Safety of Sildenafil in Premature Infants at Risk of Bronchopulmonary Dysplasia

NCT number NCT03142568
Document Date 11/06/2023

IRB Approved Template
MUST BE APPROVED
FOR SITES BEFORE USE
Nov 06, 2023

PARENTAL/LEGAL GUARDIAN PERMISSION TO PARTICIPATE IN A RESEARCH STUDY AND HIPAA AUTHORIZATION

TITLE:	Guanfacine for Hyperactivity in Children with Down Syndrome (HYPEbeGONE-DS)
PROTOCOL NO.:	NICHD-2020-HYP01
WCG IRB PROTOCOL NO.:	20234753
FUNDING SPONSOR:	The *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) The NICHD is a part of the U.S. National Institutes of Health (NIH).
INVESTIGATOR:	Name Address City, State Zip Country
STUDY RELATED PHONE NUMBER(S):	Number Number (24 hours) [24-hour number required]

Taking part in this research is voluntary. You may decide not to participate, or you may leave the study at any time. Your decision will not result in any penalty or loss of benefits to which you are otherwise entitled.

If you have any questions, concerns, or complaints or think this research has hurt you, talk to the research team at the phone number(s) listed in this document.

This study enrolls participants who may be unable to provide informed consent due to their age. The person providing permission for a child to participate in this study must be a parent or legal guardian. The terms “you” and “your” in this form refer to the parent or legal guardian. The term “your child” in this form refers to the participant.

RESEARCH CONSENT SUMMARY

We want to learn more about how guanfacine immediate release (abbreviated as GIR) acts in the bodies of children with Down syndrome (DS). GIR is a drug that is given to children by their health care providers to treat hyperactivity and Attention Deficit Hyperactivity Disorder (ADHD). By studying this drug, we hope to find the safest and most effective dose in children with DS. We are using a smaller dosage strength of GIR

for this study than is currently available through your pharmacy.

We are inviting your child to be in this research study because your child has DS with hyperactivity/ADHD. If you give permission for your child to participate in this study, your child will be in this study for up to 102 days after signing this permission form. Your child will be randomly assigned to receive either GIR or placebo (called "*study drug*" in this document), for eight weeks. We will collect blood samples from your child at three different visits during the study. We will ask you to complete questionnaires about your child's hyperactivity and sleep patterns and keep a study diary throughout the study. We will also collect certain information about your child's health from their medical records. There are some risks specific to taking GIR that are discussed later in this form. Additional study risks include mild discomfort/pain, potential bruising, risk of infection, and bleeding problems that could happen with drawing blood. There is also a potential risk of loss of confidentiality.

What we learn in this study will be put in a database run by the National Institutes of Health (NIH) to be shared for future research. Lay summaries may also be made available on the Pediatric Trials Network web site (https://pediatrictrials.org/) to share what we learn after the study. This information will not include anything that identifies your child.

If you want to learn more about this study, please continue to read below.

DETAILED RESEARCH CONSENT

You are being asked for your permission to allow your child to take part in a research study. A person who takes part in a study is called a "research participant." The term "parent" could also refer to the legal guardian of a child. "Site staff" means any person at the site investigator's location. The "study team" includes people involved with the study at the National Institute of Child Health and Human Development (NICHD), the Investigational New Drug (IND) Sponsor (the person in charge of the study overall), Duke University (Duke Clinical Research Institute [DCRI]), and The Emmes Company, LLC.

Who is paying for the study to be done?

The *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) is paying for this study and may also pay for the site staff through a contract with Duke University.

What should I know about this study?

- Site staff will explain this study to you. This form sums up that explanation. You may take a copy of this form home with you to review before making your decision.
- Taking part in this study is voluntary. Whether you allow your child to take part is up to you.
- Your decision to not allow your child to participate or to stop participation at any

time, will not be used against you or your child. It will not affect your child's access to health care at the study site. There will not be any penalties or loss of benefits to which you or your child are otherwise entitled.

- If there is anything you don't understand, ask questions. You can ask all the questions you want before you decide to participate and at any time during the study.
- Before choosing to participate, we encourage you to talk about this study with your child's health care provider, your family, and your friends.
- We will tell you about any new information that may affect your child's health, welfare, or your choice to have your child stay in this study.
- About 60 participants will take part in this study.

Why is this study being done?

Children with DS are at risk for many co-occurring conditions that require chronic medications. However, very little is known about how drugs work in children with DS. The purpose of this study is to learn more about how one of these drugs, GIR, acts in the bodies of children with DS who have hyperactivity/ADHD. We want to share what we learn with other researchers. This is important, because we do not have enough information to know if the doses of GIR used in children with DS who have hyperactivity/ impulsivity or inattention are safe or effective.

