB®)
1019 39th Avenue SE, Suite 120
Puyallup, Washington 98374-2115
Telephone: (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.

PHOTOGRAPHY PERMISSION (OPTIONAL)

We may take pictures of your child during the study. We may use these photos for our advertising flyers and sometimes in medical articles and presentations. Your child's name will not be used in any flyer, article, or presentation. People may be able to recognize your child in these photos. Once your child's photo is used in a flyer or article, you will not be able to take back your consent to use the photo.

Your child may take part in this research study without your agreement to have their photographs taken.

I will allow the CIR staff to take photos of my child.

Parent Initials _____ **Date** _____
month/day/year

SPECIMEN STORAGE PERMISSION (OPTIONAL)

If you agree, any unused blood or nasal rinse specimens taken from your child will be stored. The unused specimens may be used for screening for future respiratory virus vaccine studies and research purposes. There will be no direct benefit to your child, but we may learn more about viruses that cause illness in children. The specimens will be labeled so that your child's name cannot be easily identified. Results from future research using your child's specimens will not be put in your child's medical or study records. The results may be included in medical papers and meetings, but your child's name will not be used.

Your child's specimens will not be sold, used for human genetic testing, or used to directly make products that will be for sale. You can change your mind at any time about allowing your child's unused specimen to be used for future screening and research by contacting the study staff in writing.

The nasal rinse, blood specimens, and data collected from your child during this study are important to science. You or your child will not own the specimens or data after you give it to the study. You will not receive any financial benefit from any product or idea created by the study investigators using the data or materials collected from you.

Your child may take part in this research study without agreeing to have his/her specimens stored for future screening and research. If specimen storage permission is not given, the specimens will not be used in the future for screening or research purposes and will be destroyed.

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I will allow the use of my child's identifiable unused specimens for future screening and research as described above.

Parent Initials _____ **Date** _____
month/day/year

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

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

CONSENT

I have read the information in this consent document. All my questions about the study and my child taking part in it have been answered. I freely consent to my child taking part in this research study.

I authorize the release of my child's study records for research or regulatory purposes to the sponsor, the FDA, DHHS agencies, Johns Hopkins Bloomberg School of Public Health, and WIRB.

By signing this consent document, I have not given up any of my child's legal rights.

Print **SUBJECT'S** Name

CONSENT SIGNATURE

Signature of Parent or Guardian

month/day/year Time
Date

Print Name of Parent or Guardian

Relationship to Subject

Signature of Study Personnel
Conducting Informed Consent Discussion

month/day/year Time
Date

Print Name of Study Personnel Conducting Informed Consent Discussion