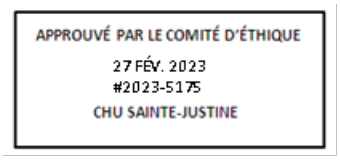
Appendix 2: Simplified fictitious ICF – English version

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



CHU Sainte-Justine
Le centre hospitalier universitaire mère-enfant
Université de Montréal

Faculté de pharmacie
Université de Montréal

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.

CHU Sainte-Justine
Le centre hospitalier universitaire mère-enfant
Université de Montréal

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

INTRODUCTION

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. We encourage you to ask questions. 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 ARE YOU BEING INVITED TO TAKE PART IN THIS STUDY?

The endocrinology department participates in research studies to try to **improve treatments** for children with **type 1 diabetes**. Today, we are inviting you to take part in a research study.

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.

Investigational drug = experimental drug: this means that Health Canada has **not** approved Insuperos for all pediatric patients with type 1 diabetes. However, its use is **authorized** for the purpose of **this study**.

<u>Type 1 Diabetes</u>

- You have a disease called type 1 diabetes.
    - Your pancreas does not produce sufficient insulin to regulate blood sugar levels.

- **Standard** treatment for this disease is subcutaneous **insulin injections**.
- Requires **several injections** every day.
    - An injection with every meal (prandial insulin = short-acting).
    - Supplementary injection before bedtime (basal insulin = long-acting)

Insuperos tablet key-points

- Closely **resembles insulin** (similar mechanism of action).
- Extended-release formulation → active for 4 weeks → taken **once a month.**
- Taken **orally**.
- Could **replace** the daily basal (long-acting) insulin **injection.**
- **Pediatric doses** were established using the data from about 40 children who received Insuperos.

WHAT ARE THE OBJECTIVES OF THE RESEARCH?

1. Evaluating the **efficacy** of Insuperos at controlling your diabetes.
2. Assessing the overall **safety** of Insuperos.

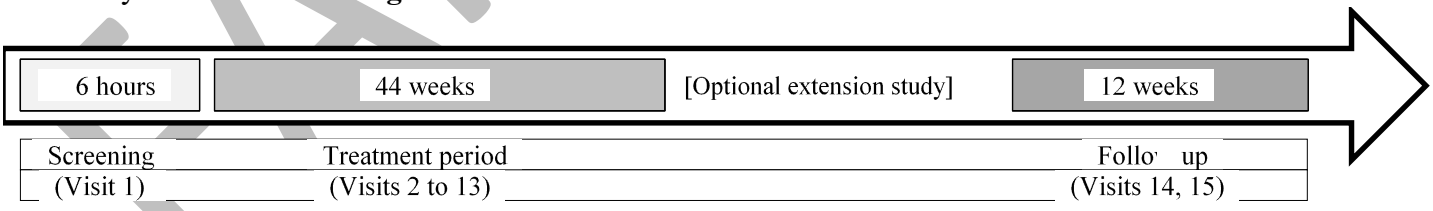
HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

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 ON 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.

This study has **3 different stages**:



You will have **15 visits** to the clinic during the study. All the visits and tests will take place at the CHU Sainte-Justine.

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

Description of the study visits

Stage 1: Screening (Duration: 1 day)

This Screening Visit is necessary to determine if you are **eligible** to **participate** in the study. The Screening Visit will take place **before** receiving the **study drug**. The **baseline assessments** will be done in this stage to determine your health status prior to starting the study drug.

Stage 2: 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.

This study is a **double-blind study**, during which you will be **randomized** to receive either Insuperos or **placebo**.

For a better understanding:

- **Double-blind study**: Neither you nor the study doctor/staff will know what treatment you are receiving nor who is receiving Insuperos or placebo.
- **Randomized**: 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. **Neither** of you will be **aware** of which **treatment** you are **taking**.
- **Placebo**: 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.

