Title of research study: ***Precise Infliximab Exposure and Pharmacodynamic Control to Achieve Deep Remission in Pediatric Crohn's Disease***

Investigator:

Contact Info:

Industry Protocol #:
REMODEL-CD

Drug Name:

Infliximab

Funding:

National Institutes of Health

National Institute of Diabetes and Digestive and Kidney Diseases

In-kind drug-only support: Janssen Scientific Affairs, LLC

Key Information:

The following is a short summary of this study to help you decide whether to be a participant in it. More detailed information about the study is listed later in this form. This document does not replace the discussion you should have with the research team about this study including having any questions or concerns answered.

If you are 18 years and older: This is a consent form. It explains this research study. If you decide that you want to be in this research study, then you will sign this form to show that you agree to be part of this study. If you sign this form, you will receive a signed copy of it for your records.

Parental Permission: If you are a parent or legal guardian of a child who may take part in this study, permission from you is required. The assent (agreement) of your child may also be required using a separate form. When we say "you" in this form, we mean you or your child; "we" means the study doctor and other staff.

Reason for the study:

Approximately 3 million people in the United States are living with inflammatory bowel disease, which includes Crohn's Disease. There are limited treatment options approved for use in children and adults with Crohn's disease. We need better ways to inform decisions on treatment.

We are asking you to be part of this research study because you have been diagnosed with Crohn's Disease and you are going to start treatment with infliximab as part of your routine clinical care.

Infliximab is a FDA-approved drug to treat Crohn's Disease. Currently, standard dosing of infliximab is based only on your weight. However, with standard dosing of infliximab, some patients may not have a complete response or may lose response over time. Several research studies have shown that response to infliximab is improved when levels of infliximab are measured more frequently and when drug levels or other blood tests are within the target range.

The main reason for this research study is to determine if a computer program that calculates an individualized dose based on your blood testing results (precision dosing) can better achieve the best possible response to infliximab compared to standard dosing (conventional dosing). This new method of precision dosing is still experimental while the conventional dosing is already approved by the United States Food and Drug Administration.

If you qualify and decide you want to be in the study, you will come to [Site Name] approximately 9 times over the next year. You will receive infliximab prescribed by your regular doctor. Most of these visits will happen when you get your infliximab infusions. You will be asked to provide blood and stool samples at specific infusions.

Your study site has been assigned to one of two groups: the conventional dosing group, which uses standard dosing based on your weight, *or* the intervention group, which uses the computer program and blood/stool tests to inform your doctor of dosing options. Which group the study site is assigned was chosen by chance, like flipping a coin. You will be told which group your study site has been assigned.

For this study, we will enroll 180 people between 6 and 22 years old with Crohn's Disease.

We expect that you will be in this research study for 12 months.

Procedures:

If you decide to participate in the research study, the following tests and procedures will take place.

Standard Dosing Group:

You will receive standard care of infliximab as ordered by your doctor.

We will:

- Collect information about you
- Measure levels of infliximab in your blood
- Perform other blood and stool tests
- Compare your results to the other group (intervention group)
- Your doctor will likely perform a colonoscopy at the end of the study so we can compare the rate of gut healing across both groups.

Intervention Group:

We will:

- Collect information about you
- Measure levels of infliximab in your blood
- Perform other blood and stool tests
- Enter the results into the computer program.
- Your doctor will likely perform a colonoscopy at the end of the study so we can compare the rate of gut healing across both groups.

Your doctor will use the computer program to inform their decision on your dose and dosing schedule. Your doctor may need to change your infliximab dose or dosing schedule in order to personalize your dosing plan.

Based on prior studies, your doctor may need to prescribe doses that are higher than the standard dosing.

More detailed information about the study procedures can be found under ***"(Detailed Procedures)"***

Risks to Participate:

Like all medicines, infliximab can have side effects. Most side effects are mild to moderate. Some may be serious and may require treatment or additional testing. Side effects may appear up to six months or longer after the last infusion.

The table below shows the most common and most serious side effects that researchers know about. We do not know all of the side effects that may occur.

