

Appendix 1: Standard fictitious ICF – English version

To obtain the French version, contact pascal.bedard.hsj@ssss.gouv.qc.ca



ÉCLAIRAGE - RESEARCH INFORMATION AND CONSENT FORMS IN PEDIATRICS

This document is provided to you on behalf of the ÉCLAIRAGE research project, following your consent to participate in the study.

As explained in the ÉCLAIRAGE research information and informed consent form, you will have 24 hours to read the following document. You may annotate the parts you consider important and the ones that you consider unclear or not essential if you want to. After the 24 hours have passed, a member of the research team will come pick up the document and will hand you the comprehension questionnaire. You will have 2 hours to complete the questionnaire.

We remind you that the research project described in the following information and informed consent form is **fictitious**.

It describes a **fake** study.

Your child does **NOT** have type 1 diabetes and will **NOT** take the medication described in this document. There is **NO** link between this research project and the hospitalization/diagnosis/treatment of your child.

No questions concerning this fictitious research information and consent form will be answered, despite what may be mentioned in the following pages.

However, if you have questions about the ÉCLAIRAGE research project, do not hesitate to ask them to a member of the ÉCLAIRAGE research team.

RESEARCH INFORMATION AND INFORMED CONSENT FORM

Research Study Title: A phase III randomized, multicenter, double-blind, placebo-controlled trial evaluating the safety and efficacy of INSUPEROS in children and adolescents with type 1 diabetes.

Protocol number: ABCD012E3456

Person responsible:

- CHU Sainte-Justine : Dr. Julie Leclair, Endocrinologist

Funding source: PharmaInc

WHY ARE YOU BEING INVITED TO TAKE PART IN THIS STUDY?

You are being invited to take part in this research study because your child has type 1 diabetes. The endocrinology department participates in research studies to try and improve treatments for children with type 1 diabetes. Today, we are inviting you and your child to take part in a research study. The following research study evaluates the safety and efficacy of a medication named Insuperos.

This form gives you important information about the study including the purpose of the study and possible risks to your participation. Please read this information to help you decide if you want to participate in this research project. It is important that you understand this information. Some terms may be unfamiliar to you. If you or your child have questions about this information at any time, please ask the study doctor or study staff to answer them. You may also discuss the study with family members, friends, and your own doctor if you wish. Please take all the time you need to make your decision.

We encourage parents to include their child in the discussion and decision making to the extent that the child is able to understand.

In this research informed consent form, “you” means you or your child.

WHY IS THIS STUDY BEING DONE?

The purpose of this study is to assess if treatment with an investigational drug, Insuperos, is safe and effective in the treatment of pediatric patients with your condition. An investigational drug is also known

as an experimental drug or a “study drug.” Investigational means that Health Canada has not approved Insuperos for all pediatric patients with type 1 diabetes, however Health Canada authorized its use for the purpose of this study.

You have a disease called type 1 diabetes. With this disease, the pancreas does not produce sufficient insulin to regulate blood sugar levels. If the blood sugar levels are not maintained within a specific range, this disease can cause multiple long-term damages to different body organs, including the heart, kidneys and eyes. The standard treatment for this disease is subcutaneous insulin injections. Insulin is an effective treatment acting as a replacement for the endogenous insulin typically produced by the pancreas, which is not functioning properly in type 1 diabetes patients. Unfortunately, this treatment requires several injections every day. Typically, insulin is administered in the following way: an injection with every meal (prandial insulin, which is short-acting) as well as a supplementary injection before bedtime (basal insulin, which is long-acting).

Insuperos is an extended-release formulation taken orally once a month that replaces the daily basal (long-acting) insulin injection. Insuperos is a molecule closely resembling the structure of endogenous insulin, therefore having a similar mechanism of action. It is coupled with another small molecule in order to prevent it from being degraded by the acidity in the stomach when taken orally. Insuperos is available in a long-acting formulation that is active for 4 weeks.

Insuperos has been tested in studies including healthy volunteers and participants with type 1 diabetes. The glycemic control with the investigative drug was similar to the one obtained with subcutaneous insulin injections in up to 94% of the adult participants, while reducing their therapeutic burden. Approximately 40 children have received Insuperos and the pediatric doses were established using their data. The use of Insuperos is experimental in this study because its efficacy and safety have not been fully evaluated in children with type 1 diabetes.

WHAT ARE THE OBJECTIVES OF THE RESEARCH?

You are being invited to participate in a research study that aims to compare monthly oral Insuperos to a placebo, for the treatment of type 1 diabetes in children between 6 months and 17 years of age. The main objectives include evaluating the efficacy of Insuperos at controlling your diabetes and assessing the overall safety of Insuperos.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

This study will include approximately 270 children (6 months to 17 years old) at about 9 research centers in the United States and Canada. At CHU Sainte-Justine, we will include approximately 10 participants.