This study is considered investigational. While GIR may be used to treat children who have hyperactivity/ADHD, the U.S. Food and Drug Administration (FDA) has not approved use of GIR in children and adolescents with ADHD. Although we worked with expert doctors to guide dosing of GIR in this trial, the best dose to use for hyperactivity in DS is not fully known. The extended release form of guanfacine, INTUNIV®, is approved by the FDA for the management of ADHD in children ages 6-17. Some doctors prescribe INTUNIV® to children with DS. However, INTUNIV® comes only as a pill, which must be swallowed whole, and comes in a lowest dosage strength of 1 mg. The GIR used in this study uses a lower dose (0.5mg) to start, and to adjust dose during the study. This may be more appropriate for determining the best dose regimen for individuals with Down syndrome.

What is involved in this study?

If your child is diagnosed with hyperactivity and/or ADHD that requires a medication to treat, they may be eligible to be in this study. After providing consent, your child will be screened to ensure they qualify to be in the study. If they qualify, your child will be put into a study group by chance (like drawing names out of a hat). You and your child cannot choose your child's group. Your child has a 2 out of 3 chance of being placed in a group to receive a study drug that contains GIR. Otherwise they will receive a placebo as their study drug A placebo looks just like the GIR study drug but does not have any drugs or medicine in it. A placebo group is used for comparison to help us determine if GIR is helpful in treating hyperactivity/ADHD. You, your child, the investigator and study team will not know if your child is receiving GIR or placebo as the study drug. However, in case of an emergency, your child's study investigator can find out what your child

received. The study drug will be increased slowly every week. Prior to each dose increase, you will be asked to measure your child's heart rate (HR) and blood pressure (BP) using an FDA cleared device that you will receive from the study team. You will be trained on how to use this device. Your child will be followed very closely with weekly telephone calls and two in-person clinic visits to determine how well they respond to the study drug, and if your child experiences any side effects. You will learn which study drug your child received after 8 weeks of participating in the study. This is done so that you and your child's healthcare provider can determine the treatment plan that is best for them to continue with after they complete the study.

How long will my child be in the study?
We expect that your child will be in this study for up to 13 weeks. If you choose to continue your child on GIR, they may be on study drug for up to an additional 7 days to give you time to work with your child's healthcare provider to obtain the GIR outside of the study.

What will happen in the study?
We will record your child's sex, date of birth, race, ethnicity, the first three numbers of your child's primary home's zip code, and information on how to contact you. Depending on the location where you are doing the study, we may create a code for the rural versus urban area where your child lives most often. Only this code will be recorded in the study records. Your child cannot be personally identified by either the zip code or the rural/urban codes we collect. We will also record information from your child's medical record at this location. If your child is seen at another location, we may ask you to sign a form to allow us to get those records. Examples include your child's medical history, current and past medicines, physical exam, laboratory results, and evaluations over the course of your child's hospitalization or clinic visits.

Screening Period
If you agree to participate in the study, your child will enter the screening period. The screening period may last up to 29 days. We expect the screening period data to be collected at one to two visits. During this time, the study team will determine if your child is eligible to be in the HYP01 study. During the screening period, the study team will:

- Collect information about your child, including gender, race, ethnicity, and date of birth.
- Collect a complete medical history.
- Complete a physical exam, including collecting your child's weight, height, BP and HR.
- Record any medications your child is taking.
- Perform an electrocardiogram (ECG) to assess your child's heart rhythm by attaching soft electrodes (small sticky pads) with a gel to your child's chest, arms and leg.
- Collect a blood sample to assess your child's blood counts, kidney, liver and thyroid function to assure they are within a healthy range to start the study drug.
- If your child menstruates, perform a pregnancy test.

- Ask for a parent/guardian to complete a questionnaire about hyperactivity behaviors (ABC).
- If your child is 8 years and older and the clinician thinks your child would understand, a questionnaire about suicide ideation (asQ) will be administered. You are welcome to be present or you may choose not to be present.

Treatment Period
The treatment period will last about 8 weeks.

Day 1 Visit
During the Day 1 visit the study team will:

- Randomly assign your child to a study group (to receive study drug that contains GIR or placebo).
- Complete a physical exam, including collecting a weight, height, BP and HR.
- Ask you to complete two questionnaires about your child's sleep patterns. These may also be completed by your child if they feel comfortable and are able.
- Give you 4-weeks' worth of study drug to take home with you along with instructions on when your child should be given the study drug and how to complete the study diary.
- Tell you how to contact the study team, should you have any questions or concerns.
- Schedule your child's next clinic visit.