Possible Infections while on Infliximab (some may be serious)
Viral Infections (affects 10% or more) o Common cold o Bronchitis (coughing up mucus) Bacterial Infections (occur between 1-10%) o Sinus infection o Sore throat o Pneumonia Tuberculosis (uncommon) Fungal infections (occur between 0.01-0.1%)

Possible Infections while on Infliximab (some may be serious)
Other Side effects of Infliximab ○ Infusion Reactions including Allergic Reactions ○ Lupus-like reactions ○ Antibodies against infliximab ○ Cancer (occur between 0.01-0.1%) ○ Abnormal liver blood tests or liver problems ○ New rash, psoriasis or hair loss ○ Blood problems (low white blood cells) or easy bruising

More detailed information about the risks of this study can be found under ***"(Detailed Risks)"***

Benefits to Participate:

We cannot promise any benefits to you or others from your taking part in this research. However, possible benefits include improved control of your Crohn's Disease and improved drug durability (longer time on the drug). In addition, you will receive infliximab at no cost during the study for up to 365 days.

This study will provide invaluable data regarding future treatment plans for dosing of infliximab.

Other Options:

Participation in research is completely voluntary. Your decision to participate or not to participate will not affect the care you receive.

Your alternative to participating in this research study is to not participate.

Cost to Participate:

You and your insurance company will be charged for the healthcare services that you would ordinarily be responsible for paying. This includes any additional fees associated with the infusion (such as, but not limited to, facility fees, professional fees and/or laboratory fees). In some cases, insurance will not pay for services ordinarily covered because these services were performed in a research study. You should check with your insurance to see what services will be covered by your insurance and what you will be responsible to pay. If your insurance company denies the dose recommended by the computer program, your doctor can appeal.

Payment:

[Sites will alter to conform to their institutions' policies.]

If you agree to take part in this research study, we will pay you for your time and effort (please see the chart below). You will receive payment for this study in the form of a reloadable debit card (Clincard). We will give you a handout that will explain how to use the card. Because you are being paid for your participation, [Site Name] is required by the Internal Revenue Service (IRS) to collect and use your social security number (SSN) or taxpayer identification number (TIN) to track the amount of money that we pay. You will need to complete a Federal W-9 form for this income tax reporting. This form requires your Social Security number. This form will be given to the [Site Name]'s business office. It will not be kept as part of your study chart. If you move, you will need to complete another W-9 with an updated address.

Your information and samples (both identifiable and de-identified) may be used to create products, including some that could be patented/licensed and sold. If this happens, there are no plans to tell you, or to pay you, or to give any compensation to you or your family.

Payment Chart

										Total
Study Activity	**Doses (infusions)**									
	1	2	3	4	5	6	7	8	9	
Questionnaire /Blood sample	$10	$10	$10	$10	$10	$10	$10	$10	$10	$90
Stool sample	$25		$25	$25		$25			$25	$125
Optional Pinch biopsy									$25	$25
Total for participation (*dependent on number of infusions in year1)										**~$240**
*You will receive $10 for each blood sample collected up to 1 year as some patients may require more or less than 9 infliximab doses in one year.										

Additional Study Information:

The following is more detailed information about this study in addition to the Key Information.

If I have Questions or would like to know about:

Who to talk to…	**You can call …**	**At …**
• Emergencies • General study questions • Research-related injuries • Any research concerns or complaints	**PI Name:** [Site PI Name]	Phone: [XXX-XXX-XXXX]
• Emergencies • General study questions • Research-related injuries • Any research concerns or complaints	**Lead Study Coordinator:** [Coordinator Name]	Phone: [XXX-XXX-XXXX]
• Your rights as a research participant	**Institutional Review Board** This is a group of scientists and community members who make sure research meets legal and ethical standards.	Phone:

Detailed Procedures:

- Consent- You will need to read and sign this consent form before doing any study procedures. You will get a copy to keep.
- Demographics – We will collect information including your current age, age of diagnosis, gender, race and ethnicity.
- Medical Record Review- We will review your medical records for information on your health, medical and surgical history, and current medications.
- Physical Exam- We will examine your temperature, heart rate, breathing rate, blood pressure, height, weight, and body mass index. We will also perform an abdomen examination and perianal examination (located around the anus, if needed).
- The study staff will ask you about any symptoms you have had since your last visit.