WHAT WILL HAPPEN IN THIS RESEARCH STUDY?

This is a clinical trial involving a medication for type 1 diabetes called Insuperos. A clinical trial is a form of research study that attempts to find or improve treatment of a disease in human patients. Clinical trials include only people who choose to participate.

Participants enrolling in this study must meet certain requirements. The study doctor will review all of the restrictions and requirements of the study with you to determine if you qualify to be in the study and to answer your questions.

This study has three (3) different stages:

- **Screening:** To take part in this study you will have to go through a screening visit. This visit will tell the study doctor if you meet all the requirements to take part in this study. If you do not meet all the requirements, you cannot continue with the study.
- **Treatment period:** If you are eligible to enter the study, you will start a 44-weeks study treatment period. You will receive either the experimental drug or the placebo.
- **Follow-up visits:** During this period, which can last up to 12 weeks, we will follow your health status every 6 weeks.

You will have 15 visits to the clinic during the study. The visits will take place at screening (when you are evaluated for study participation), every 4 weeks during the treatment phase and every 6 weeks during the follow-up period. The screening visit will take 4 to 6 hours, but the following visits should take less than 2 hours. All the visits and tests will take place at the CHU Sainte-Justine clinic. An optional extension study may be available to you after you complete the Treatment period. Your study doctor will provide you with additional information when appropriate.

Screening (Duration: 1 day)

This screening visit is necessary to determine if you are eligible to participate in the study. The research team will consult your medical record to obtain information relevant to this research. The screening visit will take place before receiving the study drug. The baseline assessments will be done in this stage, before you start the study drug, to determine your health status prior to starting the study drug. This visit lasts between 4 and 6 hours.

On your first visit to the study center, you will be told about the details of this study including any procedures or other aspects of the study which are experimental. You will be able to review the present information sheet and informed consent form. You will have the opportunity to ask any questions you may have about this study, and your questions will be answered. After you have voluntarily accepted, signed and dated the present consent form, you will receive a copy of this document to keep as a useful reference of the trial and personal contact.

At this visit the following tests will be performed:

- Medical History/ Current medical condition

- Physical examination
- Demographic
- Nutritional information
- Blood and urine samples
- Pregnancy test
- Electrocardiogram (ECG)
- Eye exam
- Coronavirus (COVID-19)

Treatment (Duration: 44 weeks)

If you meet the “entry criteria” and you agree to participate in this study, you will have to start the study treatment within 14 days after the screening visit.

You will be given tablets of Insuperos or placebo to be taken by mouth, once a month. A placebo contains no active drug but looks identical to the active study drug. A placebo is used to make sure that the changes study patients report in the study are not just happening by chance. This study is a double-blind study, meaning that neither you nor the study doctor/staff will know who is receiving Insuperos or placebo. Whether or not you receive the study drug Insuperos is decided by a process called randomization. Randomization means that the treatment is assigned based on chance. It is a lot like flipping a coin, except that it is done by computer. You have a 50% chance of receiving the placebo and 50% chance of receiving the study drug. You and your doctor will not pick whether you get Insuperos or not.

During the treatment period, you must keep using your prandial (short-acting) insulin. The study medication is used in addition to the prandial (short-acting) injections, and it does not replace them.

In order to maintain the double-blind design of the study, both treatment groups will continue to receive once-daily injections as if they were receiving a daily basal (long-acting) insulin. If you receive Insuperos, you will stop taking your daily basal (long-acting) insulin. The study team will provide you with pre-filled pens containing normal saline liquid, which is a physiological solution. It does not cause any harm and it is injected in very small quantities. If you are in the oral placebo group, you will continue receiving basal insulin. The study team will provide you with pre-filled pens containing basal (long-acting) insulin at the same dose you are using at the moment of the start of the study. The insulin and normal saline pens will be identical, so you will not know whether you inject basal insulin or normal saline. The study team may adjust the quantities you are injecting throughout the study.

The quantity of the study drug (dose) you will receive depends upon your current weight, regardless of your age, as follows:

- Body weight ≥ 60 kg: 1 tablet of 500 mg every 4 weeks.
- Body weight 30 kg to < 60 kg: 1 tablet of 400 mg every 4 weeks.
- Body weight 15 kg to < 30 kg: 1.5 tablets of 200 mg every 4 weeks.

- Body weight 5 kg to <15 kg: 1 tablet of 200 mg every 4 weeks.

The Insuperos dose you receive may change if your weight changes. If you gain weight during the study, then the dose may change to reflect the weight change, according to the study doctor's evaluation. The opposite may apply if you lose weight during the study and stay at a lower weight bracket for at least 2 visits in a row.