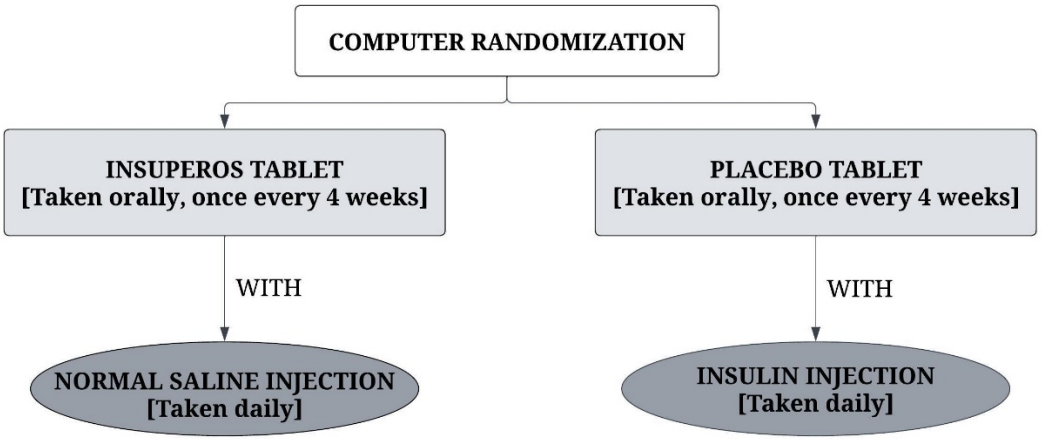
During the treatment period, you **must** keep **using** your prandial (**short-acting**) insulin. The study medication is used in **addition** to the prandial (short-acting) injections, and it does **not** replace them.

In order to maintain the double-blind design of the study, **both** study **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 (**long-acting**) 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, and the study team may adjust the amounts you are injecting throughout the study.

The following figure illustrates the medications that you will take depending on which group you are randomized to:



The quantitiy of the study drug (**dose**) you will receive depends upon your current **weight**, regardless of your age. The Insuperos dose you receive may change if your weight changes, according to the study doctor's evaluation.

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.

Stage 3: 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 l**ong-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.

Unscheduled visits

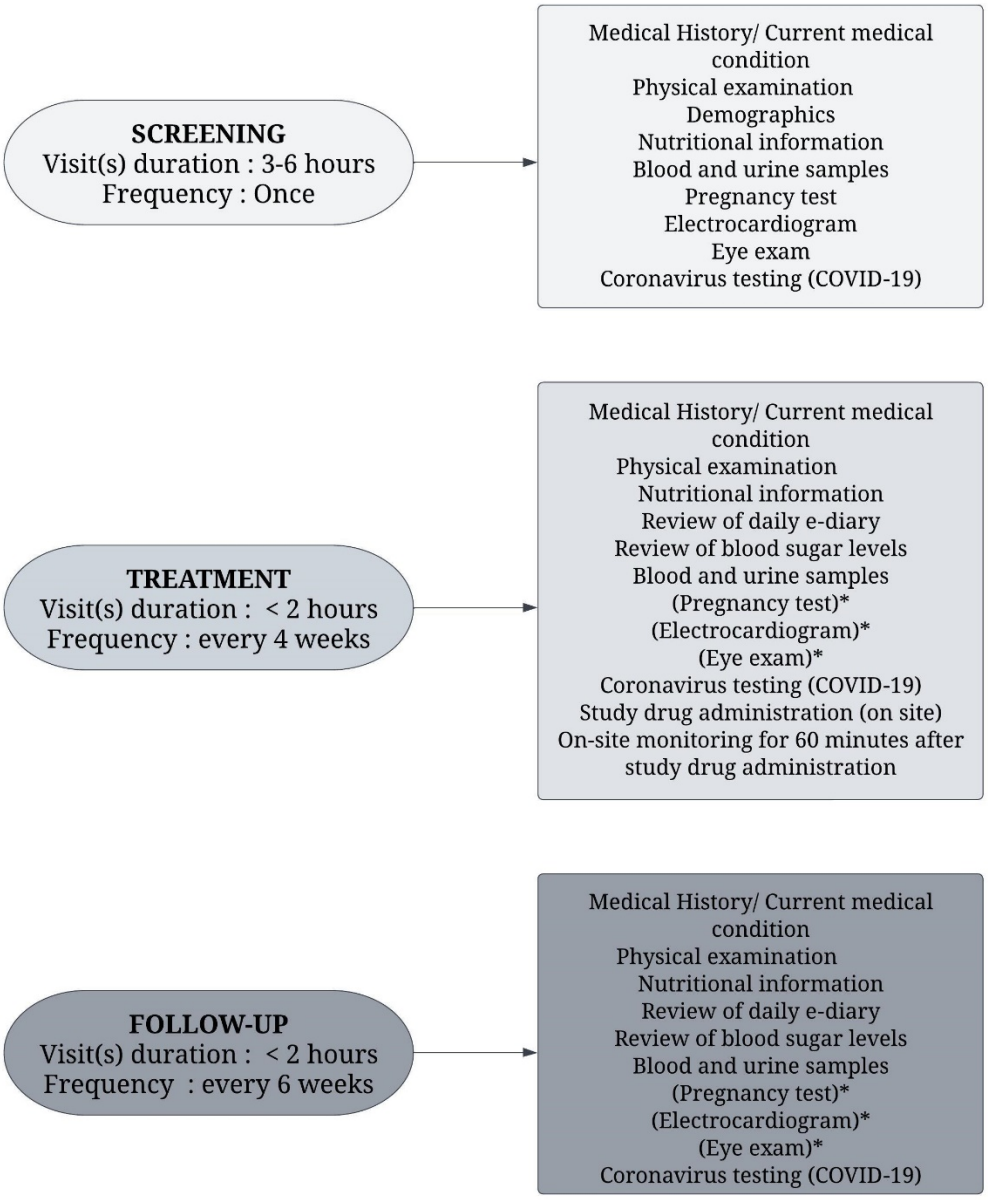
When necessary, unscheduled visits could take place. Some examples include any side effects that need a specific treatment. During these visits, the doctor may ask for any of the tests and procedures described above as well as for additional assessments depending on the reason for this visit. The duration of the visit will depend on the number of tests required.