Your child will take the first dose at home in the evening.

Weekly Telephone Calls
Your child will start the study taking 1 capsule a day before bedtime. **About every 5-7 days** the study team will call you to review the study diary and ask you questions to help the team rate how your child is responding to the study drug. Prior to each of these weekly calls, you will need to measure your child's HR and BP. Based on your child's HR, BP, and your answers to the questions, the study team will decide whether to slowly increase the dose of the study drug, keep the dose the same, or decrease the dose. Each week, the daily dose will increase by a maximum of only one capsule.

In-Person Visits
At about **week 4 and week 8** your child will need to come into in clinic for an in-person visit. During this visit the study team will:

- Complete a physical exam, including collecting a weight, height, BP and HR.
- Record any medications your child is taking.
- Perform an ECG to assess your child's heart rhythm.
- Collect a blood sample to assess study drug levels.
- Collect the study diary and any left-over study drug from weeks 1-4. At weeks 4 and 8, we will ask you to bring any unused study drug back to clinic, so we may

discard of the drug appropriately and account for any unused study drug.
- If your child is 8 years and older and the clinician thinks your child would understand, a questionnaire about suicide ideation (asQ) will be administered. You are welcome to be present or you may choose not to be present.
- **At the week 4 visit only**, you will receive 3 new bottles of study drug, enough to complete weeks 5-8 of the study. You will also be given a new study diary and asked to continue to record your child's daily doses.
- **At the week 4 visit only,** we will also collect a blood sample to assess your child's liver function. If a blood sample cannot be collected at week 4, we will collect it at week 8.
- **At the week 8 visit only**, you, your child, and the study team will learn if your child was receiving GIR or placebo. We will also discuss next steps for stopping the study drug.

Before the week 4 and week 8 in person visits, you may receive an email asking you to complete 3 online questionnaires about your child's hyperactivity and sleep patterns. If you are unable to complete the questionnaires online before the visits, we may ask you to complete them electronically or on paper during the visits.

Stopping the Study Drug and Final Safety Assessment Period
Procedures during this period will vary depending on if your child was receiving GIR or placebo.

- For participants who received placebo, the study drug will be stopped at the week 8 visit, and you will be asked to complete a final telephone safety assessment up to 7 days after final study dose is administered.
- For participants who received GIR as the study drug, the following choices will be offered:
    - 1) To continue treatment with GIR. If you and your child's healthcare provider decide your child should continue treatment with GIR, you/your child will have enough GIR from the study to last for 7 days after the week 8 visit. This will give you and your child's healthcare provider time to get GIR outside of what was provided from being in this study.
      or
    - 2) To stop treatment with GIR. If you and your child's healthcare provider decide your child should stop treatment with GIR, for your child's safety, your child will need to slowly stop using the GIR. The amount of time needed to decrease the study drug dose will depend on the final dose your child received at week 8, but will not last longer than 6 days. If you choose to stop treatment with GIR, you will be given instructions on how to safely reduce your child's GIR dosing.

For either option above, a final telephone safety assessment will occur up to 7 days after the final study provided GIR dose is taken.

Study Questionnaires
You and/or your child will be asked to complete the following questionnaires being used in this study:

- Aberrant Behavior Checklist (ABC)
  The ABC is a 58-item questionnaire that measures how significant (on a scale of 0-3) some behaviors, like hyperactivity, are observed in children. It has been used in other studies in children with intellectual disability. For this study, the ABC will be completed on paper or electronically by you. The ABC is required to enter the study and it will be collected at the 4 week and 8 week visits. This questionnaire will be one way we assess how the study drug is working to treat your child's hyperactivity.
- Sleep assessments:
  - Epworth Sleepiness Scale (ESS-CHAD): This is an 8-item questionnaire about daytime sleepiness. For this study, either you or your child will complete the assessment. It will be completed on paper or electronically. This questionnaire will be one way we assess how the study drug affects your child's sleepiness. It will be collected 3 times (at the Day 1visit, week 4 and week 8).
  - Child's Sleep Habits Questionnaire (CSHQ): This is a 35-item questionnaire that asks about sleep habits. For this study, either you or your child will complete the assessment. It will be completed on paper or electronically. This questionnaire will be one way we assess how the study drug affects your child's sleep patterns. It will be collected 3 times (at the Day 1 visit, week 4 and week 8).
- Study Diary review – From Day 1 to End of Study. This diary will tell us the dose of study drug taken, how the drug was taken (swallowed or mixed in food) and what food was taken with the study drug. The diary will also tell us what your child's HR/BP is when you take it at home. For this study, you will complete the diary. It will be collected on paper or electronically at each clinic visit.

