The Children's Hospital *of* Philadelphia®

Informed Consent Form and HIPAA Authorization

Study Title: **Nutritional Impact of Ivacaftor Treatment in 1 to 2-Year Old Children with CF Gating Mutations**

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Your child may be eligible to take part in a research study. This form gives you important information about the study. It describes the purpose of this research study, and the risks and possible benefits of participating.

If there is anything in this form you do not understand, please ask questions. Please take your time. You do not have to take part in this study if you do not want to. If you take part, you can leave the study at any time.

In the sections that follow, the word "we" means the study doctor and other research staff. If you are a parent or legal guardian who is giving permission for a child, please note that the word "you" refers to your child.

Why are you being asked to take part in this study?

You are being asked to take part in this research study because you are living with cystic fibrosis (CF) and at least one CFTR gating mutations, are 1 to 2 years old, and have not received Ivacaftor treatment but have been identified by your CF clinical team as a eligible to begin Kalydeco (ivacaftor) treatment.

What is the purpose of this research study?

The purpose of this research study is to determine the effects of clinically prescribed ivacaftor treatment on 1 to 2 year old children with CF and gating mutations on sleeping energy expenditure, growth status and gut health and function.

How many people will take part?

About 18 children will take part in this study at CHOP.

What is involved in the study?

Ivacaftor will not be administered or provided by the study. Ivacaftor will be prescribed by your clinical care provider.

How long will you be in this study?

If you agree to take part, participation is for 4 to 6 months and will require three visits:

- Visit 1 (Baseline) will occur prior to the start of clinically prescribed ivacaftor treatment
- Visit 2 (after 6 weeks of clinically prescribed ivacaftor treatment)

- Visit 3 (after 12 weeks of clinically prescribed ivacaftor treatment)

Visits 1 and 3 will take 2 or 3 days to complete. Two important tests require that you rest very quietly and still and are conducted during a nap (morning or afternoon). If these tests are not completed on the second day, then you will need a third day to complete these tests during a nap. Visit 2 is a two-day visit.

If you are not local to CHOP, you will need to stay overnight for one or two nights at a hotel near CHOP with all costs and transportation provided.

If you are local to CHOP, Visit 1 will still require a 2 or 3 day visit (depend on nap tests), however, Visit 2 may be a one-day visit and Visit 3 may be a 1 or 2 day visit depending.

What are the study procedures?

Interviews: A team member will take your medical history, along with a listing of any medications you are taking. Throughout the study, you will be asked to report if you think that anything bad has happened as a result of the study.

We will ask you to complete questionnaires by interview, including questions about who lives in the household, family contact information, and questions related to health history.

Medical Record Review: We will review your medical records throughout the study to collect information about your medical history, current health, diagnosis, treatments, medications, and results of clinical tests. If you are not a patient at CHOP, we would like to get a copy of your medical records from your regular doctor. We will ask you to sign a Release of Information form. This will allow your doctor to send us the records.

Physical Examination: We will measure your length and weight, head circumference, size of your right arm and the amount of fat stored beneath the skin. This will take approximately ten minutes.

Body Composition: We will measure your body composition (fat, muscle and bone) by a method called dual energy x-ray absorptiometry (DXA) while you are asleep. This method uses a very low-powered x-ray beam to scan the entire body (DXA). The radiation exposure is very low. The test takes about 20 minutes total.

Laboratory Test: Blood will be drawn to measure vitamins A, D, E, and K, bile acids, fatty acids, as well as your liver function, and measures of inflammation and nutritional status.

Sleeping Energy Expenditure: Sleeping energy expenditure is determined by measuring the amount of oxygen and carbon dioxide in the air you breathe. You will lay under a clear plastic hood and a metabolic cart will be used to measure oxygen and carbon dioxide as you breathe in and out. You will breathe regular room air. This test will be done at each visit while you are asleep in the morning if possible. This test does not require fasting, but we will carefully note when you last ate or drank, including the time of day, amount of food, and the feeding time prior to the test. The test lasts about 60 minutes. This test will determine the amount of energy (calories) you use in a normal resting state.

Stool Collection and Analysis: Stool samples will be collected at each visit to learn more about fat absorption, inflammation, and pancreatic function. We will provide instructions and containers for stool collection and storage.

Dietary Intake: During the study, we will ask you to keep a three-day record of the foods and beverages you eat at home. We will give you the forms, a small food scale, and measuring cups and spoons to help estimate the amounts. We will call you during the time you are expected to

keep the records in case you have questions. We ask that you mail the completed records to us within two weeks of your visit in a self-addressed stamped envelope that we provide. The information will be analyzed by a computer to determine the amount of calories, fats, and other nutrients that you ate over this three-day period.