- Questionnaires- You will answer some questions about your stomach pain, stool frequency, and general well-being.
- You will have up to 20 ml (4 teaspoons) of blood collected for research purposes prior to each infusion. In addition, about 5 ml (1 teaspoon) of blood will be collected 30-60 minutes after infusions 1, 3, 4, and 6. We will try to collect the blood sample from your IV so you do not have to have another needle stick. If we are not able to collect a blood sample at that time, you will be given the option to have another needle stick to collect the blood.
- Stool Collection- You will be asked to collect stool samples. You will be provided the kits for collection and mailing. You may also be given the option to perform additional at-home stool testing. This may include the use of a smartphone and a commercially available application that you would install on your smartphone. The study staff will provide additional information about this.
- Pregnancy Test- If you are female and able to get pregnant, you will be asked to give a small sample of urine for a pregnancy test. We will give the results of this test to the parent. If it is positive, you will not be allowed in the study.
- Drug Infusion (first 3 doses) - As part of your normal infusion visits, you will receive infliximab at 0, 2, and 6 weeks. If you are in the intervention group, you may receive doses that are higher than the FDA approved dose.
- Drug infusion (doses 4 - 9) - As part of your normal infusion visits, you will receive infliximab every 4-8 weeks. The dosing schedule and actual dose is variable and based on your site's group assignment. You may require more or less than 9 infliximab doses in one year, regardless of your site's group assignment.
- Drug infusion -You will be monitored for 30 – 60 minutes or longer following your infusion for any infusion-related side effects.
- Approximately 1 year (between 52-84 weeks) after starting treatment, you will likely have a colonoscopy as part of your clinical care.
    - We would like to collect a blood sample and up to 4 intestinal pinch biopsies for this research study. Collection of pinch biopsies is optional. You can indicate your preference on the signature page of this consent.
    - We will capture a video-image of your colonoscopy so the study doctors can review it and give it a score based on the amount of inflammation seen. The video will be labeled with your study ID and stripped of other identifiers.
- The study staff will contact you prior to visits as a reminder of upcoming visits and stool samples.

Procedures	Screen	Treatment Period														
Infusion dose number	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**Final**
Weeks (range)		**0**	**2**	**6**	**10-14**	**14-22**	**18-30**	**22-38**	**26-46**	**30-54**	**34-62**	**38-70**	**42-78**	**42-86**	**50-94**	**52-84**
Ensure you qualify to participate in this study	X	X														
Collect Demographic information	X															
Collect medical and surgical history	X															
Ask about current and past medications	X	X	X	X	X	X	X	X	X	X*	X*	X*	X*	X*	X*	X
Ask about any symptoms you are having or have experienced	X	X	X	X	X	X	X	X	X	X*	X*	X*	X*	X*	X*	X
Receive infliximab infusion		X	X	X	X	X	X	X	X	X*	X*	X*	X*	X*	X*	X
Collect vital signs (temperature, blood pressure, heart rate, weight and height)	X	X	X	X	X	X	X	X	X	X*	X*	X*	X*	X*	X*	X
Perform physical exam	X				X											X
Perform urine pregnancy test (female participants)	X															
Collect blood sample(s)	X	X	X	X	X	X	X	X	X	X*	X*	X*	X*	X*	X*	X
Collect Stool samples	X			X	X		X									X
Complete questionnaires	X	X	X	X	X	X	X	X	X	X*	X*	X*	X*	X*	X*	X
Research only pinch biopsies and blood sample at colonoscopy																X
*Some patients will have a different number of total doses during the one year study. These data are only collected up through the first year of treatment (first 365 days).																

Change of Mind/Study Withdrawal:

You can leave the research at any time; it will not be held against you.

If you decide to leave the research, contact the investigator so that the investigator can record your reason for withdrawal.

The person in charge of the research study or the sponsor (Cincinnati Children's) can remove you from the research study without your approval. Possible reasons for removal include significant failure to follow study procedures, if the investigator believes it is not in your best interest, or if your disease gets worse and the investigator believes it is best for you to be removed.

If you stop being in the research, data already collected may not be removed from the study database. You will be asked whether the investigator can collect data from your routine medical care. If you agree, this data will be handled the same as research data.

If you stop being in the research, you and your insurance company will be responsible for the cost of infliximab.