Blood Collection and Testing
Blood will be collected from a prick in the finger, a needle poke in the hand or arm or from a line that is already present and used to draw blood. To reduce the number of blood draws or "pokes," we will make every effort to collect study specific blood samples at the same time as your child's routine blood draws; however, this may not always be possible. A numbing cream/spray or other distractors may be used to reduce pain or stress during blood draws. We may ask you what will help keep your child comfortable during the research experience.

Blood samples will be collected up to 3 times from your child. These will include clinical laboratory tests to ensure it is safe to enter and continue in the trial as well as tests to measure the amount of study drug in your child's blood. This information helps researchers understand what dose of GIR should be given, and how often GIR should be given. The maximum amount of blood to be drawn is a follows:

1. Screening period—clinical labs: maximum 10 mL (about 2 teaspoons).
2. Week 4 visit—clinical lab and drug level: maximum 6 mL (1 ¼ teaspoons).
3. Week 8 visit—drug level: maximum 3 mL (about ½ teaspoon). If your child was unable to complete the Week 4 visit clinical lab, we will add it here and ask for 1 ¼ teaspoons instead.

Over the course of the whole study, blood draws will not exceed 13 mL (about 2 ½ teaspoons) for clinical labs, plus about 6ml (1 ¼ teaspoons) for drug level labs. We will use this blood for the tests we explain below.

The blood samples collected for testing will include:

- Clinical laboratory tests to assess your child's blood counts, kidney, liver and thyroid function for safety. If your child menstruates (gets their period), we will do a pregnancy test during the Screening period.
- Pharmacokinetic tests to measure the amount of study drug in your child's blood. This information helps researchers understand how much GIR to give and how often it should be given.

Urine Collection and Testing
If your child menstruates (gets their period), we will do a pregnancy test. We might use some of the blood collected to do the test, or we might collect urine instead. We will use about 1 mL (about ¼ teaspoon) of urine to do the test. Any additional urine your child provides will be discarded.

****ALL SITES:** The following risk information from [START] through [END] cannot be altered without submission of supporting documentation and/or Sponsor approval of changes. Submitted changes without appropriate documentation will be reverted during Board review.

[START]What are the discomforts or risks of the study?
Risk of Guanfacine Immediate Release:
The most common reported side effects or adverse reactions associated with GIR include:

- Dry mouth
- Drowsiness
- Tiredness
- Stomach pain
- Nausea (feeling sick to the stomach)
- Weakness
- Dizziness
- Headache
- Difficulty falling asleep
- Constipation

These reactions are mild and typically disappear after continued dosing.

Other less common, but possible, side effects are:

- low BP,
- slowed HR, or
- an abnormality in liver function tests. We will test your child at Week 4 for any abnormalities in their liver function. [END]

Risk of Placebo: There are no known risks of placebo.

Risks of Blood Drawing:
There are small risks to having blood drawn. These risks may include some pain, discomfort, or bruising where the blood is drawn. There is a small chance of infection and bleeding problems. Your child may feel dizzy or may faint.

Risks of Questionnaires:
Some of the questions asked on the questionnaires may be embarrassing or make you or your child uncomfortable. After the study ends and once your child reaches legal adulthood, there is a risk that your child could become aware of your answers to the questionnaires if your child requests a copy of their medical record and information from the study was entered into the medical record. If any question makes you or your child uncomfortable, you or your child may decline to answer.

Unforeseen Risks:
There may be risks to you from this research that are not known or foreseeable at this time.

Pregnancy Risks:
If your child becomes pregnant, the study drug may involve risks to your child or to the embryo or fetus. It is important that you notify your child's health care provider and the site staff immediately if your child becomes pregnant while in this study. You will be notified of the results of any pregnancy tests performed while your child is participating in this study, as applicable, based on your state and/or local laws and regulations. The study drug will be safely stopped if your child becomes pregnant. Your child may be contacted or asked to return for additional visits to follow your child's pregnancy until an outcome is known. There may also be other risks that we may not know about.

Risk of Loss of Confidentiality:
There is a risk of loss of confidentiality. Every effort will be made to protect your child's information, but this cannot be guaranteed.

