

**Informed Consent Form
And
Authorization To Use and Disclose Protected Health Information**

Sponsor / Study Title: **Division of Allergy, Immunology, and Transplantation,
National Institute of Allergy and Infectious Diseases
(DAIT/NIAID) / “A T cell phenotype signature driven dose
finding study with sipilizumab in type 1 diabetes mellitus”**

Protocol Number: **ITN095AI**

Principal Investigator: **«PiFullName»**
(Study Doctor)

Telephone: **«IcfPhoneNumber»**

Address: **«PiLocations»**

1. Is my participation voluntary?

Yes. It is entirely up to you to decide whether to join this research study. If you decide to join, we will ask you to sign and date this consent form and give you a copy to keep. You are free to leave the study at any time without having to give a reason. A decision not to take part in or to leave the study at any time will in no way affect the care you receive.

2. Key Study Information

This consent form contains information that should help you decide whether or not to take part in this research study. We encourage you to read the entire document. All the information is important. Here are some key points to help you understand the study. Additional information is available in the consent form in the sections noted in italics below.

- This study consists of 2 parts, Part A and Part B. Part A enrollment has been concluded. You will be joining Part B of the study. The details of both parts are included in the sections below.
- This is a 12-month research study for participants with type 1 diabetes mellitus (T1DM). See the ***Introduction and Background, and Purpose of the Study*** sections below.
- In this experimental study, researchers will try to find out if a study drug called sipilizumab can change the number and type of immune system cell called T cells that attack the cells that make insulin (beta cells) in your pancreas. This might allow the beta cells to continue to produce insulin and help to treat T1DM.
- An experimental drug is one that is not approved by the United States Food and Drug Administration (FDA). See the ***Purpose of the Study*** section below.
- The study may require up to 11 clinic visits over 12 months. See the ***What makes up this study?*** section below.

- Study participants have procedures that are not part of a routine doctor's visit. These include:
 - Extra blood draws.
 - Mixed Meal Tolerance Test (MMTT).
See the ***What am I being asked to do? How long will I be in the study?*** section below for information on all study procedures.
- Siplizumab has been tested in approximately 779 participants with different conditions such as psoriasis, transplantation, and cancer. Siplizumab is not currently FDA-approved for any disease, including T1DM. It has known side effects. The most common side effects are study injection site reactions and low levels of a type of white blood cell called lymphocytes. As with all drugs, there may be other side effects that are not known. See the ***What are the possible risks or side effects?*** section below.
- There might be no direct medical benefit to you for being in this study. The information learned from this study may someday benefit people with T1DM. See the ***Are there benefits to taking part in the study?*** section below.

3. Who is the study doctor?

The study doctor is listed as the “Principal Investigator (Study Doctor)” on page one of this consent form.

4. Introduction and Background

We are asking you to participate in this study because you were diagnosed with T1DM less than 2 years ago. T1DM is an autoimmune disease. This means that your immune system (the part of your body that helps to fight infections) mistakenly attacks your body's own cells. In T1DM, your body's T cells (immune system cells) attack the cells that produce insulin (beta cells in the pancreas). Insulin helps to keep blood glucose levels normal. As the beta cells are destroyed by your immune cells, your ability to produce insulin decreases and diabetes develops.

People with T1DM who produce some of their own insulin (even though they still need to take prescribed insulin) may have better blood sugar control than those who produce none. This may reduce long-term diabetes-related complications. Study doctors believe that using medications that affect the immune system early after diagnosis may prevent or slow beta cell destruction, leading to better blood sugar control, less need for prescribed insulin, and a lower risk of diabetes related complications.

In this experimental study, researchers will try to find out if siplizumab can change the number and type of T-cells that attack the beta cells in your pancreas. This may allow the beta cells to continue to produce insulin for you.

Siplizumab has been given subcutaneously (under the skin) (SQ) and intravenously (through IV line) (IV) to participants with psoriasis (another autoimmune disease). IV siplizumab studies were done in participants with kidney transplants, graft versus host disease (a complication of bone marrow transplantation) (GVHD), cancer, and lymphoproliferative disorders (conditions in the blood involving uncontrolled growth of white blood cells). It was generally found to be safe and well-tolerated. Siplizumab was never used in people with T1DM until this study. The safety

of siplizumab is not yet well known in participants with T1DM. Siplizumab has not been approved by the FDA to treat any illness, including T1DM.

You are considering enrolling in Part B of this study. Part A of this study has stopped adding new participants because the study team saw a lower number of T cells than expected. The long-term follow-up of enrolled participants is ongoing. The major side effects seen in part A of this study are included in this document under the risk section. The doses used in Part B are lower than in Part A.