Detailed Risks:

Infections

You may have more infections while taking infliximab or if you have an infection it could make it worse. Tell the study doctor if you have a new infection, if an infection keeps coming back, or if you have any signs of infection such as:

• Fever • Chills • Night sweats • Flu-like symptoms • Weight loss • Tiredness • Cold sores	• Headache • Coughing • Coughing up blood • Congestion • Shortness of breath • Chest tightness • Nausea • Vomiting	• Diarrhea • Frequency or burning while peeing • Redness or swelling of limbs, skin or joints • New or worsening of pain in any location

Infections seen with this treatment are colds, bronchitis (coughing up mucus), sinus infections, sore throat, and pneumonia. Those infections caused by viruses occur “very commonly” while those caused by bacteria occur “commonly.”

Some patients have had serious infections while receiving infliximab. Some of the patients have died from these infections.

Tuberculosis is a serious infection that usually develops in the lungs but can also develop in other areas of your body. Tuberculosis has been reported in patients who have received TNF-blockers, and it has been reported uncommonly in patients treated with infliximab. Tuberculosis requires prolonged treatment with specific medication. You may be more likely to develop tuberculosis while on infliximab. If you or any of your family have ever had tuberculosis you should tell your doctor. While in this study, if you come in contact with anyone who has tuberculosis, you should tell your study doctor.

Your study doctor will do a blood test to see if you have come in contact with tuberculosis.

Fungal infections have been reported in patients taking infliximab. Some of these fungal infections, such as histoplasmosis and coccidioidomycosis, occur rarely and can be serious and involve internal organs. You should find out from your study doctor which fungal infections are common where you live or travel, and what symptoms they cause. Tell your study doctor and family physician right away if you develop symptoms of such illnesses.

You should also tell your doctor if you have ever had chickenpox. If while in the study, you come in contact with someone with chickenpox tell your study doctor.

The use of live virus or bacterial vaccines when you are receiving infliximab may result in an infection. You cannot receive a live virus or bacterial vaccine during this study or for 3 months after your last dose of the infliximab. Other types of vaccines are allowed.

Congestive Heart Failure

Patients with congestive heart failure (CHF), a disease where the heart pumping action is weakened, were treated with infliximab in another study. Some of these patients had worsening of their CHF and some died. The risk is unknown. If you have a history of CHF or have received treatment for CHF, you are not allowed to participate in this study.

New cases of heart failure have been reported in patients receiving infliximab. It is not known whether or not these cases are related to infliximab. If you have shortness of breath or swelling in your ankles and/or feet, you must contact your study doctor right away.

Patients treated with infliximab have uncommonly developed worsening CHF or developed CHF for the first time.

Infusion Reactions including Allergic Reactions and Lupus-Like Reactions

Your body might have a reaction during or shortly following an infusion of infliximab into a vein. This is called an infusion reaction. These reactions are usually mild to moderate. They are managed by slowing the infusion or by giving you medication. Any drug may cause an allergic reaction in some patients. A life-threatening allergic reaction called anaphylaxis has occurred uncommonly in patients treated with infliximab.

Symptoms of an infusion reaction or an allergic reaction may include 1 or more of the following:

• Fever • Chills • Hives • Rash • Swelling • Itching	• Headache • Flushing • Nausea • Light-headedness • Chest pain or tightness • Wheezing	• Difficulty breathing or swallowing • Decrease or increase in blood pressure • Anaphylaxis (life-threatening allergic reaction

If the symptoms cannot be managed or become serious or life threatening, the infusion will be stopped and additional treatment will be provided immediately if necessary.

If you have an allergic reaction your regular doctor may give you a medication used to treat allergic symptoms (such as an antihistamine), or to reduce aches, pains, and fever (such as acetaminophen or paracetamol). Antihistamines can make you sleepy, so please use caution when driving a car or operating machinery.

Cases of seizures have also been reported uncommonly. Cases of temporary loss of vision occurring during or within 2 hours of an infliximab infusion have also been reported. Patients have experienced a stroke, heart attack (sometimes resulting in death), or abnormal heart rhythm within 24 hours of the start of their infusion with infliximab.

Another type of reaction is called a delayed hypersensitivity reaction, which as occurred uncommonly in patients treated with infliximab. This reaction can occur 1 to 14 days after the infusion. Symptoms such as fever, rash, muscle aches, and/or joint pain may develop. You should report any of these symptoms to your study doctor right away.