For the 44 weeks of treatment, you will return to the study site for repeat testing of many of the tests that you experienced in the first study visit. The visits are scheduled every 4 weeks on site. Some evaluations will be repeated at every visit, while others will be performed only if considered as needed by a member of the research team.

The following procedures will be performed by your doctor or study staff at every visit on site:

- Medical History/ Current medical condition
- Physical examination
- Nutritional information
- Review of daily e-diary
- Review of blood sugar levels
- Blood and urine samples
- Coronavirus (COVID-19) testing

The following procedures will be performed by your doctor or study staff only if deemed necessary:

- Eye exam
- Electrocardiogram (ECG)
- Pregnancy test

If you permanently discontinue the study medication, you will be asked and encouraged to return to the study site for the follow-up phase of the study.

Follow-up (Duration: 12 weeks)

After receiving 44 weeks of treatment, the experimental treatment will be stopped. During the follow-up period, you will not receive the investigational drug. During this period, we want to monitor the long-term effects of the medication.

If you are willing and you qualify to enter an extension study, then you may not need to participate in these follow-up visits. If you do not go into the extension study, you will return to the study site once every 6 weeks during the post-treatment follow-up period.

During the follow-up study visits your doctor or study staff will perform the following procedures:

- Medical History/ Current medical condition
- Physical examination
- Nutritional information
- Review of daily e-diary
- Review of blood sugar levels
- Blood and urine samples
- Pregnancy test*
- Electrocardiogram (ECG)*
- Eye exam*
- Coronavirus (COVID-19) testing

* The following procedures will be performed by your doctor or study staff only if deemed necessary.

Unscheduled visits

When necessary, unscheduled visits could take place, for example in case of any side effects that need a specific treatment, or some changes or discontinuation of the study treatment. During these visits, the doctor may ask for additional assessments depending on the reason for this visit.

During your participation in this research study, the study doctor or a member of the research team will conduct the following tests and procedures:

Medical History/ Current medical condition: Your study doctor will ask you a series of questions regarding how you are feeling, your health conditions and medical history. You will also be asked about procedures and any medications you have been taking, including all non-prescription medications (such as vitamins, herbal supplements, aspirin, and other over-the-counter medications). You will also be asked information about healthcare visits/hospitalizations/interventions due to type 1 diabetes. Please answer the questions transparently and tell the study doctor if you feel different or something is wrong.

Physical examination: A complete physical examination will be performed. This includes measurement of your body weight and height (or length for children under 2 years of age), blood pressure, heart rate and body temperature.

Demographic: Your demographic data (including age, race, nationality and ethnicity) will be collected.

Nutritional information: You are expected to maintain a similar diet to the one you had before entered the study. Information on your nutritional habits will be recorded. If you are hospitalized, information on the type of nutritional (food) support you have been given will be collected.

Daily e-diary: You will have to fill out a daily diary documenting any diabetes-related symptoms, potential side effects from Insuperos as well as the impact of the disease/medication on your quality of life.

Blood sugar level: Your blood sugar levels will be continuously measured via a continuous glucose monitoring device. A small sensor under your skin will measure your glucose levels in the blood vessels under your skin. This enables blood glucose levels tracking throughout the day and night. You will be able to see your glucose level anytime at a glance. The monitoring device will be installed and explained by the research team at the first in-clinic visit for treatment. It will be changed every 4 weeks by the research team when you come to the clinic. The average daily value, the minimal and maximal values as well as 2 additional values throughout the day will be automatically and electronically transmitted to the research team. These results will be checked daily to see if any emergency intervention is needed. The results will be inserted in your medical file and discussed at each visit.

Blood and urine samples: These will be collected for standard laboratory testing such as hematology (blood cell counts), chemistry (sugar, minerals, enzymes, HbA1c, and lipids) and insulin levels. On some days, you will have to fast to test your glucose properly. These days will be specified to you during the first visit. To fast means you are not to eat any food or drink except water and coffee/tea (unsweetened and without milk) for the previous 4-12 hours, depending on your age.

Pregnancy test: If you are a woman, your fertility (ability to become pregnant) will be assessed by the study doctor. If appropriate, you will be asked to do a pregnancy test and your blood will also be tested to see if you are pregnant. The study doctor or study staff will tell you if the pregnancy test results are positive. The results of the pregnancy testing must be negative in order for you to be in the study.

Electrocardiogram (ECG): This is a heart tracing which records the electrical activity of your heart. Leads (like stickers) will be placed on your skin and you will be asked to lie down during the exam.

Eye exam: A series of tests to evaluate your vision and check for eye diseases will be done by an ophthalmologist at CHU Sainte-Justine.

Coronavirus (COVID-19) testing: Depending on the circumstances local to the site, the study doctor may require you to be tested for coronavirus. A swab of the area at the back of your nose will be taken for this assessment.