<u>Tests and procedures</u>

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

Informations collected	
Medical History/ Current medical condition	• The research team will **consult** your **medical record** to obtain information relevant to this research. • You will be asked a **series of questions** regarding your medical history, your current condition as well as your medications (prescription and non-prescription).
Demographic data	• Age, race, nationality and ethnicity.
Nutritional information	• Nutritional habits **questionnaires**.
Daily e-diary	• **Daily** documentation of: any diabetes-related symptom, potential side effects from Insuperos and the impact of the disease/medication on your quality of life.
Tests and procedures	
Physical examination	• Body weight and height, blood pressure, heart rate and body temperature.
Blood sugar level	Continuously measured via a continuous glucose monitoring device: • A small sensor under your skin measures blood glucose levels day/night. You can see your glucose levels anytime. • 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**. The average daily value, the minimal and maximal values, and 2 more 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) • Insulin levels On some days, you will have to **fast** to test your glucose properly. These days will be specified on 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 applicable)	• If you are a female, your fertility (ability to become pregnant) will be assessed and urine and blood pregnancy tests will be done, if appropriate.
Electrocardiogram	• Leads (like stickers) will be placed on your skin to record the electrical activity of your heart.
Eye exam	• A series of tests to evaluate your vision and check for eye diseases will be done by an ophthalmologist.
Coronavirus (COVID-19) testing	• A swab of the area at the back of your nose will be taken.

The figure below details the tests and procedures that will take place at the different visits during the study:



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

FOR HOW LONG WILL YOU PARTICIPATE IN THIS STUDY?

