JOHNS HOPKINS BLOOMBERG SCHOOL OF PUBLIC HEALTH

RESEARCH SUBJECT INFORMED CONSENT DOCUMENT
RSV-SERONEGATIVE INFANTS AND CHILDREN

TITLE:	Phase I Placebo-Controlled Study of the Infectivity, Safety and Immunogenicity of a Single Dose of a Recombinant Live-attenuated Respiratory Syncytial Virus Vaccine, RSV 6120/ΔNS1, Lot RSV#018A, or RSV 6120/F1/G2/ΔNS1, Lot RSV#016A, 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 330 WCG IRB Protocol #20181405
SPONSOR:	National Institute of Allergy and Infectious Diseases (NIAID), National Institutes of Health (NIH)
INVESTIGATOR:	Ruth A. Karron, MD Center for Immunization Research (CIR) Johns Hopkins Bloomberg School of Public Health (JHSPH) 624 N. Broadway, Hampton House Room 217 Baltimore, MD 21205 United States
STUDY-RELATED PHONE NUMBERS:	Ruth A. Karron, MD (410) 955-1624 Kristi Herbert, CRNP-P Cell: (410) 627-8067 (24 hours)
STUDY COORDINATOR:	Kristi Herbert, CRNP-P Cell: (410) 627-8067

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 2 experimental (investigational) nose drop vaccines that are 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 vaccines are referred to as "study vaccine".
- In this study, your child may receive a salt-water placebo instead of a 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 will monitor the safety of this research study.
- 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 older infants and toddlers. This study involves 2 investigational RSV vaccines which are given as nose drops. The vaccines contain a live, weakened form of the virus.

The purpose of this study is to look at the safety (side effects) of 2 experimental RSV vaccines. In addition, scientists will look at the antibody response (germ fighters) to the vaccines in healthy children. The FDA has not licensed these vaccines. We have tested very similar vaccines in adults and young children. There will be up to 50 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)

Although 2 products have been developed to protect healthy young infants against RSV disease, there is currently no product available to provide long-lasting immunity to older infants and children.

PROCEDURES

Your child cannot take part in this study if she or he:

- has been previously diagnosed with wheezing more than once, or within the past 12 months
- lives in a house with people with weak immune systems
- lives with or is in a daycare room with babies younger than 6 months of age for the first 28 days after your child receives study vaccine or placebo
- has contact with a person diagnosed with COVID-19 disease or active SARS-CoV-2 infection within the past 10 days
- has received an RSV vaccine or monoclonal antibody (mAb) or enrolled in a study of an RSV vaccine or mAb within the past 6 months
- has received an immunoglobulin (IVIg) within the past 6 months

Your child must wait 2 to 4 weeks after receiving routine vaccines, or inactivated influenza vaccine within 3 days before receiving a study vaccine or placebo.

In addition, after receiving a 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 will be completed at your child's primary medical practice or at one of the CIR sites. It will take about 1 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 your child's blood to test for antibodies against RSV
- a physical exam of your child

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 follow all current CDC and local guidance regarding the use of personal protective equipment (PPE) during all study visits. We will give your child either a single dose of one of the 2 study vaccines or one dose of placebo by nose drops. Placebo is a salt water nose drop without a study vaccine. Study doctors will compare results from children who receive placebo to the results of children who receive a study vaccine. Whether your child receives a study vaccine or placebo will be decided by chance (like tossing dice). About 2 of each 5 enrolled children will get 1 of the RSV vaccines, and about 2 of each 5 enrolled children will get the other RSV vaccine. Approximately 1 of each 5 enrolled children will get nose drops without vaccine (placebo). Neither you nor the study doctors or study nurses will know whether your child received 1 of the 2 study vaccines 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 complete physical exam.
- a blood draw if not enough blood was collected at the screening visit
- a nasal swab to check for other viruses in the nose.
- having your child lie on his or her back while receiving a single dose of 1 of the 2 study vaccines or placebo given by nose drops using a small syringe without a needle
- having your child continue to lie down for 1 minute after receiving study vaccine or placebo
- staying in the clinic for 30 minutes after a 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 ± 1 day). These visits will take place at your home or an agreed upon location. If a Stay at Home Order is started during the study, we may replace in-person visits with remote research visits, and you may be asked to swab your child's nose. We will show you how to do this, and we would provide the swabbing kit and arrange transport of the sample. During a remote research visit, you may also be asked to measure your child's temperature and count your child's pulse and breathing rate. 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
- swabbing the nose 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)

Any required blood draws during a Stay at Home Order will be collected in-person as soon as possible once the order is lifted.