The table below details when the tests and procedures will take place during the study:

	Screening	In-Clinic Visit (Treatment)														Follow-up Visit	Unscheduled Visit**
In-Clinic Visit (V)	V 1	V 2	V 3	V 4	V 5	V 6	V 7	V 8	V 9	V 10	V 11	V 12	V 13	V 14	V 15	N/A	
Duration of visit (hours)	4 to 6	<2	<2	<2	<2	<2	<2	<2	<2	<2	<2	<2	<2	<2	<2	TBD***	
Week (W)		W 0	W 4	W 8	W 12	W 16	W 20	W 24	W 28	W 32	W 36	W 40	W 44	W 50	W 56	N/A	
Medical History	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Current medical condition/medication	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Physical examination	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Demographics	X																
Nutritional information	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Review of daily e-diary			X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Review of blood sugar levels		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Blood sample	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Urine sample	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Blood or urine pregnancy test for girls of childbearing potential*	X															X	
Electrocardiogram (ECG)*	X															X	
Eye exam*	X															X	
Coronavirus testing (COVID-19)	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Study drug administration every 4 weeks (on-site)		X	X	X	X	X	X	X	X	X	X	X	X				
On-site monitoring for 60 minutes after study drug administration		X	X														

*: The following procedures will be performed by your doctor or study staff only if deemed necessary.

** : During an unscheduled visit, any of the listed tests could be performed according to what your doctor or study staff consider necessary.

***: TBD: To be determined. The duration of the visit will depend on the tests that will be performed.

FOR HOW LONG WILL YOU PARTICIPATE IN THIS STUDY?

If you participate in this clinical trial, you will receive the experimental treatment for a period of 44 weeks. We would like to continue to check on your health for about 12 weeks after your participation in the research project. Keeping in contact with you for some time after your active participation ends may help us to learn about the long-term effects of the experimental treatment being studied. The total duration of your participation in the study will be 56 weeks.

This timeframe is used if you don't want to continue, or if you do not qualify for continuing in the 1-year open extension trial (a separate extension study with a separate Informed Consent Form).

WHAT ARE THE RISKS?

You may experience side effects from the drugs or procedures used in this study. Side effects can be mild to severe or very serious, and they can vary from person to person. You should talk to your study doctor about any side effect that you have while taking part in the study.

Risks associated with Insuperos

The side effects associated with Insuperos are listed below. They come from information known from its use in adults. There may be side effects that are not known at this time.

Insuperos may cause all, some, or none of the side effects listed below. These side effects can be mild but could also be serious, life-threatening, or even result in death.

Very common side effects (may affect one or more in 10 people)
<ul style="list-style-type: none">• Weight gain• Headache• High blood pressure: A transitory increase in blood pressure could be observed in patients taking Insuperos. Some symptoms of high blood pressure could include headaches, nosebleeds, fatigue, confusion, vision problems, chest pain, anxiety, shortness of breath or palpitations.• Gastrointestinal toxicity: Nausea, vomiting, abdominal pain and diarrhea can occur in individuals taking Insuperos. If the vomiting is too inconvenient or if it prevents you from hydrating or nourishing yourself, you need to alert the study doctor and study staff as soon as possible.
Common side effects (may affect 1 to 10 in 100 people)
<ul style="list-style-type: none">• Dehydration• Hypoglycemia: Temporary lowering of the blood glucose levels has been observed (<4 mmol/L) in patients taking Insuperos. This side effect is mostly seen in cases where the dosage is too high. Hypoglycemia can present itself with multiple

symptoms: headaches, weakness, tremors, fatigue, somnolence, confusion, palpitations, drowsiness, increased sweating, trouble focusing and mood changes. The severity of these symptoms can vary according to the blood glucose levels. A lower blood glucose level will cause more severe symptoms.

- **Kidney toxicity:** Acute kidney injury is a decrease in how well your kidneys work. Symptoms may include lower amounts of urine than usual, swelling in legs, ankles, and around the eyes, tiredness, confusion, nausea, seizure, chest pain.
- **Liver toxicity:** Insuperos may cause an increase in certain enzymes in the blood which may indicate liver disease or bile duct obstruction. In more severe cases, liver toxicity can also cause nausea, vomiting, diarrhea, abdominal pain, fatigue, appetite loss, jaundice (yellow coloration of the eyes and/or skin), intense skin itchiness, dark urine and muscle pain. If these symptoms occur, you need to alert the study doctor and study staff as soon as possible.

Uncommon (less than 1 in 100 people)

- **Eye disorders:** This side effect has been observed in adults taking Insuperos for longer than 16 weeks (4 doses). According to recent studies, it is a side effect that is reversible upon stopping the medication. Insuperos needs to be stopped immediately when symptoms arise. Some possible symptoms include blurry vision, seeing flashes of light, sensitivity to light and headaches.
- **Hypokalemia:** Some cases of lowering of potassium levels in the blood have been observed in patients who were treated with Insuperos. Hypokalemia could cause arrhythmias, which are irregular heartbeats.