5. What is the purpose of this study?

The main purpose of this study is to:

- Study the effects of siplizumab on T cells in two different groups of participants with T1DM.
 - Group 1: 18 to 45 years old
 - Group 2: 8 to 17 years old
- Find out if there are side effects from siplizumab in participants with T1DM.
- Find out if siplizumab allows participants with T1DM to continue to make their own insulin by preserving insulin-producing beta cells.

6. What makes up this study?

Who is sponsoring this study?

This study is sponsored by the National Institutes of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health (NIH). It is being conducted by the Immune Tolerance Network (ITN), funded by NIAID, NIH. ITB-Med, LLC is the pharmaceutical manufacturer providing the study drug.

How many participants will be in the study? How many centers will conduct this study?

The study plans to enroll about 90 participants at about 20 clinics in the United States (US). If these participants do not complete the study, additional participants may be treated.

What am I being asked to do? How long will I be in the study?

You are being asked to take part in this study because you have T1DM. There are three periods to this study:

- **Period 1** is the screening (SCR) to see if you qualify for this study.
- **Period 2** is the study injection visit. All eligible participants will receive siplizumab.
- **Period 3** is the follow-up period to see if you develop any side effects and if there was a change in the number and type of T-cells.

Description of Study Procedures

Physical Exam 	You will have a complete physical examination, similar to those done for regular medical care during some visits. Partial physical exam will be done based on your health status at other visits.
Medical History, Medication, and	This will include questions about your age, sex, past health history, vaccination history, what medications you have taken, past surgeries, and

<u>Health Status Review</u> 	your race and ethnicity. Your medical chart will be reviewed by the study doctors. Your study doctor will discuss with you the medications you need to avoid while you are in this study. At each follow-up visit, the study staff will ask you about any medications you are taking or have used since your last visit, your health, and your diabetes including your insulin use and glucose meter or continuous glucose monitor readings.
<u>Vital Signs</u> 	Your vital signs (blood pressure, heart rate, temperature, and breathing rate) will be taken during all visits. Your height and weight will be taken at certain visits.
<u>Blood Draw</u> 	Blood samples will be taken to assess your general health diabetes, past or recent infections and for research tests at the visits. • Clinical tests: Standard medical laboratory tests to provide ongoing care. Your study doctor will be able to give you the results of these tests. • Infectious Disease Testing: Tests will be run for certain infections such as HIV, tuberculosis, and hepatitis as part of screening for this study. The study doctor may be required by law to report the result of these tests to the local health authority. A skin test called Purified Protein Derivative (PPD) skin prick test may be done to screen for tuberculosis instead of a blood test. Your study doctor will tell you how you will be tested for tuberculosis. Tests for other viral infections like Epstein-Barr virus (EBV) and cytomegalovirus (CMV) will also be done at screening and follow-up visits. • Research tests: Special laboratory tests that may provide information about T1DM, viral infections, the immune system (the body's natural defense system against illness), and response to the study drugs and other medications will be done at screening and follow-up visits. • Genetic tests: Laboratory tests that study the inherited (present from birth) characteristics that are present in each of your cells. Genetic testing may help researchers learn more about T1DM or may help to find treatments for T1DM during follow-up visits. Genetic samples will not be used for genetic cloning, paternity testing, or to identify you. Whole genome sequencing (determining a complete DNA profile of a person) may be performed as part of these tests. The results of the genetic and research tests will not be shared with you. They are not likely to affect you as a participant.

<u>Mixed Meal Tolerance Test (MMTT)</u> 	You will have an MMTT to assess your ability to produce insulin. You will be given specific instructions on insulin dosing and diet for 3 days prior to the MMTT. You will be asked to fast for about 10 hours but no more than 16 hours before coming for the test on that morning. During the fasting period, you should only drink water. If you use a hybrid closed loop CSII system (for example, Control IQ or Omni Pod 5), you will need to switch to manual mode 2 hours before you begin the test. You will be asked to check your blood glucose on your glucometer or continuous glucose monitor about 2 hours before you begin the test in case you need some short-acting insulin to meet the target glucose level. The target glucose is between 70 and 200 mg/dL. You should plan to start the MMTT before 10:00 am. An IV needle will be used to place a thin plastic tube in your arm. You will be asked to drink about 12 ounces of “Boost High Protein Nutritional Energy Drink” within 5 minutes. Blood will be drawn from the IV over the next 2 hours. After the last sample is taken, your insulin dose will be adjusted as necessary to control your blood sugar.
<u>Pregnancy Test</u> 	If you are a female who can get pregnant, blood or urine will be collected for pregnancy testing. Your study team will determine which sample will be used.
<u>COVID-19 Test</u> 	A COVID-19 test will be done if you have any symptoms of COVID-19. Your study doctor will tell you how you will be tested for COVID-19.
<u>Siplizumab Injection</u> 	Siplizumab will be given as a single injection under your skin by the study staff. The injection could be given in your abdomen, arms, thighs, or buttocks. Your study doctor will discuss injection site options with you and will choose the best site to administer your medication. Your vital signs (blood pressure, pulse, temperature, and breathing rate) will be checked just before you receive the study drug injection and 15 and 30 minutes after you receive the study injections. You will be given acetaminophen (for example, Tylenol), ibuprofen (for example, Motrin) or a similar medication and also diphenhydramine (for example, Benadryl), hydroxyzine (for example, Atarax) or a similar medication by mouth before the study drug administration to prevent any allergic reactions that may occur. Please let the study team know if you are on a regular dose of antihistamine or if you have taken a dose of antihistamine on the day of the injection.
<u>Telephone Calls</u> 	The study team will call you to give instructions about the MMTT and to follow-up any side effects you may be experiencing. You can also call your study doctor if you are experiencing any side effects.