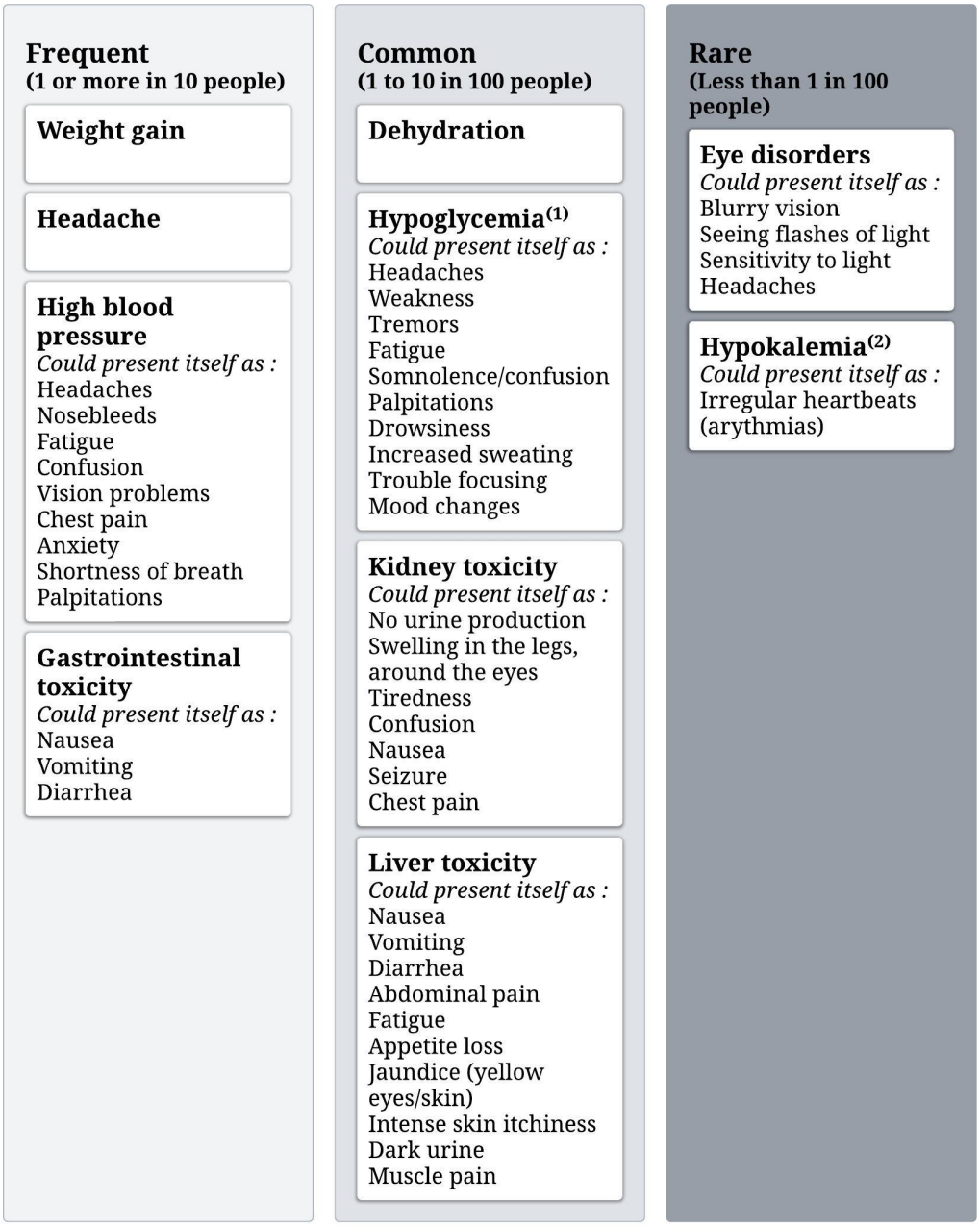
The **total** duration of your participation in the study will be **56 weeks**.

WHAT ARE THE RISKS?

You may experience side effects from the drugs or procedures used in this study. You should talk to your study doctor about **any** side effect that you have while taking part in the study.

Risks associated with Insuperos

Here are the potential side effects that were reported in adult clinical trials. Insuperos may cause all, some, or none of the side effects listed below. These side effects can be mild but could also be serious, or even life-threatening. There **may** be side effects that are **not known** at this time.



(1) Hypoglycemia: lowering of blood glucose <4 mmol/L. The severity of symptoms can vary according to bloodsugar levels. Lower blood sugar = more severe symptoms.