Adverse Events Diary: We will ask you to keep a record of any signs or symptoms that you may have had since you started the study. We will collect these diaries from you at each study visit and provide you with a new diary for the next study period. We will also ask you about any adverse events in person at the 6 and 12 week visits (Visits 2 and 3) and also during phone calls at 3 weeks and 9 weeks.

Adherence: We will ask you in person at the 6 and 12 week visits (Visits 2 and 3) about adherence to your ivacaftor treatment, that is, how many doses you missed. We will ask about adherence to pancreatic enzyme medication use over this time period. We will also call you by phone at 3 weeks and 9 weeks to ask about how many of ivacaftor or pancreatic enzyme medications you missed.

Delay of Ivacaftor treatment: You will be asked to plan the start of your clinically prescribed ivacaftor treatment until all baseline (Visit 1) procedures have been completed.

Visit Schedule

We will ask you to sign consent forms for the study in person at Visit 1 on Day 1 before you start the study. Many of the study assessments could occur on any of the visit days (i.e.questionnaires, spot stool sample). The baseline (Visit 1) and 12 week (Visit 3) visits are identical with the exception of obtaining informed consent which will occur at Visit 1 on Day 1 prior to any assessments being done or specimens being collected. The Tables below provide a brief description of the purpose and duration of each study visit. If you are not local to CHOP, Visits 1 and 3 will be 2 or 3 day visits and Visit 2 will be a two-day visit as described below. If you are local to CHOP, Visit 1 will be a 2 or 3 day visit, Visit 2 may be a one-day visit and Visit 3 may be a 1 or 2 day visit as Days 1 and 2 for Visits 2 and 3 can be combined to complete study protocol procedures.

Visit 1 (Baseline)

Day 1 – Consent (2-3 hours)	• Informed consent • Instructions in preparation for study procedures
Day 2 (5-6 hours)	• Sleeping energy expenditure • Blood draw • Stool sample • Body measurements • Whole body DXA • Questionnaires
Day 3 (if needed) (1-2 hours)	• Whole body DXA or sleeping energy expenditure if not performed on Day 2
Post Visit Follow-up (3-4 days)	• 3-day weighed food records • Begin clinically prescribed ivacaftor treatment
(6 weeks)	• Maintain adverse events diary

Visit 2 (Week 6 of ivacaftor treatment)

Day 1 (2-3 hours)	• Instructions in preparation for study procedures
Day 2	• Sleeping energy expenditure

(5-6 hours)	• Blood draw • Stool sample • Body measurements • Whole body DXA • Questionnaires
Post Visit Follow-up (3-4 days)	• 3-day weighed food records
(6 weeks)	• Maintain adverse events diary

Visit 3 (Week 12 of ivacaftor treatment)

Day 1 (2-3 hours)	• Instructions in preparation for study procedures
Day 2 (5-6 hours)	• Sleeping energy expenditure • Blood draw • Stool sample • Body measurements • Whole body DXA • Questionnaires
Day 3 (if needed) (1-2 hours)	• Whole body DXA or sleeping energy expenditure if not performed on Day 2
Post Visit Follow-up (3-4 days)	• 3-day weighed food records • Maintain adverse events diary until 3-day food records are completed • Send food records and adverse events records to CHOP

What are the risks of this study?

Taking part in a research study involves inconveniences and risks. If you have any questions about any of the possible risks listed below, you should talk to your study doctor or your regular CF doctor.

While in this study, you are at risk for the following side effects:

Risks associated with study:

Delaying treatment with ivacaftor: There is minimal risk associated with planning the start of ivacaftor treatment until all baseline (Visit 1) procedures have been completed.

Blood draw: There is a small risk of pain, infection and local irritation associated with the blood draw. A skilled pediatric research nursing staff person will draw the blood. You will have approximately 18cc (1.2 tablespoon) of blood drawn at Visit 1 and 3, and approximately 5cc (1 teaspoon) at Visit 2 and no more than 5cc/kg body weight over an eight week period.

DXA scans: This research study involves exposure to radiation from the DXA scans. Therefore, you will receive a very low radiation dose. This radiation dose is not necessary for your medical care and will occur only as a result of your participation in the study. At doses much higher than you will receive, radiation is known to increase the risk of developing cancer after many years. At the doses you will receive, it is very likely that you will see no effects at all.

Sleeping Energy Expenditure: This assessment poses minimal risk.

Physical measurements: There are no physical risks but you might experience momentary embarrassment or discomfort. The exam is similar to those that are performed as part of routine medical care.

Questionnaires: Sharing dietary intake, demographic information, health history and medical information poses minimal risk

Stool collection: Collection and storage of stool is associated with a small risk of fecal contamination. However, for safety and convenience, you will be provided with proper stool collection instructions and supplies (gloves, disposable collection containers, storage freezer container).