Screening Period

If you agree to participate, you will have a screening visit to see if you qualify for the study. The screening visit is expected to take a few hours and consists of exams, tests, or procedures to find out if you can be in the main part of the study. The screening period may last up to 37 days.

Screening visit procedures:

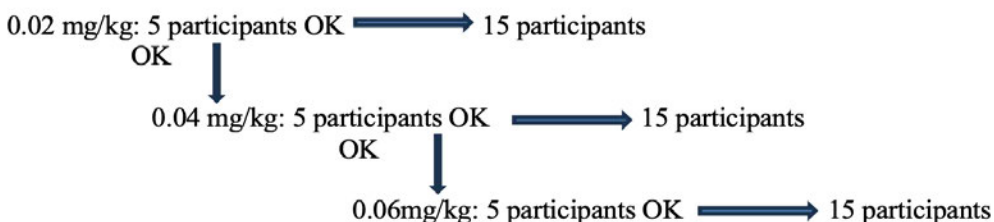
- **Informed consent form:** You will review and sign this informed consent form
- **Medical history and physical exam**
- **Medical chart review and vital signs check**
- **Blood draw:** Blood samples to check your overall health, diabetes, and possible recent infections such as HIV, tuberculosis hepatitis, other viruses (EBV and CMV), and a pregnancy test if you can get pregnant
- **COVID-19 test:** If you have any symptoms of COVID-19
- **MMTT**

Study Drug Injection Visit (Visit 0/Week 0)

Part A participants were randomly assigned into 4 dosing groups. Injections were given every week for 12 weeks. These dosing groups have been stopped. You will not receive one of these doses.

In Part B, if you qualify and decide to continue in the study, you will return for the study injection. There will be one (1) injection of the study drug with different participants receiving different doses of the study drug to see which dose is safe and causes a change in the number and type of T cells.

The first group of participants will receive the lowest dose of the study drug, starting at 0.02 mg/kg. If there are no safety concerns, the dose will be increased to 0.04 mg/kg for the next group of participants. If there are no safety concerns with the 0.4mg/kg dose, the dose will be increased to 0.06 mg/kg for the next group of participants. Each group will have 5 participants at first. If there are no important safety concerns and the dose seems to be effective in changing the number and type of the T cells, another 10 participants will be treated in each group. The study will add more participants in each group only if the doses are found to be safe and effective. You and your study doctor will know which dosing group you are assigned to. If there is more than one dosing group open at a time, you will be randomly (like flipping a coin) added to a group.



Visit 0 procedures:

- **Physical exam**
- **Vital signs, medications, and health status check**
- **Blood draw:** Blood will be collected for clinical labs, research labs, genetic tests, and virus testing
- **COVID-19 test if indicated**
- **Urine pregnancy test if indicated**

- **Siplizumab injection:** You will receive a single dose of siplizumab if you are eligible based on the test results and your health status

Study visit 0 may take about 4 hours.

Follow-up Period (Visits 1-9/Weeks 1-52)

After you complete the study drug injection visit, you will be asked to come to the clinic for 9 more visits for follow-up. The follow-up phase is to monitor any changes in your T1DM status and to assess overall safety.

Follow-up visit procedures:

- **Partial physical exam at some visits (V1, V2, and V4) and a complete physical exam at the other visits**
- **Vital signs, medications, and health status check**
- **Blood draw:** Blood will be collected for clinical labs, research labs, genetic tests, and virus testing
- **COVID-19 test if indicated**
- **Urine pregnancy test if indicated**
- **Mixed Meal Tolerance Test (MMTT)**

Each study visit may take up to 2-4 hours depending on which assessments are done at each visit.

You may also be required to return for unscheduled visits, or an end-of-study visit to check on your health and have additional lab tests performed. These visits will last about the same time as the follow-up visits. The study doctor will also schedule a telephone follow-up if you develop any symptoms of infection.