(2) Hypokalemia : lowering of potassium levels in the blood

Diabetic acidosis and coma

This is **not** a side-effect of the medication, but it remains **a risk** associated with this treatment. Some individuals may respond less than others to Insuperos. Therefore, in some rare cases, the treatment with Insuperos is not efficient enough to control your type-1 diabetes (blood sugar levels).

Cause: high blood glucose levels (>20 mmol/L) for a long period of time

Symptoms: fruity breath, difficulty breathing, headache, nausea, vomiting.

Allergic reaction (drug hypersensitivity)

There is a risk that Insuperos, like any other medication, could provoke an allergic reaction in people who receive it. This allergic reaction could range from mild to life-threatening. If you suspect that you are having an allergic reaction, **call 911** or go to the **closest emergency room**.

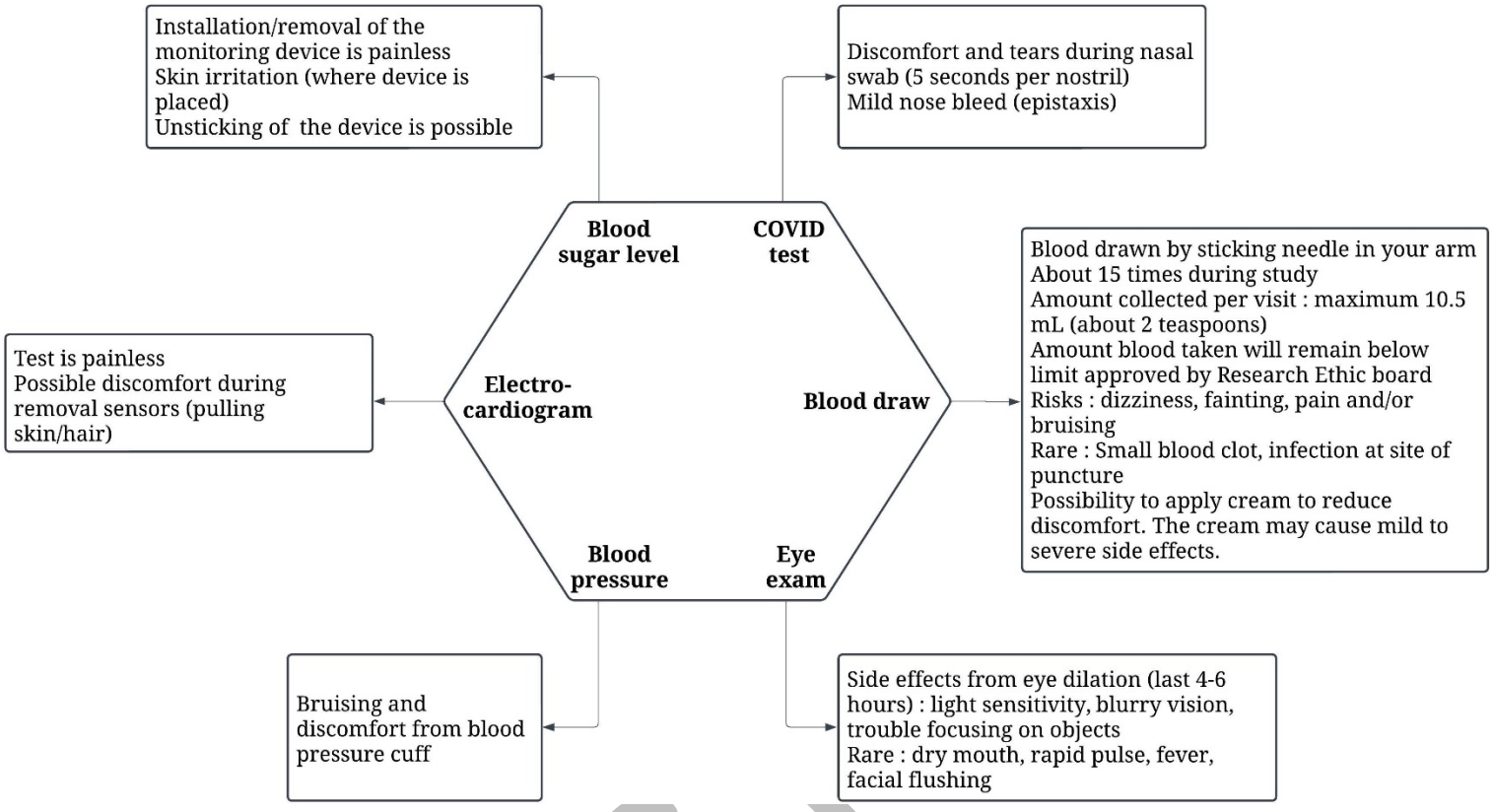
Symptoms of a **life-threatening** allergic reaction
Difficulty breathing, rapid heartbeat, tongue swelling, nausea, fainting,hives, fever, and dizziness

