Information for legal guardians of children regarding follow-up in the PI4 study

We wish to ask you whether you would like your child to take part in the follow-up to the PI4 clinical trial. In this document, you will find information about the follow-up and what it means to take part. You will also find information here about what will be expected of your child if you choose for your child to take part, and about any risks and benefits of the study.

# What is the aim of the study, and why do you wish for my/our child to take part?

The aim of this study is to follow up how children develop after their mothers have taken part in PI4 and been treated with metformin or a placebo during their pregnancy. The main aim of PI4 is to see whether treatment with metformin can prolong pregnancy and therefore reduce the degree of premature birth in children. You have come to our attention as the mother of the child has taken part in PI4.

This study is being run at the *Research Hospital* in collaboration with Region Västra Götaland. The entity responsible for research in the trial is Region Västra Götaland. ‘Entity responsible for research’ means the organisation responsible for the trial. The Sponsor of the trial is Region Västra Götaland.

This clinical trial has been reviewed and approved by the Swedish Medical Products Agency (Läkemedelsverket) and the Swedish Ethical Review Authority (Etikprövningsmyndigheten).

# How is the study conducted?

If you agree to your child taking part in the study, any normal treatment received by your child will not be affected. This is what will happen if your child takes part in the study:

## After birth

The samples from the umbilical cord and placenta taken at the time of the birth may be analysed for biomarkers relating to pre-eclampsia and metformin, in order to understand the effect of metformin. After the birth, information will be obtained about your child, such as weight, height, any illnesses and duration of hospital stay.

## Follow-up visit two to three months after the birth

After two to three months, there will be a follow-up where you are asked questions about your child’s health, while information about the duration of your child’s stay in hospital and birth weight will be collected.  
 **Follow-up visit after 2 years**

After two years, there will be a follow-up visit where you will answer questions about the child's development. The child´s weight and height will also be measured.   
  
**Follow-up in registers**

To evaluate whether treatment with metformin provides health economic benefits for society,

the National Prescribed Drug Register, the National Medical Birth register, the Swedish Neonatal Quality Register, the National Cause of Death Register, local hospital registers, the National Patient Register, the Swedish Social Insurance Agency´s register MiDas and LISA will be used up to two years after the child is born.

# Possible consequences, risks and inconveniences of taking part in the study

The questions asked are harmless and have previously been validated in children of the same age. You are entitled to cancel your child’s participation in the study at any time.

# What will happen with your child’s details?

In this clinical trial, information about your child will be collected and recorded. This information will be obtained from questionnaires, interviews and your child’s medical records. All

information is recorded in a database using a data processing system owned by Region Västra Götaland. This information may also be linked to Swedish registers from birth to school age. Data will be stored using a unique study code. The final database will be stored on a secure data storage platform. Personal details such as the personal ID number and address linked to the study code will be stored separately from the database. Information about your child will be saved for at least 25 years.

## What will happen with your child’s samples?

The samples taken in connection with the trial will be stored in a biobank in accordance with the Swedish Biobank Act *(2023:38)*, which regulates the way in which samples may be stored and used. During the study, the samples that you provide will be stored in biobanks at the participating hospitals. A Swedish biobank will be responsible for the samples. On completion of the study, any samples may be sent to the responsible biobank for final storage. The sample is stored in coded (pseudonymised) form, which means that the sample cannot be traced to your child as a person. Each sample has a unique code to avoid confusion. The sample and associated identification list (key code) will be stored at Biobank Väst, separately from each other and protected against unauthorised access. The key code will be stored by the local biobank and/or local investigator and may be shared with the principal investigator and responsible biobank. Your child’s blood sample may be sent for analysis to our laboratory or to our partner’s laboratory, both within and outside the EU/EEA. Biomarkers and genes may be analysed. Following any analysis other than by the entity responsible for the study, the samples will either be returned to the entity responsible for the study or destroyed. The samples will be saved for a maximum of 25 years.

# Data collection

During the study, information will be collected about age, sex, health (e.g. current and previous illnesses), as well as the results of any examinations. Data collected will be stored and processed in a database. An analysis of your child’s data will be conducted by the principal investigators who form part of the researcher group for the study, or by other researchers following an approved ethical review. However, this personal data will be coded at the time of transfer and the other researchers will not have access to the key code.

Information may also be obtained from Swedish registers. The registers in question, in addition to the hospital’s administrative register, are: the Patient Register, which holds data on diagnoses and resource use in specialised care; the Medical Birth Register, which holds data on pregnancy and childbirth; the Neonatal Care Register, which holds data on specialised care for newborn children; the Prescribed Drug Register, which holds data on prescribed medication and related costs; and Statistics Sweden, which holds data on deaths and emigration. The information will only be collected until the follow-up at 2–3 months.

In order to perform an economic evaluation and to monitor your child’s health and development, surveys and register data for the period from recruitment to the 2–3 month visit will be used, such as the use of different types of medication and related costs from the registers mentioned above.