You will be in the study for a total of 1 year and 1 month if you finish all 3 periods of the study. Your participation in the study will end at Visit 9 unless you experience any side effects that require more monitoring. Some participants may enter the long-term monitoring period to closely follow any persistent side effects.

The table lists the study tests, procedures, and study drug you will receive at each study visit.

Study Period	Screening	Injection Visit	Follow-up								
WEEK		0	1	2	4	6	8	12	24	36	52
VISIT	-1	V0	V1	V2	V3	V4	V5	V6	V7	V8	V9
Physical exam and vital signs	X		X	X	X	X	X	X	X	X	X
Siplizumab injection SQ		X									
Mixed meal tolerance test	X							X	X	X	X
Blood samples	X		X	X	X	X	X	X	X	X	X

Study Period	Screening	Injection Visit	Follow-up								
WEEK		0	1	2	4	6	8	12	24	36	52
VISIT	-1	V0	V1	V2	V3	V4	V5	V6	V7	V8	V9
Clinical blood volume in teaspoons	3	2	1	1	2-2.5	1-1.5	2-2.5	2-2.5	2-2.5	2-2.5	2-2.5
Research blood volume (includes genetic testing)	3	8	6	7	7-7.5	6-6.5	8-8.5	0-0.5	10-10.5	10-10.5	10-10.5
Urine pregnancy test if indicated			X	X	X	X	X	X	X	X	X

Long-Term Safety Monitoring Period (Visits 1SM- 4SM/Weeks 64-100)

If you experience a side effect that is ongoing at the end of the study (week 52), you may be requested to come for additional visits to be monitored closely by the study doctors. This may include telephone calls, additional visits, and the collection of laboratory samples approximately every 12 weeks for 48 weeks or until the side effect has improved.

The below table lists the study tests and procedures you will receive at each long-term safety visit.

Study Period	Long Term Safety Monitoring			
DAY	48	532	616	700
WEEK	64	76	88	100
VISIT	1SM	2SM	3SM	4SM
Physical exam and vital signs	X	X	X	X
Blood samples	X	X	X	X
Clinical blood volume in tablespoons	1-1.2	1-1.2	1-1.2	1-1.2

7. What are the possible risks or side effects?

Below is the list of all potential risks associated with participating in this study. If you experience any of the side effects described below, you will be monitored closely by the study doctor.

Study Drug Risks

Siplizumab may cause all, some, or none of the side effects listed below. These side effects might be mild but might also be serious, life-threatening, or even result in death. There is less experience with the lower doses and single injection being used in this study, and not all of these side effects have been seen as commonly in studies using lower doses or in all of the diseases studied. For example, rare and unusual infections occurred less often in participants with psoriasis and there were no deaths in participants with psoriasis. Also, deaths have been reported only in studies using IV siplizumab but not SQ siplizumab. The potential risks associated with the use of siplizumab are the following:

Cytokine Release Syndrome (CRS): A whole-body inflammatory response that can be caused by infections and certain drugs. It has been seen with the use of medications similar to

siplizumab. Symptoms of CRS include flu-like illness that resolves on its own. Less frequently, CRS may cause a shock-like reaction that includes heart, lung, and nervous system problems. So far, no serious events of CRS have been seen with siplizumab.

Infections: Siplizumab can reduce the number of a kind of white blood cells called lymphocytes that help you fight off infections. If you experience any signs of an infection (for example, fever, chills, cough, congestion, lack of energy, or sore throat) contact your study doctor. Rare or unusual infections that are more common in people with weakened immune systems might also occur. Please note that there could be symptoms of infections that are not listed here. If you have any new symptoms, please notify the study staff.

Lymphopenia: Low levels of a type of white blood cell called lymphocytes. This may occur as a result of siplizumab reducing the number of lymphocytes in your blood. You will have blood tests to closely monitor if the lymphocytes are below a certain level. Your study doctor will recommend taking precautions to reduce your risk of infection. You should take precautions such as wearing a well-fitted facemask, washing hands frequently, and avoiding large crowds and close contact with sick people until your study doctor tells you that your lymphocyte count has recovered enough.

COVID-19: Siplizumab could put you at an increased risk for infection with SARS-CoV-2 (COVID-19). You will be tested for SARS-CoV-2 infection (COVID-19) as indicated in this document. We strongly recommend that you follow the current Centers for Disease Control and Prevention (CDC) and local public health authorities' recommendations for reducing the risk of SARS-CoV-2 infection during study participation. If you develop SARS-CoV-2 infection during study participation, contact your study doctor immediately. There may be treatments that could help with your infection.