What other choices are there besides taking part in this study?
This study is not designed to diagnose, treat, or prevent any disease. Your child's

alternative is to not take part in the study. Even if you don't allow your child to participate, they will have access to standard medical care at the study site. Standard medical care might also include GIR or GER (INTUNIV®) prescribed by your child's medical doctor.

Will I/my child be paid for taking part in this study?
[There will be no money paid to you or your child for being in this study.

OR

You / your child will be reimbursed for time and travel up to $[Amount] for each sample collection, visit or completed study assessment in the form of a [form of payment]. You / your child may be paid up to a maximum total of $200 for study participation.**]**

Will I/my child receive any payment if there is a commercial profit?
Your child's study data and/or samples will not be sold to anyone. However, the use of study data and/or samples may result in commercial profit. You and your child will not receive any payment if there is commercial profit.

Will I/my child have to pay to take part in this study?
There will be no additional costs to you or your child as a result of being in this study. Any study specific procedures or study specific tests will be provided to your child free of charge. However, you or your child's insurance company will be charged for the routine medical care your child would receive whether or not your child participates in this study. You may wish to contact your child's insurance company to talk about this further.

Taking part in this study may lead to added costs to you, such as: travel expenses to attend research visits or time away from school or work to attend research visits.

What if my child is injured because of taking part in this study?
If your child is injured or gets sick because of being in this study, seek immediate medical attention, and then call the site investigator named on this form. The investigator will provide your child with treatment or refer your child for treatment; you and/or your child's insurance will be billed for this.

Who will pay if my child is injured?
There is no plan by the study site to provide free medical care or money for injuries to participants in this study. There is no plan by the National Institute of Child Health and Human Development (NICHD), Duke University (Duke Clinical Research Institute [DCRI]), or Duke University Health System to provide any reimbursement or payment for any study-related injury costs. You are not giving up any of your legal rights by signing this permission form.

Are there benefits to taking part in this study?

We cannot promise any benefits to your child from taking part in this study. Participation in the study may result in improvement in hyperactivity/impulsivity or inattention behaviors in participants; however, it is unknown if there will be a direct benefit to your child for being in this study. Being part of a randomized clinical trial allows for close follow up and monitoring of all participants in the study. We hope participation will also provide important information about the safety and efficacy of GIR in children with DS, which is greatly needed. We hope the information learned from this study will benefit children in the future.

Confidentiality

What happens to my child's study data and samples?

All data we record as part of this study will be stored in a secure database on a server in the U.S. All study data in the database and samples will be given a unique code number and will not be labeled with your child's name or initials, social security number, address, or telephone number. The database will include your child's date of birth, 1st three numbers of your child's zip code, sex, and dates of study visits. Only the site staff, study team and their authorized representatives and others listed under the "authorization" section will have access to information that may identify your child including the list that can match your child's name to the unique code number. Separate from the study database, electronic copies of documents may also be provided to The Emmes Company, LLC that contain your child's identifying information. These electronic copies will be checked for accuracy and then immediately destroyed following review. All study members, who accesses your child's information, will keep it confidential and secure.

All participants' de-identified study data and any remaining de-identified study samples will be submitted to a NIH-designated storage location, such as the NICHD Data and Specimen Hub or DASH (https://dash.nichd.nih.gov) from which the data will be shared with other researchers. Your child's study data, study samples and health information, stored in these databases, will not be labeled with your child's name or other information that could be used to identify them. Researchers approved to access information in these databases will agree not to attempt to identify your child.

De-identified samples may also be used by researchers in the future to conduct tests separate from those being done in the current study. These researchers may conduct whole genome sequencing (WGS); by doing WGS, these researchers may have information that is unique to your child.

The purpose of sharing this information is to make more research possible that may improve children's health. This will be done without obtaining additional permission from you.

The data and samples collected in this study may be kept forever. We may publish the results of this study. However, we will not include your or your child's name or any other identifying information.

What is a Certificate of Confidentiality?
The study data and specimens are covered by a Certificate of Confidentiality (CoC) from the National Institutes of Health (NIH). The CoC further protects you and your child's privacy. It keeps the courts and other agencies from forcing the U.S. study team to share information or body fluid samples that may identify your child during a legal proceeding unless you agree to this. If you want your study information shared with insurers, medical providers, or others not connected with this research, you must ask the investigator to release it.

Information and body fluid samples can only be shared without your permission if:

1. There is a law that requires us to share this with an agency. An example of this would be to report child abuse or contagious diseases; or
2. The information is used for other research, as allowed by federal rules.

We must share information for program reviews with the NIH or the U.S. Food and Drug Administration (FDA) who may request these.