In order to **minimize** and **manage** the allergy **risks** and inconveniences the doses will be **administered under supervision** of the study research team at the 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 figure identifies the possible risks associated with the procedures and tests done in the study:



Reproductive Risks

Studies in pregnant animals have shown that the medications you are required to take in this study can **harm** an **unborn** or **nursing baby**. You should **not conceive** a baby **during** your **participation** in this research project, but also for **3 months after** your participations ends. If this does happen, you must **inform** the **study doctor** immediately.

If you or your partner are old enough to get pregnant, you should use a **birth control method** or **abstain** from having sex during the time you are **participating** in this research study but also **3 months after** your participation ends. Talk to your doctor about which birth control method would be best for you.

Women should **not** breastfeed a baby while **participating** in the research but also for **3 months after** their participation ends.

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 hope that this study will help you personally by allowing a simplification of your type 1 diabetes treatment, but we can't guarantee that it will. You will receive close attention and monitoring of your type 1 diabetes from the study staff during this study. We hope that the study results will provide knowledge allowing to benefit other patients with this disease 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. Instead of participating in this research project, you could receive **standard** long-acting insulin or an insulin pump. If available, other research projects may be possible. Please talk to your doctor if you have any questions concerning alternative treatments.

PARTICIPANTS RESPONSABILITIES

By signing this consent form, you agree to commit to the following **responsibilities**.

- Providing **truthful information** about :
    - Any changes in your current medical condition or in your medication (prescription, over the counter or herbal supplements)

- **Compliance** to the study doctor's **instructions**:
    - Adherence to the study visits, procedures and assessments schedule (as planned in the protocol).
    - Respect of authorized and non-authorized medication during the study

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?

<u>Data collection</u>

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.

The study file may include the following **information** from your **medical charts**:

- Your identity (name, gender, date of birth, ethnicity, address)
- Past and present health status
- Lifestyle
- Results of all tests, exams, and procedures that will be performed during this research project.

To ensure your **safety**, the following elements will be **included** in your **medical chart**:

- A document indicating your **participation** in this **study** such (a copy of the Informed Consent Form)
- The **results** of certain **tests** conducted as part of the research and the **drug administration forms**

Any **person** or **company** to whom you **give access** to your **medical chart** will have **access** to this **information**.

Data management

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 doctor in charge of this research study will keep the key to the code linking your name to your study file.

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?

Voluntary participation

Your participation in this research study is **voluntary**. Therefore, you may **refuse** to participate. 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.

Your doctor could be one of the investigators in this study. As such, your doctor's interest lies primarily in your well-being and 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.

Withdrawal

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

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 **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**.

The doctor in charge of this research study, the Research Ethics Board or the funding agency **may put an end** to your **participation without** your **consent** 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
- If you become pregnant (if applicable).

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.

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

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.

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, extension 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:

CHU Sainte-Justine: 514-555-4587, extension 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 (Print)	Assent of minor, capable of understanding the nature of the research (signature) or Verbal assent of minor obtained by: _____	Date
Name of parent(s) or legal guardian (Print)	Signature	Date
Name of participant (18 years +) (Print)	Signature	Date

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	Signature	Date

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	Signature	Date

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.