Allergic Reaction: You may also experience an allergic reaction that has not been seen before with siplizumab. In general, symptoms of an allergic reaction may include:

- Headache
- Rash
- Itching
- Reddening/Flushing
- Swelling
- Shortness of breath
- Nausea
- Vomiting
- Pain, redness, rash, and swelling at the site of the study injection

Severe allergic reactions that could be life-threatening can cause:

- Dizziness
- Severe skin reactions
- Difficulty breathing or swallowing
- Decrease in blood pressure

Your study doctor will be monitoring you after you receive your dose of siplizumab. You should seek immediate care if you experience any symptoms of an allergic reaction during the study.

Cancer: Long-term use of medications like siplizumab may result in an increased risk of developing certain types of cancer. There are no reports of newly diagnosed cancer associated with the use of SQ siplizumab in the available data. There are reports of recurring cancer in the studies conducted using IV siplizumab. These cancers occurred in participants with preexisting conditions and other treatments that have an additional risk of cancer. There was one report of skin cancer in a transplant participant. Additionally, new white blood cell cancers have been reported in people being treated with siplizumab for other cancers and GVHD. The rates of these cancers in study participants were similar to rates in participants who were not treated with siplizumab. The effect of siplizumab on cancer risk in T1DM is not known. The study doctor will monitor you for any signs or symptoms of cancer while participating in this study.

The **most commonly reported signs and symptoms** associated with the side effects noted were:

- Headache
- Fever
- Chills
- Nausea
- Low heart rate
- Muscle and/or joint pain
- Flu-like symptoms
- Study drug injection site reactions
- High blood pressure

The **most commonly reported laboratory abnormalities** were:

- Low levels of lymphocytes, which might not improve right away if you stop taking siplizumab
- Low levels white blood cells

Low levels of lymphocytes were observed in DESIGNATE Part A participants. Based on earlier psoriasis studies using a single dose of siplizumab, the persistent low levels of lymphocytes seen in Part A are less likely to occur in Part B.

Less commonly reported signs and symptoms of side effects included:

- Increased breathing/respiratory rate
- Diarrhea
- Lack of energy

Participants recovered from these side effects before their end of participation in the completed studies. The recovery from the most commonly reported lab abnormalities was longer compared to the other side effects. Some of the Part A participants in this study are in the long-term follow-up period.

You may experience any of the above symptoms with the use of the study drug. Please notify your study doctor if you experience any new symptoms. Your study doctor will monitor you

closely for any symptoms. If any side effects are ongoing at the end of the study, the study team may continue to follow-up with you. This may include telephone calls, additional visits, or the collection of laboratory samples.

Reproductive Risks: You should not get pregnant while you are in this study. If you can get pregnant, you must agree to use a type of birth control that works well. You will have to use an acceptable method of birth control while you are in this study until the end of study week 52.

The possible risks of the study drug to those who are pregnant, unborn babies, and newborn babies are unknown. The possible risks of breastfeeding while receiving the study drug are also unknown.

Study Procedure Risks

Blood Draw/IV Line Risks: Possible side effects from having blood drawn include dizziness, redness and swelling of the vein, pain, bruising, or bleeding from the site of the needle puncture. There is also a very small chance of infection.

Study Injection Site/PPD Skin Test Risks: Symptoms may include tenderness, swelling, or a rash at the site of the study injections or PPD skin test. Cold packs can be applied to the area to help with any tenderness or swelling from the study injections.

MMTT Risks: There may be a risk of high or low blood sugar from this preparation or the test. During the test, you will be closely checked for changes in your blood glucose and how you are doing. Otherwise, you may not like the taste of the nutritional supplement drink used during this test.

Premedication Risks: The medicines given before siplizumab include antihistamines (allergy medicines). They can cause drowsiness, dizziness, constipation, stomach upset, blurred vision, or dry mouth/nose/throat.

Unforeseen Risks

As with any research study, there might be side effects that are unknown at this time. You should report any concerns to the study staff.

8. Are there benefits to taking part in this study?

There may be no direct medical benefit to you for taking part in this study. Information from this study may help doctors learn more about the treatment for T1DM. This information could help future T1DM patients.

9. What other choices do I have if I do not take part in this study?

Before you decide to take part in this study, your study doctor will talk with you about other options available to you. If you decide not to join the study, your study doctor can recommend other treatments. You do not need to participate in this study to be treated for your T1DM.

10. What about new findings?

During your participation in this study, your study doctor will inform you of any new findings from this or other research that may affect your willingness to continue in this study.

11. May I leave this study at any time?

Yes, you may leave the study at any time. If you decide to leave the study, there is no penalty or loss of benefits in your routine medical care or any other benefit(s) that you would otherwise be entitled to receive.

You will be asked to come back for one more visit to have some end-of-study tests for your safety.

In addition, you should consult with the study doctor listed on page one of this consent form who will discuss treatment and procedures for your continued care when you are no longer in this study.