This Certificate does not keep you from sharing information about yourself/your child or your/your child's participation in this research.

What information will be in my child's records at the study location?
Study data entered in your child's medical records will be kept per the study site policies. Other study records will be kept until the FDA has completed their review of the results or for a minimum of 2 years after the study has ended, whichever is longer. A copy of this signed form may go into your child's medical record. This will allow the health care providers caring for your child to know what tests your child is receiving as part of the study and to know how to take care of your child if they have other health problems or needs during the study. It is possible that you may not be able to see the information that has become part of your child's records until the entire study is over.

Authorization for the Use and Disclosure of Protected Health Information
The United States government has a Privacy Rule to protect the privacy rights of patients. The Privacy Rule protects the confidentiality of personal health information that can be linked to a specific individual. The information protected under the Privacy Rule is often referred to as "protected health information" or PHI. This section, called an "Authorization," explains how your child's PHI will be used and shared, and it also describes your child's rights.

Your child's PHI, which may include your child's date of birth, sex, dosing information, medical records, medical history, and the dates or results of any tests, therapies, or procedures that your child has for their medical care will be shared by site staff with individuals and organizations that oversee this study, including:

- Site staff (including those named on the first page of this form),
- The study team and their authorized representatives, including laboratories that may be hired to perform tests,
- Government agencies, such as the U.S. FDA and NIH, who will obtain information from this study under the data collection authority given to them under U.S. law,
- The Institutional Review Board (IRB), Ethics Committee(s) (US or global) that reviews the ethical conduct of this study. The IRB or ethics committee is a group of scientists and non-scientists who review the ethics of research. The goal of the IRB or ethics committee is to protect the rights and welfare of study participants.

The sponsor and the groups above will use your child's health information:

- to complete this research
- to evaluate the results of the study
- to check that the study is being done properly
- to obtain marketing approval for new products resulting from this research

We try to make sure that everyone who sees your and your child's PHI keeps it private, but we cannot guarantee this. If your child's information is shared by any of the groups named above with anyone outside the study team, it may be further shared by them and may not be covered by U.S. privacy laws. Except when required by law, we will only use or share information outside the study team in a way that nobody can tell it is yours and your child's information.

[For IL Sites Only: You have the right to review any mental health information collected about you and shared with others.]

You do not have to sign this form, but if you want your child to be in this study, you must sign/date this form. By agreeing to be in this study, you are giving permission (also called authorization) for us to use and disclose your child's PHI as described in this form. If you refuse to allow the study team to share your child's PHI, your child will not be able to be in the study. However, not signing this form will not affect your child's access to medical care.

If you do not stop this authorization, it will remain in effect indefinitely or if the study site is located in California, Delaware, Illinois, Indiana, Washington, or Wisconsin it will expire on 31Dec2070 or if the study site is located in Maryland, this authorization will expire one year after being signed and dated.

You have the right to stop this Authorization at any time. Your decision to stop your authorization will not involve any penalty or loss of access to treatment or other benefits to which you/ your child is otherwise entitled. If you decide you no longer want your child to participate in this study, but do not stop your Authorization, new health information may be collected until this study ends.

To stop this Authorization, you should inform the site investigator, as named on the first page of this form, of your decision in writing. Stopping your authorization will prevent sharing of PHI in the future but will not affect any PHI that has already been gathered or shared.

You have the right to review and copy your child's health information. However, your access to this information may be delayed until the study is complete.

Will I see any study results?
You may be contacted by the study team conducting this research in the future to be provided with overall study results (summary results from all participants). This means you will not know the results as they relate to your child specifically. You can contact the site staff if you have any questions about study results availability.

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 website will not identify your child either.

You will not be provided with overall results from future studies that use de-identified data and specimens from this study that have been submitted to an NIH storage location such as DASH.

Who can answer my questions about this study?
If you have questions about this study, complaints, or concerns that your child was harmed as a result of participation, call the site staff at the phone number(s) listed on this form.

An IRB is overseeing this study. An IRB is a group of people who perform independent review of research studies. You may contact them at 855-818-2289 or clientcare@wcgclinical.com:

- You have questions, concerns, or complaints that are not being answered by the site staff.
- You are not getting answers from the research team.
- You cannot reach the research team.
- You want to talk to someone else about the research.
- You have questions about your child's rights as a study participant.