Diabetic acidosis and coma

High blood glucose levels (>20 mmol/L) can lead to ketoacidosis (high levels of ketones cause the blood to become more acidic). This is not a side-effect of the medication, but it remains a possible risk associated with this treatment. It is possible that Insuperos will not be efficient enough in controlling your type-1 diabetes. If the Insuperos dose is insufficient (too low), it could be insufficient to maintain an optimal blood glucose. This could be explained by the fact that some individuals may respond less than others to Insuperos, therefore putting them at risk for this manifestation. This is considered a rare risk. It is important to take the Insuperos doses when indicated, as well as the prandial (short-acting) subcutaneous insulin in order to maintain good control of the blood glucose levels. Some possible symptoms include fruity breath, difficulty breathing, headache, nausea, vomiting. If not treated, it can evolve into a coma. This condition may require hospitalization. This manifestation could arise at any moment if the blood glucose level is not under control.

Allergic reaction

There is a chance that you may experience a local or generalized allergic reaction (also known as hypersensitivity reaction) to the study drug. One kind of allergic reaction can happen immediately (within minutes or hours) after taking study drug. Symptoms of immediate allergic reaction may include skin flushing, rash or hives, sneezing, runny nose, difficulty breathing, wheezing, a sense of choking, sudden change in blood pressure (causing dizziness or light-headedness), swelling around the mouth, throat, or eyes, fast pulse or sweating, abdominal cramps, diarrhea, etc. The severity of this type of immediate reaction ranges from mild to severe. A mild reaction may progress to a more severe one, so you should contact the study staff if you experience any new symptoms occurring within a couple of hours after taking Insuperos .

A severe allergic reaction requires immediate medical treatment and could result in permanent disability or death if not treated promptly. If you believe you are having a severe allergic reaction, you should immediately seek emergency medical treatment and alert the study doctor and study staff as soon as possible.

In order to minimize and manage the allergy risks and inconveniences, the doses will be administered under supervision of the study research team at CHU Sainte-Justine. You must be carefully monitored for symptoms that may suggest an allergic reaction for at least 60 minutes after administration.

Risks associated with research procedures

The tests done at each visit are standard medical tests, however they may cause some discomfort. The following risks have been identified for the procedures and tests done in the study:

Blood pressure measure: You may experience bruising and discomfort from the blood pressure cuff.

Questionnaires/Diaries: Some people feel uncomfortable when answering questions about their habits and their life. Though it is always better to have fully completed questionnaires, you do not need to answer any questions that make you feel uncomfortable.

Blood sugar level: The installation and removal of the monitoring device is painless. However, there can be some inconveniences caused by the device itself. There can be skin irritation in the region where the device is placed. The device could also unstick under certain circumstances. It is important to follow the instructions given for maintenance.

Blood draw: As part of this study, you will have your blood drawn. The study doctor or study staff will take your blood by sticking a needle in your arm. The risk of collecting

blood may include dizziness, fainting, pain, and/or bruising. Rarely, there may be a small blood clot or infection at the site of the needle puncture or central line.

Blood will be taken about 15 times during the study. During the screening visit, approximately 10.5 mL of blood will be collected (about 2 teaspoons or 3/4 tablespoon). After the first visit, approximately 7.5 mL of blood will be collected at each visit (about 1.5 teaspoon or 0.5 tablespoon). In total, approximately 206 mL of blood will be collected from you. More blood may be collected if extra tests are needed for your health and safety. The amount of blood taken will remain below the limit approved by the Research Ethic board.

In order to reduce the discomfort that can be related to blood sampling, the research team can offer you, if there is no known contraindication, the possibility of using an anesthetic cream. The use of this cream is not mandatory in the context of research and the decision to use it belongs to you. This cream is contraindicated in patients who are allergic to lidocaine or other topical anesthetics (creams or gels, for example). If you want to use the cream, the minimum amount required to be effective will be applied (about the size of a pea) in order to limit the amount that will be absorbed into the blood and that could cause serious side effects. Be aware that serious side effects related to the use of cream have been described, especially when used on a regular basis and / or when applied over large areas.

Electrocardiogram (ECG): This test is painless, and you should not feel anything while the ECG is done. Because the ECG machine will be connected to your body with sticky patches, like bandages, you may experience temporary discomfort (pulling on the skin/skin hair) during removal of the sensors.

Eye exam: You may experience some side effects following the eye exam because of the eye dilation performed. These side effects typically last around 4 to 6 hours and may include: light sensitivity, blurry vision, trouble focusing on objects. In very rare cases, you may experience dry mouth, rapid pulse, fever or facial flushing.