12. Can I be taken off this study without my consent?

You may be removed from the study without your consent at any time. Reasons why you may be removed from the study include, but are not limited to, the following:

- Your study doctor decides that it is best for you not to continue
- You are unable to complete study tests
- The study is stopped by the institution, the Sponsor(s), or other health authorities
- You become pregnant or plan to get pregnant during this study
- You take medications that suppress your immune system
- You have severe side effects from the study drug, sipilizumab
- You have recurrent side effects from the study drug, sipilizumab

If you are removed from the study, your study doctor will notify you about treatments or procedures for your future care. You will be asked to come back for one more visit to have some end-of-study tests for your safety.

13. What about pregnancy and birth control?

You cannot participate in this study if you are pregnant, breastfeeding, or planning to become pregnant while in the study.

If you can get pregnant, you must either be sexually inactive by complete abstinence from vaginal intercourse or use a medically acceptable form of birth control while in the study. Periodic abstinence from vaginal intercourse and withdrawal are not acceptable methods of contraception. Abstinence must start two weeks before the study drug is given.

Acceptable forms of birth control include oral birth control pills (combined hormone or progestin alone), injectable or implantable progestogens, intrauterine devices, estrogen vaginal rings, male partner sterilization, or double barrier methods (for example, condom and occlusive cap with spermicidal agent). If using male partner sterilization, records of sterilization should be provided.

Birth control must be used throughout the study, starting at two weeks before the study drug is given until visit 9/week 52. If you leave the study early, you should be on birth control for 40 weeks after the study drug was given.

Even if you are using birth control, you will be given a pregnancy test before and during the study. You and the study doctor will discuss acceptable methods of birth control.

If you become pregnant or think that you have become pregnant while in this study, you must contact your study doctor right away. If you are still receiving the study drug, your study doctor will stop your study drug. You will continue to be followed until the baby is born or the pregnancy is stopped. Information requested about the delivery shall include gestational age at delivery and any birth defects.

Male participants are not required to use birth control during the study. However, you should let your female partner know that you are in this study.

14. What will it cost me to be in the study?

The costs of all study drugs, tests, and procedures described above that are required by the study will be paid for by NIAID through the ITN. You will be responsible for any expenses related to your routine clinical care. Please ask your study doctor about any expected added costs that you may incur. Insurance companies and other carriers sometimes refuse to pay the costs of study treatment when individuals are participating in research. Check with your health plan or insurance company to find out what they will pay for. Taking part in this study may lead to added costs to you or your insurance company.

15. Will I be paid for taking part in this study?

You will receive payments per the following table for participating in the study.

Item	Amount
Travel expenses (All visits)	\$50.00/visit
Visit -1 (Screening)	\$100.00
Visits 0	\$80.00/visit
Visits 1-9, unscheduled, Visits 1SM-4SM (if applicable)	\$60.00/visit
MMTT visits -1 (Screening), 6-9 (Additional payments)	\$250.00/visit

Please contact your study staff for assistance with any additional travel costs. If for any reason you do not complete the study, you will be paid for each study visit you do complete.

16. What if I am injured during the study?

If you are injured or get sick while in this study, it is important to tell your study doctor listed on page one of this consent form.

Emergency medical treatment will be available to you. The study site will bill you or your insurance company in the normal way for the cost of such care. No payment or additional compensation is available to you for such injuries. There is no provision for medical care at no

cost to you or monetary compensation from the study sponsor, the NIAID, NIH. You do not lose any legal rights by signing and dating this form.

17. Will I be tested for HIV?

Yes, you will be tested for HIV as part of the screening visit before you start the study. If you are found to be HIV positive, you will not be permitted to participate in the study. Your medical records will be kept confidential to the extent permitted by law. However, as mentioned earlier in this consent form, the study doctor may be required by law to report the result of this test to the local health authority.

18. Will my identity be kept private/confidential?

Your medical and research records will be confidential to the extent permitted by law. Every effort is made to keep your identity private. However, we cannot always guarantee complete confidentiality.

Medical and research records from this study will be reviewed by the United States agency funding this study (NIAID, NIH), including its representatives, agents, employees, contractors, and other persons assisting in conducting, monitoring, or analyzing the study.

In addition, the FDA, or other health authorities, and pharmaceutical drug manufacturer, ITB-Med, LLC, may review your medical and research records for regulatory purposes.

You will be identified by a study code, not your name. The key to the code is kept in a secured file at the study site. Personal data from your records will not be released without your permission. You will not be named in any publication about this study. After the study is completed, this study data may be placed in a central storage location. The purpose is to make study data available to other researchers. This data does not include identifiers (for example, name and contact information). Information from this study may be put into databases along with information from other studies. There are different kinds of databases. Some are publicly accessible, and some are restricted. Anyone on the internet can access publicly accessible databases. Only researchers who apply and are approved can access restricted databases. Traditionally used identifying information about you (such as name, phone number, address) will NOT be included or shared with others.