Risks associated with breach of confidentiality: As with any study involving collection of data, there is the possibility of breach of confidentiality of data. Every precaution will be taken to secure participants' personal information to ensure confidentiality. At the time of participation, each participant will be assigned a study identification number. This number will be used on data collection forms, blood samples, stool specimens and in the database instead of names and other private information. A separate list will be maintained that will links each participant's name to the study identification number for future reference and communication.

If any of the blood tests done for this study result in information that your doctor should know about, we will ask your permission to share these results with your doctor.

Are there any benefits to taking part in this study?

There will be no direct benefit to you from taking part in this study. The knowledge gained from this study may help doctors determine the mechanisms for the benefits of ivacaftor treatment in young children, such as improved growth status and weight gain when they begin treatment with ivacaftor.

Do you need to give your consent in order to participate?

If you decide to participate in this study, you must sign this form. A copy will be given to you to keep as a record.

What are your responsibilities?

Please consider the study time and responsibilities as a research subject when making your decision about participating in this study. You will need to follow the study doctor's instructions and keep all study appointments.

What happens if you decide not to take part in this study?

Participation in this study is voluntary. You do not have to take part in order to receive care at CHOP.

If you decide not to take part or if you change your mind later there will be no penalties or loss of any benefits to which you are otherwise entitled.

Can you stop your participation in the study early?

You can stop being in the study at any time. You do not have to give a reason.

Can the study doctor take you out of the study early?

The study doctor may take you off of the study if:

- Your condition worsens
- The study is stopped
- You cannot meet all the requirements of the study
- New information suggests taking part in the study may not be in your best interests

What choices do you have other than this study?

- Not participating in this study
- You can discuss other options available to you with your doctor

What about privacy, authorization for use of Personal Health Information (PHI) and confidentiality?

As part of this research, health information about you will be collected. This will include information from medical records, procedures, interviews and blood and stool tests. Information that could identify you will not be shared with anyone – unless you provide your written consent, or it is required or allowed by law. Laboratory test results will not appear in your medical record. We will do our best to keep your personal information private and confidential. However, we cannot guarantee absolute confidentiality. Your personal information may be disclosed if required by law.

The results of this study may be shown at meetings and published in journals to inform other doctors and health professionals. We will keep your identity private in any publication or presentation.

Several people and organizations may review or receive your identifiable information. They will need this information to conduct the research, to assure the quality of the data, or to analyze the data or samples. These groups include:

- Members of the research team and other authorized staff at CHOP.
- People from agencies and organizations that perform independent accreditation and/or oversight of research; such as the Department of Health and Human Services and the Office for Human Research Protections.
- Public health authorities that are required by law to receive information for the prevention or control of child abuse.
- Data may be shared with the study sponsor, Vertex Pharmaceuticals. Your data will be labeled with a unique number and will not include information that can identify you. The sponsor will not know who you are. Private information such as your name, birth date or medical record number will not be shared with them.
- Your samples/data will be shared with outside laboratories so they can be analyzed. Your samples/data will be labeled with a unique number and will not include information that can identify you. The outside laboratories will not know who you are. Private information such as your name, birth date or medical record number will not be shared with them. These laboratory results will not appear in your medical record. The outside laboratories are:
    - ARUP Laboratories
    - Craft Technologies Laboratories

- Gundberg Laboratory, Yale University

By law, CHOP is required to protect your health information. The research staff will only allow access to your health information to the groups listed above. By signing this document, you are authorizing CHOP to use and/or release your health information for this research. Some of the organizations listed above may not be required to protect your information under Federal privacy laws. If permitted by law, they may be allowed to share it with others without your permission.

There is no set time for destroying the information that will be collected for this study. Your permission to use and share the information and data from this study will continue until the research study ends and will not expire. Researchers continue to analyze data for many years and it is not possible to know when they will be completely done.

Can you change your mind about the use of personal information?

You may change your mind and withdraw your permission to use and disclose your health information at any time. To take back your permission, it is preferred that you inform the investigator in writing.

Virginia Stallings, MD
The Children's Hospital of Philadelphia
2716 South Street, 14FL, Rm 14473
Philadelphia, PA 19146

In the letter, state that you changed your mind and do not want any more of your health information collected. The personal information that has been collected already will be used if necessary for the research. No new information will be collected. If you withdraw your permission to use your personal health information, you will be withdrawn from the study.

Financial Information

All costs of participating in this study will be covered by the study. There are no costs to you or your insurance company. All travel expenses to Philadelphia will be covered by the study. Lodging will also be arranged and paid for by the study team.

Will you be paid for taking part in this study?