Can my child be removed from this study without my approval?
Your child may be removed from this study by the site investigator or the sponsor without your approval. Possible reasons for removal include:

- Your child's condition changes, and the study is no longer in your child's best interest
- The entire study is stopped by the FDA, NICHD, or the IND sponsor
- The investigator is no longer participating in the study
- Your child does not follow the study rules

While your child will not be removed from this study if they are to become pregnant, we request that you let the site staff know and inform your child's healthcare provider. We will ask you and your child return to complete a final study visit where we will tell you if your child's study drug was GIR or placebo, instructions for stopping the study drug, conduct safety assessments, an ECG, collect a blood sample, and ask you to complete questionnaires.

How will I be informed about new information?
We may learn new information during the study that you may need to know. We may also learn about things that might make you want to stop your child's participation in the study. If this happens, you will be notified about any new information in a timely manner. You may also be asked to sign a new permission form that describes these new findings if you decide to continue in the research study.

What happens if I agree to have my child participate in this study, but I change my mind later?
You can withdraw from the study at any time.

If you decide you no longer want your child to participate in this study, call the site staff at the phone number listed on the first page of this form.

Any information and study samples collected before your decision to no longer have your child participate in this study will remain a part of the study records.

If you choose to withdraw early from the study, you will learn if your child is receiving GIR or placebo. If they are receiving GIR, they might require a slow reduction of the study drug lasting up to 6 days, and you will receive instructions on how to do this safely. In addition, the study team will request the following to be completed:

- Safety assessment via telephone questionnaire
- Perform an ECG to assess your child's heart rhythm (in-person only)
- Request the parent/guardian complete a final ABC questionnaire
- Blood collection for PK analysis (in-person only)

No further samples will be collected and no new information about your child will be collected for study purposes unless your child has a side effect related to being in this study. If a side effect occurs, the site staff may need to contact you or review your child's medical records.

Any information and study samples collected before your decision to no longer have your child participate in this study will remain a part of the study records.

Future Contact for New Research Opportunities
At the end of this permission form, you will have the chance to tell us whether or not you will allow the study team to contact you in the future about opportunities for additional research studies that your child may be eligible to participate in. If you choose not to allow researchers to contact you in the future, your child can still participate in this research study.

Optional: Decision to Allow Contact about Opportunities for Future Research Studies	
Please **initial** the appropriate line to indicate whether or not you agree to allow contact about opportunities for future research.	
The information below can only be completed by the parent or legal guardian.	
Initials	**Yes,** I give study team permission to contact me about opportunities for future research studies.
Initials	**No,** I do not give study team permission to contact me about opportunities for future studies. I understand that my child may still participate in this study without providing permission to contact me about opportunities for future research studies.

- Minor participants are required to sign, if able, the "Children's Assent Form" that will be provided.**"**
- Parent/Legal Guardians of minor participants are required to sign under **"Parental Permission"**
- The person obtaining permission is required to sign under "**Parental/Legal Guardian Permission"**

STATEMENT OF PARENTAL PERMISSION
(Parent or Legal Guardian providing permission for a minor participant)

By signing this form, I confirm that:

- I have read this permission form and was given enough time to consider the decision for my child to participate in this study.
- The purpose of this study, procedures to be followed, risks, and benefits have been explained to me.
- I have been encouraged to ask questions, and my questions have been answered to my satisfaction.
- I have been told whom to contact if I have questions, to talk about problems, concerns, or suggestions related to this study.
- I have read this form and agree to give permission for my child to participate in this study and for the use of associated protected health information.
- I understand that participation in this study is voluntary, and I may choose to stop my child's participation in this study at any time without any penalty or loss of access to treatment or other benefits to which my child is otherwise entitled.
- I have been told that I will be given a signed and dated copy of this form[, as well as a signed and dated copy of the Experimental Subject's Bill of Rights]. ***For CA Sites Only***

_____
Printed Name of Participant

The information below can only be completed by the Parent or Legal Guardian capable of providing permission for a minor participant.

For Parents or Legal Guardians (Individual Authorized to Consent to the Child Participant's General Medical Care): By signing below, I certify that I am the parent or legal guardian of the participant named above. I am permitted under state law to sign this form on behalf of the participant.