Some patients have developed symptoms or developed abnormal blood tests that look like a disease called lupus. These symptoms may include muscle aches, joint pain, fever, prolonged chest discomfort or pain, rash (including a rash on the cheeks or arms that gets worse in the sun) and shortness of breath. You should report any of these symptoms to your study doctor.

Antibodies against Infliximab

Your body may make antibodies against infliximab. These antibodies might cause an allergic reaction if you receive infliximab in the future.

Cancer

Cancers have been reported in patients who have received infliximab and other TNF-blockers. Lymphoma (a cancer of lymph nodes) has been reported rarely in patients treated with infliximab (affects between 1 and 10 in 10,000 patients). Cases of leukemia (a cancer of the blood) have also been reported in patients taking TNF-blockers. It has been reported rarely in patients treated with infliximab (affects between 1 and 10 in 10,000 patients).

Rarely (between 0.01-0.1%), patients who received infliximab developed skin cancers, including melanoma.

A very aggressive rare type of lymphoma, called hepatosplenic T-cell lymphoma, has been reported in patients treated with TNF-blockers including infliximab. This type of cancer usually causes death. Almost all patients had received azathioprine or 6-mercaptopurine (6-MP) in combination with or immediately prior to a TNF-blocker. The vast majority of infliximab cases have occurred in patients with Crohn's disease or ulcerative colitis, and most were reported in adolescent or young adult males. Cases of hepatosplenic T-cell lymphoma have also occurred in patients with Crohn's disease and ulcerative colitis receiving azathioprine who were not treated with infliximab. It is unclear what role of infliximab may have in the development of the lymphoma.

Some women being treated for rheumatoid arthritis with infliximab have developed cervical cancer. For women taking infliximab, including those over 60 years of age, your doctor may recommend that you continue to be regularly screened for cervical cancer.

You should tell your study doctor prior to participating in this study if you have a history of lymphoma or cancer, and if you develop lymphoma or cancer, including skin or cervical cancer, during or after you have participated in this study. You should also regularly discuss cancer screenings with your study doctor, and the impact of life-style choices (for example, smoking) on the risk of developing cancer.

Central Nervous System

Some patients, who have a disease of their nervous system, have reported that this disease got worse. You should tell your doctor if you have a disease of your nervous system. Seizures and multiple sclerosis are examples of nervous system diseases. While in this study, if you are diagnosed with a nervous system disease discontinuation of infliximab should be discussed with your doctor.

Rarely, people who did not have a nervous system disease developed one after taking infliximab. Signs of nervous system disease include:

• changes in your vision • seizures	• numbness or tingling in any part of your body • weakness in your arms and/or legs

Lung

Interstitial lung disease is the name for diseases that inflame or scar the lungs and may cause long term complications. The inflammation and scarring may make it difficult to breathe and get enough oxygen in your blood.

Patients treated with infliximab have rarely developed interstitial lung disease and in some cases, the disease progressed quickly.

Liver

If you currently or at any time in the past have had any liver problems, including hepatitis B, you should tell your doctor. Treatment with TNF-blocking agents such as infliximab may result in a reactivation of the hepatitis B virus in people who have been known to carry this virus. Hepatitis B reactivation has been reported rarely in patients treated with infliximab. You will have a blood test to see if you have hepatitis B prior to treatment with infliximab.

Some patients develop abnormal liver blood tests, often without symptoms. If this happens, your doctor may stop your treatments for a period of time or permanently. In most cases the liver tests return to normal after stopping treatment.

There have been cases where people taking infliximab have developed serious liver problems, resulting in liver transplantation or death. Signs that you could be having a problem include:

• skin and/or eyes turning yellow • dark brown urine • right-sided stomach pain	• nausea • vomiting • loss of appetite • fever • extreme tiredness

Skin

Hair loss has commonly occurred in patients treated with infliximab.

Patients treated with infliximab have commonly developed a worsening of psoriasis or new onset psoriasis, including a type called pustular psoriasis. Symptoms may include dry, red skin with yellow blisters, often on the palms of the hands or soles of the feet, although it can occur elsewhere.

Rarely, a type of rash called vasculitis resulting from inflammation of blood vessels in the skin has occurred in patients treated with infliximab.