You will be compensated $150 for each Visit for your time and effort associated with the protocol procedures. You will be reimbursed to cover the costs of travel, parking and meals that have not been pre-arranged by the study team. In order to be reimbursed, you must provide receipts for these items. Visit 1 (baseline) and Visit 3 (12-week) may require a third day. If you require an additional day for Visit 1 or Visit 3 to complete the protocol procedures, you will be compensated an additional $150 for your time and effort. Visit 2 (6-week) will not have an additional day option. If your total compensation is more than $600 in a calendar year, you will receive a W9 form.

Summary of Range of Payment

	Each Visit	If Additional day required
Visit 1 (Baseline)	$150	$300
Visit 2 (6-weeks)	$150	$150*
Visit 3 (12 weeks)	$150	$300
	$450 (minimum)	$750 (maximum)

*The compensation for Visit 2 (6 weeks) will always be $150.

Who is funding this research study?

This study is supported by Vertex Pharmaceuticals, Inc. Vertex Pharmaceuticals, Inc. is a drug company that makes the medication being studied in this research project. Vertex Pharmaceuticals is giving money to Children's Hospital of Philadelphia for the costs of the study. The results of the study will be reported to Vertex Pharmaceuticals. If the study shows that the ivacaftor may be useful for a new purpose, this could benefit Vertex Pharmaceuticals financially.

Please ask a study team member if you have any questions about how this study is funded.

What if you have questions about the study?

If you have questions about the study, call the study doctor, Dr. Stallings at 267-425-1633. You may also talk to your own doctor if you have questions or concerns.

The Institutional Review Board (IRB) at The Children's Hospital of Philadelphia has reviewed and approved this study. The IRB looks at research studies like these and makes sure research subjects' rights and welfare are protected. If you have questions about your rights or if you have a complaint, you can call the IRB Office at 215-590-2830.

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.

Consent for Use of Data or Specimens for Future Research

As part of the study, we will collect blood and stool samples. We may wish to use these samples in a future study about CF and nutrition. The information and samples will be given a unique code and will not include information that can identify you.

If you leave the study, the data and specimens will remain part of the research. You can ask to have the data collected about you removed or your samples destroyed. You can also ask us to remove information that identifies you from the data or samples.

Please indicate whether you will allow your data or samples to be used for future research by putting your initials next to one of the following choices for both blood and stool:

_____ (initials) The blood may be used for this study only.

_____ (initials) The blood may be used for other future research studies. If the specimens are shared outside of CHOP, no identifiable information will be included.

_____ (initials) The stool may be used for this study only.

_____ (initials) The stool may be used for other future research studies. If the specimens are shared outside of CHOP, no identifiable information will be included.

Consent to Take Part in this Research Study and Authorization to Use and Disclose Health Information for the Research

The research study and consent form have been explained to you by:

Person Obtaining Consent	Signature of Person Obtaining Consent
	Date

By signing this form, you are indicating that you have had your questions answered, you agree to take part in this research study and you are legally authorized to consent to your child's participation. You are also agreeing to let CHOP use and share your child's health information as explained above. If you don't agree to the collection, use and sharing of your child's health information, your child cannot participate in this study. **NOTE:** *A foster parent is not legally authorized to consent for a foster child's participation.*

Name of Subject	
Name of Authorized Representative (if different than subject)	Relation to subject: ☐ Parent ☐ Legal Guardian
Signature of Authorized Representative	Date

Consent to Take Part in this Research Study and Authorization to Disclose Health Information for Research

_____
Name of Subject

Name of Authorized Representative (if different than subject)	Relation to subject: ☐ Parent ☐ Legal Guardian

The research study and consent form have been explained to the subject or parent/legal guardian.

By signing this form, you are indicating that you have answered the subject's or parent's/legal guardian's questions, they have agreed to take part in this research study and they are legally authorized to consent to their or their child's participation. They have also agreed to let CHOP use and share their or their child's health information as explained above. If they don't agree to the collection, use and sharing of their or their child's health information, they cannot participate in this study.

Person Obtaining Consent	Signature of Person Obtaining Consent
	Date

Witness/Interpreter

By signing this form, you are indicating that:

- The information in the Summary Document as well as any additional information conveyed by the person obtaining consent was presented to the subject in a language preferred by and understandable to the subject or parents/legal guardian's; and
- The subject's or parent's/legal guardian's questions were interpreted and the responses of the person obtaining consent were presented in a language preferred by and understandable to the subject or parent/legal guardian.
- At the conclusion of the consent conference, the subject was asked in a language preferred by and understandable to the subject if s/he understood the information in the Summary Document as well as an additional information conveyed by the person obtaining consent (including responses to the subject's questions) and responded affirmatively.

Name of Witness/Interpreter	Signature of Witness/Interpreter

Date