COVID test: You may experience some discomfort during the nasal swab. Experiencing a mild nosebleed (epistaxis) is also possible. The procedure can trigger tears when performed, because it activates a reflex in your body. The procedure does not last for more than five seconds per nostril, and there are no other long-term harms from the test.

Reproductive Risks

Women should not get pregnant, and men should not conceive a baby during their participation in this research project. Studies in pregnant animals have shown that the medications you are required to take in this study can harm an unborn or nursing baby.

Women

Pregnant or breastfeeding women and women planning to become pregnant or planning to breastfeed should not participate in this study.

If you are unable to become pregnant (that is, not sexually mature), the use of birth control methods is not required during this study.

If you could become pregnant (that is, sexually mature and sexually active), you:

- should let your sexual partner know you are in the study,
- must agree to practice abstinence (not have sex) or must agree to use a highly effective method of birth control during treatment with Insuperos and for an additional 3 months after the last dose of Insuperos,
- must discuss your pregnancy prevention method with the study doctor to ensure it is the best option for you; even with the use of a highly effective method of birth control, there is still a small chance that a pregnancy could occur.

Highly effective methods of birth control include: combined (estrogen and progestogen) hormonal methods (pills, vaginal ring, or skin patch), intrauterine device (IUD), intrauterine hormonal-releasing system (IUS), surgery to tie both fallopian tubes (bilateral tubal ligation/occlusion), your male partner has had a vasectomy and testing shows there is no sperm in the semen or sexual abstinence (have no sex).

If you become pregnant or suspect being pregnant during study treatment or within 3 months after completing study treatment you must inform the study doctor immediately, and you have to stop ongoing study treatment immediately. You will not be allowed to continue study treatment if you are pregnant. Your study doctor will medically follow your pregnancy until delivery to monitor your child and your safety.

Women should not breastfeed a baby while participating in the research and for 3 months following the last dose of Insuperos.

Men

Men should not conceive a baby during their participation in this research project. As a male participant in the study, you must agree to use a condom during intercourse while taking the drug and not to father a child during the study and for a period of 3 months after stopping Insuperos. In addition, it is advised that your female partner uses a highly effective form of birth control method (contraception) if she is sexually active and may become pregnant. In case you father a child while in this study, you are asked to report the pregnancy to the study doctor. Consent from your partner will be needed to allow your study doctor to medically follow this pregnancy until delivery to monitor the mother's and child's safety.

Unknown Risks

Participation in this research project may also have other risks that we do not know or have not predicted.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY

We think that it is possible that Insuperos may allow a simplification of your type 1 diabetes treatment regimen. However, since Insuperos is still currently under

investigation as a treatment, you cannot be assured of any benefits for this condition. Your condition may get better, but it could stay the same or even get worse.

You will be given close attention from the study staff during the study. You will receive information about your health from physical examinations and medical tests done in this study.

We hope that the information obtained in this study will lead to favorable results and, along with additional studies, lead to approval by the regulatory authorities of Insuperos for use in children, therefore providing benefits for other patients in the future.

WHAT OTHER OPTIONS ARE THERE?

You do not have to be in this study to get treatment for your type 1 diabetes. There are other treatments available to treat signs and symptoms of the disease if you decide to not participate in the study. Your study doctor will detail the alternative treatments to you. Some options that may be available to you include receiving the standard treatment (subcutaneous basal, long-acting, insulin injection), an insulin pump or participating in another research project (if available). If you have any questions concerning alternative treatments including any questions about their risks and benefits, please ask your study doctor. You and the study doctor can decide what is best for you.

PARTICIPANTS RESPONSABILITIES

Your adherence to the study visits, procedures and assessments schedule, as planned in the protocol, is of utmost importance in order to prevent missing data and to be able to fully evaluate the efficacy and safety of the study drug.

It is essential that you provide truthful information about your medical history and current conditions.

It is important that you tell the study doctor about any health problems, medications (prescription, over the counter, or herbal supplements) and doctors' visits you have had in the past few months or at the present time. Tell the study staff if you stop taking any medications that you were previously taking. This is very important. Please tell your study doctor or site staff if you have any unusual symptoms.

While you are involved in the study, you should not start new therapies for your type 1 diabetes. If you enter the study, the study doctor will discuss with you whether you should stop or continue any therapies you may be taking.

Inform the study doctor and/or staff if you have been in a research study in the last 2 months or are in another research study now. If you decide to participate in this study, you can not join or be a part of another research study at the same time.

By signing this consent form, you agree to follow the study doctor's instructions and attend all study-related visits.

IS ANY COMPENSATION BEING OFFERED?

You will not receive direct monetary compensation for your participation in this study. Your expenses for your travels, parking and meals related to your participation in this research study will be reimbursed upon presentation of receipts.