Stevens-Johnson syndrome and toxic epidermal necrolysis are two forms of a life-threatening skin condition that have been reported rarely in patients treated with infliximab. Another skin condition called erythema multiforme has been reported rarely in patients treated with infliximab.

A skin condition called linear IgA bullous dermatosis has been very rarely reported in patients treated with infliximab. Rarely, another skin condition called acute generalized exanthematous pustulosis has been reported in patients treated with infliximab.

Rarely, lichenoid reactions (itchy reddish-purple skin rash and/or threadlike white-grey lines on mucous membranes) have occurred in patients treated with TNF-blockers, including infliximab.

Blood Problems

With the use of TNF-blockers, including infliximab, sometimes the body fails to make enough white blood cells that help the body fight infection or fails to make enough red blood cells, resulting in anemia. In some instances, the number of white blood cells was severely decreased. In addition, sometimes the body fails to make enough platelets, the cells that help you stop bleeding. Some patients have died from this failure to produce blood cells. Your study doctor will monitor the results of tests done on your blood during the study. If you develop a fever that does not go away or infection, bruise or bleed very easily, look very pale or become tired easily, tell your study doctor right away.

Other Risks

Rarely, people develop sarcoidosis, a multisystem immune disorder which is characterized by the formation of lesions (granulomas) in body organs that could affect the lungs, lymph nodes, skin, and other body systems.

A serious inflammation of the blood vessels called vasculitis may occur and in severe cases may result in permanent damage of the affected internal body organs. Vasculitis has been reported rarely in patients treated with infliximab.

Rarely, patients treated with infliximab have developed a pericardial effusion which is an abnormal amount of fluid between the heart and the sac around the heart. Hemophagocytic lymphohistiocytosis (HLH), a life-threatening condition, has been very rarely reported in patients treated with infliximab. This condition is identified by fever, enlarged liver or spleen, decreased number of blood cells, and neurological abnormalities.

There may be other discomforts or risks to you from this study that we do not yet know about.

Your study doctor and staff will ask you about any side effects you have at every visit. If you have any problems, you should let the doctor know right away.

Risk of blood collection

When we collect blood from you for this study, you may experience slight pain at the location of the blood draw. Some bleeding, bruising or discoloration of the skin is common at the site after a blood collection. In rare instances, infection at the site may occur. The study doctor will be able to treat any symptoms you may have.

To reduce risks associated with the blood draw, we will try to take the blood sample at the time the IV is placed so you do not have to have another needle stick.

Risk of colonoscopy pinch biopsy

If you agree to additional pinch biopsy samples for research, obtaining the additional intestinal biopsies may not significantly increase the patient's risk of perforation, bleeding, or infection associated with the colonoscopy. As the colonoscopy will be performed at the discretion of your regular doctor, all potential risks of the procedure, including risks of anesthesia will be discussed with you and separate consent documents will be obtained (separate from this research study).

Risk of high doses of infliximab

If you are in the intervention arm, you may receive doses that are higher than the FDA approved dose. These higher doses have been shown to be safe in uncontrolled studies (real world practice).

Risk of loss of confidentiality

Your privacy is of great concern to us. There is a minimal risk of loss of confidentiality and we have taken steps to minimize this risk which include removing all identifiable patient information from biospecimens collection tubes, providing a unique study ID number for each participant, using a secure, password protected electronic data collection database (Medidata Rave®) and secure web portal (RoadMAB™), and storing all study related paper materials in a locked cabinet.

Pregnancy Risks

The effect of infliximab on the ability to have children is unknown. However, we are not fully aware of the effects of the study drug on unborn babies, on human sperm, or pregnant or breastfeeding women. Pregnant women and women making breast milk to feed infants cannot participate in this study. Female patients (if they have had a first menses) must have a urine or blood test when beginning this study that shows they are not pregnant.

It is very important that women taking part in this study do not become pregnant while taking part in this study. It is very important that men taking part in this study do not get a woman pregnant while participating in this study.

During this study and for 6-months after the last dose of infliximab, women of childbearing potential and men must use proven birth control methods (such as avoiding sex, birth control pills or injections, or an intrauterine device). Your study doctor will discuss birth control methods with you.
If you are pregnant, or may become pregnant, treatment with the study drug may lead to new, previously unknown, side effects, and this may involve risks to you and your unborn baby. You will be withdrawn from the study.