Your privacy is important to us, and we will use safety measures to protect your privacy. Despite the safety measures that we use, we cannot guarantee that your identity will never become known. Although your genetic information is unique to you, you share some genetic information with your children, parents, brothers, sisters, and other blood relatives. It may be possible that genetic information from them could be used to help identify you. It may also be possible that genetic information from you could be used to help identify them.

While we will not use information that is traditionally used to identify you, people may develop ways in the future that would allow someone to link your genetic or medical information in our databases back to you. For example, someone could compare information in our databases with information from you (or a blood relative) in another database and be able to identify you (or your blood relative).

It is also possible there could be violations to the security of the computer systems used to store the codes linking your genetic and medical information to you. There may also be other privacy risks that we have not foreseen.

Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The National Institute of Allergy and Infectious Diseases (NIAID), the sponsor of the research
- NIAID representatives, agents, employees, contractors, and other persons assisting in conducting, monitoring, or analyzing the study
- FDA
- Other State and Local health authorities
- Pharmaceutical company, ITB-Med, LLC, may review your medical and research records for regulatory purposes

Certificate of Confidentiality

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence (for example, if there is a court subpoena) unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except if there is a federal, state, or local law that requires disclosure (see below), if you have consented to the disclosure, including for your medical treatment, or if it is used for other scientific research as allowed by federal regulations protecting research participants.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by the agency which is funding this project or for information that must be disclosed in order to meet the requirements of the FDA. You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law of, for instance, child abuse or neglect, harm to self or others, and communicable diseases.

The Certificate of Confidentiality will not be used to prevent disclosure for any purpose you have consented to in this informed consent document.

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.

19. Whom To Contact About This Study

Please contact the study doctor at the telephone number listed on the first page of this consent document if you experience any medical problems, suffer a research-related injury, or have questions, concerns, or complaints about the study such as:

- Whom to contact in the case of a research-related injury or illness
- Payment or compensation for being in the study, if any
- Your responsibilities as a research participant
- Eligibility to participate in the study
- The study doctor's or study site's decision to withdraw you from participation
- Results of tests and/or procedures

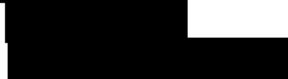
If you seek emergency care or hospitalization is required, alert the treating physician that you are participating in this research study.

An institutional review board (IRB) is an independent committee established to help protect the rights of research participants. If you have any questions about your rights as a research participant, contact:

- By **mail**:



- or call **toll free**:
- or by **email**:



Please reference the following number when contacting the Study Subject Adviser:
Pro00067421.

20. Will any of my samples, information, or data be stored for future use and shared with others?

If you agree, we will store your blood and information in the central ITN repository located in the United States for a minimum of 10 years. The purpose is to make these samples and information available for future research which is not yet planned and to share the stored samples with other researchers.

Information about you, including your samples, collected for this study may be shared with other researchers. It may also be used for other research studies. We will make sure that your identity cannot be linked to the information we share. We will not ask you for additional permission before sharing the information.

ITB-Med (the pharmaceutical company providing sipilizumab) may receive samples from this study. These samples will be labeled with a number. Your personal information such as your name and contact information will not be included with these samples.

Your decision to allow samples and data to be stored and shared is separate from your decision to participate in this study. If you decide to allow storage, your samples and data may be stored for an unknown length of time but for a minimum of 10 years. Blood samples used for research tests can include analysis of deoxyribonucleic acid (DNA). The samples will be stored using a code and may be sent to be tested in outside labs. All data are kept confidential, and the people testing the DNA will not have any of the other identifiers (for example, name and contact information).

Researchers can look closely at large amounts of your genetic information by sequencing, or “reading,” every letter in your DNA (your genome). Reading a person’s entire genetic code is called whole genome sequencing. Future research may look at large chunks of your DNA (whole exome testing) or all of your DNA at once (whole genome testing).

Your biospecimens collected during this study may be used for commercial profit (even if identifiers are removed), and you will not share in this profit.

The results of tests done on your stored samples will not be given to you or your study doctor. The results will not be put in your records and will not change your medical care. There will be no benefits to you from the storage of these samples and information. However, the use of your samples and information may help researchers learn more about your disease or help study the genetics related to your disease.

There may be risks in allowing the storage, sharing, or analysis of samples and information. For example, if future research is for genetic testing and because genetic information is unique to you there is a risk that someone using your sample could trace it back to you. Researchers are required to protect your privacy and to keep your information private to the extent permitted by the law. This does not occur all the time when information is shared with others.