	Relationship to participant, if applicable (check one)
	☐ Legal Guardian
_____ Printed Name of Parent or Legal Guardian	☐ Parent
	Date:
_____ Signature of Parent or Legal Guardian	Time: ☐ AM / ☐ PM (check one)

STUDY STATEMENT OF PERSON OBTAINING PARENTAL/LEGAL GUARDIAN PERMISSION My signature below documents that: I have fully explained the study described by this form in a language the above person(s) signing this form understood. I have answered their questions and will answer any future questions to the best of my ability. I will tell the above person(s) signing this form of any changes in procedures or in the possible harms/possible benefits of the study that may affect their willingness to provide Permission to stay in the study. Permission was freely given, and I will provide the above person(s) signing this form with a signed and dated copy of this form.		
The information below can only be completed by the person obtaining permission.		
❑ I have explained the study to the above person(s) signing this form, and the above person(s) signing this form have agreed to be in the study.		
_____ Printed Name of Person Obtaining Permission	_____ Signature of Person Obtaining Permission	Date:

CALIFORNIA HIPAA AUTHORIZATION

****This HIPAA section will be for sites that are only located in CA****

Federal regulations give you certain rights related to your health information. These include the right to know who will receive the information and how it will be used. The study doctor must obtain your authorization (permission) to use or release any health information that might identify you.

In this form "you" generally refers to the research participant.

WHAT INFORMATION MAY BE USED AND SHARED?

The study doctor and study staff will use and share your health information as part of this research study. Except when required by law, you will not be identified by name, address, telephone number or other facts that could identify the health information as yours.

Examples of the information that may be used are:

- Medical records (from any doctor, hospital, or other healthcare provider)
- Information created or collected during the research. This could include your medical history, and dates or results from any physical exams, laboratory tests or other tests.

WHO WILL RECEIVE INFORMATION ABOUT YOU?

The study doctor and study staff will share your personal health information with:

- the sponsor, including persons or companies working for or with the sponsor
- Independent/Institutional Review Board (IRB)
- the U.S. Food and Drug Administration (FDA)
- Department of Health and Human Services (DHHS) agencies
- other regulatory agencies

WHY WILL THIS INFORMATION BE USED AND/OR GIVEN TO OTHERS?

The sponsor and the groups above will use your health information:

- to complete this research
- to evaluate the results of the study
- to check that the study is being done properly
- to obtain marketing approval for new products resulting from this research

IS MY HEALTH INFORMATION PROTECTED AFTER IT HAS BEEN GIVEN TO OTHERS?

Your health information may be further shared by the groups above. If shared by them, the information will no longer be covered by this Authorization. These groups are committed to keeping your health information confidential.

WHAT IF I DECIDE NOT TO ALLOW THE USE OF MY HEALTH INFORMATION?

You do not have to sign this form. If you do not sign this form, you cannot take part in this research study.

MAY I WITHDRAW OR REVOKE (CANCEL) MY PERMISSION?

YES. You may withdraw your permission to use and disclose your health information at any time. You can do this by sending written notice to the study doctor. If you withdraw your permission, you will not be able to continue being in the research study.

WHAT HAPPENS IF I WANT TO WITHDRAW MY AUTHORIZATION?

Information that has already been gathered may still be used and given to others. If you withdraw your permission, no new health information will be gathered unless you have a side effect related to the study.

If you withdraw from the study but do not withdraw your Authorization, new health information may be collected until this study ends.

WILL MY AUTHORIZATION EXPIRE?

This Authorization will expire December 31, 2070, unless you withdraw it in writing before then.

MAY I REVIEW OR COPY THE INFORMATION OBTAINED OR CREATED ABOUT ME?

YES. You have the right to review and copy your health information.

However, your access to this information may be delayed until the study is complete.

Your decision to withdraw your Authorization or not to participate will not involve any penalty or loss of access to treatment or other benefits to which you are otherwise entitled.

AUTHORIZATION
By signing this form, I allow the use or disclosure of my health information. I will receive a signed and dated copy of this Authorization.

<table>
<tr><td colspan="2">_____
Printed Name of Participant (if not signing the Authorization)</td></tr>
<tr><td colspan="2">The information below can only be completed by a Participant’s, a Parent or a Legal Guardian capable of providing permission.</td></tr>
<tr><td colspan="2">For Parents or Legal Guardians (Individual Authorized to Consent to the Child Participant’s General Medical Care): By signing below, I certify that I am the parent or legal guardian of the participant named above. I am permitted under state law to sign this form on behalf of the participant.</td></tr>
<tr><td rowspan="4">_____
Printed Name of Parent or Legal Guardian</td><td>Relationship to participant, if applicable (check one)</td></tr>
<tr><td>☐ N/A - Self</td></tr>
<tr><td>☐ Parent</td></tr>
<tr><td>☐ Legal Guardian</td></tr>
<tr><td rowspan="2">_____
Signature of Parent or Legal Guardian</td><td>Date:</td></tr>
<tr><td>Time:
☐ AM / ☐ PM (check one)</td></tr>
</table>