If you think that you have become pregnant, have a confirmed pregnancy or may have fathered a child while taking part in the study, you must tell the study doctor immediately. The study doctor will follow your pregnancy to its outcome. You should also notify your childbirth doctor that the mother/father received infliximab.

Infliximab crosses the placenta. If you received infliximab while you were pregnant, your baby may be at a higher risk for getting an infection. It is important that you tell your baby's doctor and other health care professionals that you have received treatment with a study drug before the baby receives any vaccine. A 12-month waiting period following birth is recommended before the administration of a live vaccine (like BCG and rotavirus) to a baby whose mother received infliximab while she was pregnant. Administration of BCG vaccine within 12 months after birth to the baby whose mother received infliximab while pregnant may result in infection in the newborn with severe complications, including death. For other types of vaccines, discuss with your doctor.

Severely decreased numbers of white blood cells have also been reported in infants born to women treated with infliximab during pregnancy. If your baby has continual fever or infections, contact your baby's doctor immediately.

If you are a female study patient, you must agree to not donate eggs (ova, oocytes) during the study and for 6 months after your last dose of study drug.

If you are a male study patient, you must not donate sperm while you are in the study and for 6 months after your last dose of study drug.

If you are a male study patient, and you father a child during your participation in this study, the study doctor will ask for your partner's permission to stay in contact with her throughout the length of the pregnancy.
There may be other risks that we do not know about yet.

Privacy:

Efforts will be made to limit the use and disclosure of your personal information, including research study and medical records, to people who have a need to review this information. We cannot promise complete privacy. Organizations that may inspect and copy your information include the IRB, the Medical Monitor, your doctor, the Food and Drug Administration, National Institutes of Health (NIH), Janssen Scientific Affairs, LLC, and other representatives of this organization.

As approved by the CCHMC Institutional Review Board, de-identified samples will be stored in the Minar Laboratory. These samples could be used to research the causes of Crohn's disease, its complications and other conditions for which individuals with Crohn's disease are at increased risk, and to improve treatment. The Minar laboratory personnel will also be provided with a code-link that will link the biological specimens to each participant, maintaining the blinding.

Samples and/or data collected for or generated from this study could be shared and used for future research. Samples and /or data may be shared with other collaborators at Cincinnati Children's and possibly with outside collaborators, who may be at another institution or for-profit company.

If information that could identify you is removed from your information or samples collected during this research, that information or those samples could be stored and used for future research studies or distributed to another investigator for future research studies without your additional informed consent.

All future researchers will be given the least amount of information needed to meet the goals of their research project. Researchers that use these samples and information must agree to never try to re-identify a participant from a coded dataset. Researchers will only be allowed to use the provided samples and information for approved research purposes. Any researchers planning to do research with information that may identify you will need to have extra review and approval by the Cincinnati Children's Institutional

Review Board (IRB). An IRB is a group of scientists and non-scientists who look at research projects like these and make sure research participants' rights and welfare are protected.

The sponsor (Cincinnati Children's), monitors, auditors, the IRB, the Food and Drug Administration will be granted direct access to your medical records to conduct and oversee the research. By signing this document, you are authorizing this access. We may publish the results of this research. However, we will keep your name and other identifying information confidential.

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

Federal Certificate of Confidentiality:
This research is covered by a Certificate of Confidentiality from the National Institutes of Health. This means that the researchers cannot release or use information, documents, or samples that may identify you in any action or suit unless you say it is okay. They also cannot provide them as evidence unless you have agreed. This protection includes federal, state, or local civil, criminal, administrative, legislative, or other proceedings. An example would be a court subpoena.

There are some important things that you need to know. The Certificate DOES NOT stop reporting that federal, state or local laws require. Some examples are laws that require reporting of child or elder abuse, some communicable diseases, and threats to harm yourself or others. The Certificate CANNOT BE USED to stop a sponsoring United States federal or state government agency from checking records or evaluating programs. The Certificate DOES NOT stop disclosures required by the federal Food and Drug Administration (FDA). The Certificate also DOES NOT prevent your information from being used for other research if allowed by federal regulations.

Researchers may release information about you when you say it is okay. For example, you may give them permission to release information to insurers, medical providers or any other persons not connected with the research. The Certificate of Confidentiality does not stop you from willingly releasing information about your involvement in this research. It also does not prevent you from having access to your own information.