You will not have to pay for any study treatment or any study-related tests while you are in the study. The prandial (short-acting) insulin, basal (long-acting) insulin, and the study drug will be offered to you free of charge for the duration of this research study.

SHOULD YOU SUFFER ANY HARM

Should you suffer harm of any kind following administration of the study drug or any other procedure related to this research study, you will receive all the care and services required by your state of health.

By agreeing to participate in this research study, you are not waiving any of your rights nor discharging the doctor in charge of the study, the sponsor, or the institution of their civil and professional responsibilities.

HOW IS PRIVACY ENSURED?

During your participation in this study, the doctor in charge of the study and the research team will collect in a study file the information about you needed to meet the scientific objectives of the study. They will only collect information required to meet the scientific goals of the study.

The study file may include information from your medical charts including your identity, such as your name, gender, date of birth, ethnicity, address, past and present health status, lifestyle, and the results of all tests, exams, and procedures that will be performed during this research project.

All study data collected during this research study (including personal information and samples) will remain confidential to the extent provided by law. You will be identified by a code number only. The key to the code linking your name to your study file will be kept by the doctor in charge of this research study.

To ensure your safety, a document indicating your participation in this study such as a copy of the Informed Consent Form is included in your medical chart. The results of certain tests conducted as part of the research and the drug administration forms will also be included in your medical chart. As a result, any person or company to whom you give

access to your medical chart will have access to this information.

The doctor in charge of this research study or a member of the research team will forward your coded data to the sponsor or its representatives. However, the sponsor and any partners outside of Quebec are required to respect confidentiality rules equivalent to those in effect in Quebec and Canada, regardless of the country to which your data may be transferred.

Study data will be stored for at least 15 years following the end of the study by the doctor in charge of this research study and the study sponsor (PharmaInc).

The study data may be published or shared at scientific meetings; however, it will not be possible to identify you.

For monitoring, control, safety, security, and approval of the study drug by regulatory agencies, your study file as well as your medical charts may be examined by a person mandated by Canadian or international regulatory authorities, such as Health Canada, as well as by authorized representatives of the study sponsor, the institution, or the Research Ethics Board. All these individuals and organizations will have access to your personal data, but they adhere to a confidentiality policy.

You have the right to consult your study file in order to verify the information gathered, and to have it corrected if necessary.

However, to protect the scientific integrity of this study, you may have to withdraw from the study if you access certain information before the study ends.

IS YOUR PARTICIPATION VOLUNTARY AND CAN YOU WITHDRAW?

Your participation in this research study is voluntary. Therefore, you may refuse to participate. You may also withdraw at any time, without giving any reasons, by informing the doctor in charge of this research study or a member of the research team. If you decide you do not want to take part in this study, your study doctor and the study team will respect your decision and will not change their attitude towards you.

Your doctor could be one of the investigators in this study. As such, your doctor's interest lies primarily in your well-being and also in the successful pursuit of this study. Therefore, before you sign up for the study and at any time thereafter, you may wish to consult with another doctor who is not part of this study. You are by no means obligated to participate in whatever study is offered to you. Your decision not to participate in the study, or to withdraw from it, will have no impact on the quality of care and services to which you are otherwise entitled, or on your relationship with the teams providing them.

The doctor in charge of this research study, the Research Ethics Board, the funding

agency, or the sponsor may put an end to your participation without your consent. This may happen if it is discovered that you do not meet the study requirements, if new findings or information indicate that participation in this research study is no longer in your best interests, if you do not follow study instructions, if there are administrative reasons to terminate the study or if you become pregnant (if applicable).

If you permanently discontinue the study medication, you will be asked and encouraged to return to the study site for the follow-up phase of the study. The purpose of this follow-up period will not be to convince you to remain in the study, but it will allow you to stop the medication in a safe and controlled manner.

If you withdraw or are withdrawn from the study, no further data or biological samples will be collected. However, the information, blood, urine, the test results, the questionnaires and ECGs already collected for the study will be stored, analyzed and used for safety reasons.

Any new findings acquired during the course of the study that could influence your decision to continue your participation will be shared with you quickly.

You have the right to modulate your withdrawal from the study at any time, by:

- Stopping the study drug (Insuperos),
- Stopping the follow-up visits on site,
- Allowing only medical chart information to be transmitted to the sponsor, or
- Withdrawing from the study completely.

If you stop taking part in the study, or the study ends early, you will stop receiving the study drugs.

RESULTS AFTER THE STUDY

Your study doctor will receive a summary of the study results after the study is completed and all data examined. The study doctor may share these results with you.

About a year after the study is completed, a summary of the results, will be publicly available at www.pharmainc123.com.

The study results will also be made publicly available at <http://www.ClinicalTrials.gov> , and at the European Clinical Trials Database (EudraCT, <https://eudract.ema.europa.eu/>).