Data collection is done for research purposes. The legal basis for processing personal data is that research is considered to be a matter of public interest. Your child’s details are protected by confidentiality and there is no unauthorised access to the register. Your/your child’s answers and results will be processed in such a way as to prevent unauthorised access. During data processing, it will not be possible to identify individual participants when the results of the trial are reported or published.

# My rights

Your answers and your child’s results will be processed in such a way as to prevent unauthorised access.The Sahlgrenska University Hospital is responsible for the processing of your personal data. The Data Protection Officer is the person responsible for making sure that your child’s personal data is processed in a legal and correct manner. According to the EU General Data Protection Regulation (GDPR), you have the right to access the data about your child that is processed in the study free of charge, and, where appropriate, to have your child’s data corrected. You can also request the erasure of any data held about your child, and for restrictions to be placed on the processing of your child’s personal data. If necessary, the Data Protection Officer can assist you with this. You can contact the Data Protection Officer at the following address: Sahlgrenska University Hospital, Data Protection Officer, SE-413 45 Gothenburg.Telephone:+46 (0)31-343 27 15, [sahlgrenska.universitetssjukhuset.dso@vgregion.se](mailto:sahlgrenska.universitetssjukhuset.dso@vgregion.se). If you are unhappy with how your child’s personal data is being processed, you have the right to file a complaint with the Swedish Authority for Privacy Protection, which is the supervisory authority. Your child’s personal data will only be used for the purposes given above. It may only be used for other purposes if you/your child has given new consent and/or the Swedish Medical Products Agency/other medicines authority in the EU and the Swedish Ethical Review Authority have issued a new approval.

# Quality control and archiving

In order to safeguard quality and to check that the study is being conducted correctly, it may be appropriate for someone appointed by the sponsor/entity responsible for research or other person in authority to compare the data collected with your child’s medical records.

The quality reviewer must sign a confidentiality agreement in order to have access to your child’s medical records. By signing the consent form, you are giving your permission for this access to your child’s medical records. Data will be saved for at least 25 years after completion of the study.

# How will I receive information about the results of the study?

The results will be published in a shared EU-wide database of clinical drug trials (CTIS) and scientific journals, and will be presented at national scientific meetings. Only statistics at group level will be presented, and it will not be possible to identify any individual person. Published data will also be shared on the research group’s website, [www.preeclampsiaresearch.com](http://www.preeclampsiaresearch.com/)

# Insurance and compensation

As elsewhere in the healthcare system, your child will be covered by the Swedish Patient Injury Insurance Scheme and the Swedish Pharmaceutical Insurance Scheme. Taking part in the trial will not entail any additional cost to you. Reasonable travel costs will be paid on production of a receipt. A symbolic gift will be given to your child at the follow-up visit at 2–3 months.

# Participation is voluntary

It is your choice whether you wish for your child to take part in this study, and you may cancel your child’s participation at any time without giving a reason. Nor will this affect your child’s future care or treatment. If you choose to cancel your child’s participation, any data already collected will still be used in the study. No further data will be collected, however*.* You may request the destruction of your child’s samples at any time.

Your child’s samples may only be used in the manner for which you have given your consent. All future, as yet unspecified, research will entail a new ethical review, and the Swedish Ethical Review Authority will then decide whether or not you need to be contacted again with a new request for consent. If you agree to us storing and using your child’s samples for future purposes, you will need to give specific consent for this.

If you wish to cancel your child’s participation you must contact the people in charge of the study (see below).

# People in charge of the study

## Principal investigator:

Name: Telephone number: E-mail address: **Research nurse:**

Name:

Telephone number:

E-mail address:

# Consent to take part in this study

I/we have been given verbal and written information about the trial and had the opportunity to ask questions. I/we may keep a copy of the written information.

I/we confirm that:

* I/we consent to my/our child taking part in the study and know that participation is completely voluntary.
* I/we have studied how my/our child’s personal data will be processed and how any data collected about my/our child will be stored and processed.
* I am/we are aware that I/we may withdraw my/our consent and end my/our child’s participation at any time and without giving a reason.
* I/we consent to my/our child’s samples being stored in a biobank in the manner described in the information to research participants.

## Consent to future research

I have been informed that the samples that my/our child provides may be of relevance to future research that has not been described in the information provided to me as the legal guardian of the research participant. I have also been informed that, if my/our child’s samples are to be used in future research, then the Swedish Ethical Review Authority must perform a review of the new project and, as part of its review, decide whether or not we/our child needs to be asked again.

I consent to my/our child’s samples being saved for future research.

I/we hereby consent to our child taking part in the study:

Signature (legal guardian 1) Print Date

# If there are two legal guardians:

Signature (legal guardian 2) Print Date

**Signature of clinic**

I have provided information about the study, verified that the legal guardian(s) has/have understood the information and received answers to their questions regarding the trial.

|  |  |  |
| --- | --- | --- |
| Signature of doctor responsible for inclusion | Print name | Date |

***A copy of this signed information should be given to the legal guardian(s).***