If injured while in the study:

If you believe that you have been injured as a result of this research, you should contact [Site PI Name] as soon as possible to discuss the concerns. Treatment for injuries is available at [Site Name]. If you go to the Emergency Room or to another hospital or doctor, it is important that you tell them that you are in a research study. If possible, you should give them a copy of this consent form.

[Site Name] follows a policy of making all decisions about compensation for the medical treatment of physical injuries that happened during or were caused by research on an individual basis.

Return of results:

Most tests done on samples or images obtained in research studies are only for research and have no clear meaning for healthcare. At certain time points, you and your treating physician will be made aware of select results of your stool and blood testing and amount of infliximab in your blood and may contact you.

AUTHORIZATION FOR USE/DISCLOSURE OF HEALTH INFORMATION FOR RESEARCH

[Sites may use their own HIPAA language OR use the CCHMC language below]

To be in this research study you must also give your permission (or authorization) to use and disclose (or share) your "protected health information" (called PHI for short).

What protected health information will be used and shared during this study?

[Site Name] will need to use and share your PHI as part of this study. This PHI will come from:

- Your [Site Name] medical records
- Your research records

The types of information that will be used and shared from these records include:

- Laboratory test results, diagnosis, and medications
- Reports and notes from clinical and research observations
- Imaging (like CT scans, MRI scans, x-rays, etc.) studies and reports
- Physician reports and video/photo images of a previous recorded colonoscopy

Who will share, receive and/or use your protected health information in this study?

- Staff at [Site Name] and Cincinnati Children's
- Personnel who provide services to you as part of this study
- Other individuals and organizations that need to use your PHI in connection with the research, including people at the sponsor (Cincinnati Children's), Janssen Scientific Affairs, LLC and organizations that the sponsor may use to oversee or conduct the study.
- Government agencies who oversee this study, including the FDA and NIH
- The members of the Cincinnati Children's Institutional Review Board and staff of the Office of Research Compliance and Regulatory Affairs.

How will you know that your PHI is not misused?

People that receive your PHI as part of the research are generally limited in how they can use your PHI. In addition, most people who receive your PHI are also required by federal privacy laws to protect your PHI. However, some people that may receive your PHI may not be required to protect it and may share the information with others without your permission, if permitted by the laws that apply to them.

Can you change your mind?

You may choose to withdraw your permission at any time. A withdrawal of your permission to use and share your PHI would also include a withdrawal from participation in the research study. If you wish to withdraw your permission to use and share PHI you need to notify the study doctor, listed on the first page of this document, in writing. Your request will be effective immediately and no new PHI about you will be used or shared. The only exceptions are (1) any use or sharing of PHI that has already occurred or was in process prior to you withdrawing your permission and (2) any use or sharing that is needed to maintain the integrity of the research.

Will this permission expire?

Your permission will expire at the end of the study.

Will your other medical care be impacted?

By signing this document, you agree to participate in this research study and give permission to [Site Name] to use and share your PHI for the purpose of this research study. If you refuse to sign this document, you will not be able to participate in the study. However, your rights concerning treatment not related to this study, payment for services, enrollment in a health plan or eligibility of benefits will not be affected.

While you/your child are participating in this research study you may not be able to access some of your/your child's health information that is related to the study. Any request for this information can be fulfilled once the study is completed.

SIGNATURES

The research team has discussed this study with you and answered all of your questions. Like any research, the researchers cannot predict exactly what will happen. Once you have had enough time to consider whether you should participate in this research, you will document your permission by signature below.

You will receive a copy of this signed document for your records.

Optional procedure:

Indicate if you **AGREE or DO NOT AGREE** to the following optional procedure:

Initials: _____ Yes, I AGREE to the collection of extra gastrointestinal biopsies for research.

Initials: _____ No, I DO NOT AGREE to the collection of extra gastrointestinal biopsies for research.

_____

Printed Name of Research Participant

_____ _____

Signature of Research Participant Indicating Consent — Date

_____ _____

Signature of Parent or Legally Authorized Representative* — Date

_____

* If signed by a legally authorized representative, a description of such representative's authority must be provided

_____ _____

Signature of Individual Obtaining Consent — Date