If information resulting from the analysis of your samples is shared publicly, it will not contain the identifiers (for example, name and contact information). The samples and information will not be sold. However, the results of the tests could lead to the development of commercial products. You will not receive any money from research using your stored samples and information.

You can change your mind at any time during the study and ask to have your stored samples destroyed. This request should be made to the study doctor. If your samples have not been used, they will be destroyed. If your samples have already been tested or shared before your request is made, the information from these tests will be used and cannot be destroyed.

Please indicate your response below:

I agree to the storage and sharing of samples (blood) for genetic tests and sharing of information/data resulting from the analysis of my genetic tests not currently planned.

☐ Yes ☐ No

Initials of Research Participant

I agree to the storage and sharing of samples (blood) and sharing of information/data resulting from the analysis of my samples for other tests (not genetic) not currently planned.

☐ Yes ☐ No

Initials of Research Participant

FUTURE CONTACT

May we contact you by phone to find out if you are interested in hearing about new research studies or to ask you about how your current health is? Contact would be made by the lead study doctor's staff. If you decide at any time that you no longer want to be contacted, please tell us and we will stop calling you.

Would you like us to contact you about future research studies?

☐ Yes ☐ No

Initials of Research Participant

Would you like us to ask you about how your current health is?

☐ Yes ☐ No

Initials of Research Participant

If you say "no" to this question, this will not affect your participation in this study.

21. SIGNATURE PAGE

Please sign and date below if you agree to take part in this study.

- You have read the informed consent, and/or had it explained to you
- You were given the opportunity to ask questions about the information
- You voluntarily agree to take part in the study

Research Participant's Name
(Typed or printed)

Research Participant's Signature

Date

Signature of person explaining and obtaining the consent:

Name and Title
(Typed or printed)

Signature

Date

WITNESS SIGNATURE FOR PARTICIPANTS WHO CANNOT READ

The study participant has indicated that he/she is unable to read. The consent document has been read to the participant by a member of the study staff, discussed with the participant by a member of the study staff, and the participant has been given an opportunity to ask questions of the study staff.

Name of Witness
(Typed or printed)

Signature

Date

AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION

If you decide to be in this study, the study doctor and study staff will use and share health data about you to conduct the study. Health data may include:

- Your name.
- Address.
- Phone number.
- Date of birth.
- Medical history.
- Information from your study visits, including all test results.

Health data may come from your study records or from existing records kept by your doctor or other healthcare workers.

For this study, the study staff may share health data about you with authorized users. Authorized users may include:

- Representatives of the National Institute of Allergy and Infectious Diseases (NIAID), NIH.
- Representatives of Advarra IRB (an Institutional Review Board that reviews this study).
- The Food and Drug Administration (FDA) and other US federal and state agencies.
- Government agencies to whom certain diseases (like HIV, hepatitis, and STDs) must be reported.
- Outside individuals and companies, such as laboratories and data storage companies, that work with the researchers and sponsor and need to access your information to conduct this study.
- Other research doctors and medical centers participating in this study, if applicable.
- A data safety monitoring board which oversees this study, if applicable.

Your health data will be used to conduct and oversee the research, including for instance:

- To see if the study drug works and is safe.
- To compare the study drug to other drugs.
- For other research activities related to the study drug.

Once your health data has been shared with authorized users, it may no longer be protected by federal privacy law (HIPAA) and could possibly be used or disclosed in ways other than those listed here.

Your permission to use and share health data about you will end in 50 years unless you revoke it (take it back) sooner.

You may revoke (take back) your permission to use and share health data about you at any time by writing to the study doctor at the address listed on the first page of this form. If you do this, you will not be able to stay in this study. No new health data that identifies you will be gathered after your written request is received. However, health data about you that has already been gathered may still be used and given to others as described in this form.

Your right to access your health data in the study records will be suspended during the study to keep from changing the study results. When the study is over, you can access your study health data.

If you decide not to sign and date this form, you will not be able to take part in the study.

STATEMENT OF AUTHORIZATION

I have read this form and its contents were explained. My questions have been answered. I voluntarily agree to allow study staff to collect, use and share my health data as specified in this form. I will receive a signed and dated copy of this form for my records. I am not giving up any of my legal rights by signing and dating this form.

Printed Name of Participant

Signature of Participant

Date

Printed Name of the Person Obtaining Date
the Authorization

Signature of the Person Obtaining the Date
Authorization

WITNESS SIGNATURE FOR PARTICIPANTS WHO CANNOT READ

The study participant has indicated that he/she is unable to read. This Authorization document has been read to the participant by a member of the study staff, discussed with the participant by a member of the study staff, and the participant has been given an opportunity to ask questions of the study staff.

Printed Name of Witness

Signature of Witness

Date