NON-VISIT STUDY DAYS

After your child is enrolled, the study staff will be in contact with you for 21 non-visit day reports. On study days 1-28 (each ± 1 day) and study day 29 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 a remote or in-person 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 nasal swab to check for study vaccine and other viruses

Your child may catch other germs that may cause illness during or after the study. During a remote research visit, you may be asked to do the nasal swab, and the clinical assessments may be done remotely during which we may ask you to measure your child's temperature and to count your child's pulse and breathing rate.

RSV-SURVEILLANCE SEASON

Your child's health will be monitored weekly for illness during the RSV surveillance season. 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 nasal swab.

A blood sample will be collected after the RSV-surveillance season. You may choose to have your child receive numbing cream before the blood draws to decrease pain. This sample is collected to check for an antibody response to RSV infection. Any required blood draws during a Stay at Home Order will be collected in-person as soon as possible once the order is lifted.

RISKS AND DISCOMFORTS

RISKS OF THE STUDY VACCINES

- If a 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.
- A study vaccine virus could spread from your child to other people and may make them sick.
- A 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 a 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 SWAB

- A nasal swab may cause brief discomfort and may rarely cause a nosebleed.

RISKS OF 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 1 of the 2 study vaccines, 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 or pre-paid card at the scheduled follow-up visit about 56 days after enrollment. This payment will include:

- $50 for enrollment visit
- $30 for each completed scheduled and unscheduled study visit
- $5 for each completed non-visit contact

You will receive the final payment at the visit after RSV-surveillance season. This payment is for activities during the RSV-surveillance season and will include:

- $5 for each weekly report to study staff
- $30 for the visit after RSV-surveillance season
- $30 for each illness visit
- $50 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 RSV vaccines for healthy infants and children in this age group. 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 vaccines' safety is available
- it is in your child's best interest
- the FDA, study sponsor, or the Institutional Review Board (IRB) decide to end the study

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 study information is protected by the NIH Certificate of Confidentiality. This Certificate allows us, in some cases, to refuse to give out your child's information even if requested using legal means. The researchers cannot be forced to disclose information that may identify your child, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings.

It does not protect information that we have to report by law, such as child abuse or some infectious diseases. The Certificate does not prevent us from disclosing your or your child's information if we learn of possible harm to your child or others, or if your child needs medical help. 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.

Disclosures that you consent to in this document are not protected. This includes putting research data in the medical record or sharing research data for this study or future research. Disclosures that you make yourself are also not protected.

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
- WIRB- Copernicus Group (WCG IRB)
- NIAID
- DSMB
- Legal counsel
- Office for Human Research Protections
- FDA
- Study sponsor and sponsor contractors

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.

SOURCE OF FUNDING FOR THE STUDY

The Johns Hopkins CIR receives funding from the NIH to conduct this study.

IN CASE OF INJURY

If you need to talk with someone about this research study, then call Dr. Ruth Karron at (410) 955-1624, Kristi Herbert, CRNP-P at (410) 627-8067 (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 a study vaccine, contact:

Dr. Ruth Karron at (410) 955-1624 or
Kristi Herbert, CRNP-P at (410) 627-8067 (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:

WCG IRB
1019 39th Avenue SE, Suite 120
Puyallup, Washington 98374-2115
Telephone: (800) 818-2289
E-mail: Researchquestions@wcgirb.com

WCG IRB is a group of people who perform independent review of research. WCG IRB will not be able to answer some study-specific questions, such as questions about appointment times. However, you may contact WCG IRB 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 his or her photograph taken.

Select your choice:

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

_____ No, I will <u>not</u> 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 and nasal swab 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 swab, 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 your agreement to have his or 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.

Select your choice:

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

_____ No, I will <u>not</u> allow the use of my child's 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 WCG IRB.

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

Assent instructions:
Assent of children is not required because their capability is so limited that they cannot reasonably be consulted.

_____
Print **SUBJECT'S** Name

CONSENT SIGNATURE

_____ _____ _____
Signature of Parent or Guardian month/day/year Date Time

_____
Print Name of Parent or Guardian

_____
Relationship to Subject

_____ _____ _____
Signature of Study Personnel Conducting Informed Consent Discussion month/day/year Date Time

_____
Print Name of Study Personnel Conducting Informed Consent Discussion