These websites will not include information that can identify you.

You can search the websites at any time using the study code ABCD012E3456

POSSIBILITY OF COMMERCIALIZATION

The results of the research derived in part from your participation in the study may lead to the commercialization of Insuperos. However, you will not be entitled to any financial gain thereof.

WHERE CAN I GET MORE INFORMATION?

A description of this clinical trial is available at <http://www.clinicalTrials.com>, in accordance with American and Canadian law. This website will not contain any information that would identify you. It will provide a summary of the research results once ready. You may search the website at any time.

You may ask to receive a copy of the results of this research project; these will only be available after the entire project has been completed.

You will receive a signed copy of this form. You may ask the research team questions at any time.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

In case of emergency, please go directly to the closest emergency room.

If you have any questions or if you have a problem you think might be related to your participation in this research study, or if you would like to withdraw, you may communicate with the doctor in charge of this research study:

CHU Sainte-Justine : Dr. Julie Leclair (514-555-4587, poste 6802)

For any questions regarding your rights as a research participant in this study, or if you have comments or wish to file a complaint, you may communicate with the local service quality and complaints commissioner at:

CHU Sainte-Justine : 514-555-4587, poste 5255

OVERVIEW OF ETHICAL ASPECTS OF THE RESEARCH

The Research Ethics Board of the CHU Sainte-Justine has given ethics approval to this research study and is responsible for monitoring the study at all participating institutions in the health and social services network in Quebec.

CONSENT AND ASSENT FORM

Research Study: A phase III randomized, multicenter, double-blind, placebo-controlled trial evaluating the safety and efficacy of INSUPEROS in children and adolescents with type 1 diabetes.

I have reviewed the Informed Consent Form. Both the research study and the Informed Consent Form were explained to me. My questions were answered, and I was given sufficient time to decide. After reflection, I consent to participate, or that my child will participate in this research study in accordance with the conditions stated above, including the use of all personal data and samples collected.

I authorize the study team to access my medical chart or the medical chart of my child.

In addition, I authorize the researcher or research team to inform the family doctor or treating physician, in writing, that I am/my child is taking part in this research study, and to send them all relevant information.

Name of participant Date (Print)	Assent of minor, capable of understanding the nature of the research (signature) or Verbal assent of minor obtained by: _____
--	--

Name of parent(s) or legal guardian Date (Print)	Signature
--	-----------

Name of participant (18 years +) Date (Print)	Signature
---	-----------

I have explained the research study and the terms of this Informed Consent Form to the research participant, and I answered all questions asked.

Name of the person obtaining consent
Date

Signature

SIGNATURE OF WITNESS

YES **NO**

A witness' signature is required in the following cases:

- Reading disability or inability to read – The witness (impartial) signing below attests to the fact that they read the Informed Consent Form, that the research study was precisely explained to the participant, and that the participant seems to have understood it.
- Foreign language (participant does not understand the language in which the Informed Consent Form was written) – The signatory attests to acting as interpreter for the participant throughout the consent process.

Name of witness
Date

Signature

Additional Information on Data Privacy Following the Application of the *General Data Protection Regulation (GDPR)*

Research Study: A phase III randomized, multicenter, double-blind, placebo-controlled trial evaluating the safety and efficacy of INSUPEROS in children and adolescents with type 1 diabetes.

Sponsor: PharmaInc , 1234 Rue de La Seine, Paris, France, postal code : 70123

Dear Sir/Madam,

The international sponsor of this research study, PharmaInc has a head office in Europe. As such, the sponsor must comply with the *European Union General Data Protection Regulation (GDPR)*. The GDPR gives you additional rights that are not specified in Canadian and Quebec legislation and that therefore do not appear in the Informed Consent Form that you signed for the research study stated above. For more information, see below.

As per the GDPR, you have the following rights to data privacy, in addition to those specified in the Informed Consent Form you signed:

- Should you request corrections to the data collected about you during the project, please note that you have the ***right to restrain*** the processing and use of that data while your request is being evaluated. For example, you may ask that your data not be processed until your request has been reviewed.
- You have the ***right to request a transfer of*** your study data to yourself or to anyone else in any commonly used, and accessible format, such as a computer-readable.
- You have the ***right to file a complaint*** with a European data protection authority, such as :

French Protection of Clinical Research Data (FPCRD) :

Address : 56 Rue Saint-Rustique, Paris, France, postal code : 72165

Email : fpcrd.france@yahoo.com

Phone number : +33357897524

- You have the ***right to request the deletion*** of your study data. These will be deleted if no longer needed or if there is no other legal requirement for their use.

The study data collected from you will be stored for at least 25 years after the end of the study, or longer, if needed for legal requirements.

If you have any questions, please contact the doctor in charge of this study.