Date of document update: 10th of Dec 2020

Unique study approval ID (Sweden): 2019-05490

Official title: Improving care for children with congenital heart disease by cardiovascular biomarker profiling and advanced non-invasive cardiac imaging techniques.

Consent form in English language
(translated from the original version in Swedish language):

Information for guardians of children / young people <18 years of age on participation in a scientific study

We want to ask you as a guardian / parent about your child's participation in a research study. The purpose of this study is to improve the early diagnosis of children with congenital heart defects and compare these children to those without heart disease. We aim to better understand what drives heart disease inside the body, partly at the cellular level and how congenital heart defects affect heart function. Below we provide more information about the project and what it means to participate.

The research study is conducted at Ryhov University Teaching Hospital in the county of Jönköping in collaboration with the Child Heart Center at Skåne's University Hospital in Lund, the national screening laboratory for newborns at Karolinska University Hospital in Stockholm, the Children's Heart Service at Linköping University Hospital and the research department at Perkin Elmer in Turku, Finland. The main providers responsible for the study are Region Jönköping County and Region Skåne. The project is called in English: "Improving the care of children with congenital heart disease through cardiovascular biomarker profiling and advanced non-invasive cardiac imaging techniques." The study will help us find new reference values for substances in the blood and in some cases also in the body's tissue from the heart or vessel (so-called biomarkers). The purpose is to examine children and adolescents with congenital heart disease and compare these with those who do not have

congenital heart disease. The project will also help us establish new ultrasound examinations of the heart and circulatory conditions that could be used during follow-up and treatment of children with congenital heart defects such as atrial or ventricular septal defect (so-called "holes in the heart").

How is the study conducted?

All participating children will undergo pain-free cardiac examinations that involve a clinical assessment as well as ECG analysis of the heart rhythm and an ultrasound of the heart. For children where there is a clinical suspicion of heart rhythm disorders, a so-called long-term ECG may be ordered, which is painless and means that the child carries a small ECG tape recorder. We want to compare two different long-term ECG analysis methods in that case at the same time (approximately 24 hours and approximately 72 hours). In addition, we try to detect changes in circulation from birth with analysis of previously saved dried blood samples taken from your child after birth in connection with the national screening examination (so-called Guthrie cards). Part of your child's Guthrie card test is taken from the Karolinska University Laboratory for analysis of biomarkers in connection with the study (approximately 30 microliters).

We will take a saliva sample from the mouth and a regular blood sample (approximately 2 milliliters) in connection with your child's visit to the hospital. Blood sampling is performed after local anesthesia of the skin once for healthy children and approximately once a year during the research period for children with heart disease over a maximum of 3 years. All examinations are done at your visit to the children’s heart clinic.

Children and young people to be treated at the children’s heart center in Lund

If your child is to be treated at a child heart center in Lund, you can also take the saliva and blood samples in Lund. In case your child has already undergone a heart operation or during the course of the project undergoes a heart operation, we ask you that we can save a small tissue sample from the child's heart or blood vessels for analysis of biomarkers (approximately 5 grams). In that case, part of an already saved tissue sample is taken from the respective research department in Sweden (biobank) or we ask that a small tissue sample be preserved in connection with the heart operation in Lund for analysis in

connection with the study.

In the case your child needs a heart surgery treatment or a cardiac catheter based intervention at the children's heart center in Lund during the course of the study, we will offer your child two additional complementary heart examinations with magnetic resonance imaging (MRI). This is done before and about 6-12 months after the procedure. MRI involves a thorough imaging and functional examination of your child's heart that can be helpful when establishing new ultrasound examinations of the heart. Your child needs to lie still during the MRI examination time (approximately 45 minutes) and unfortunately a crackling sound is heard from the MRI camera. You and your child get headphones and can bring an audiobook or a favorite music tape or movie that is easy to relax to during the examination. Smaller children or more anxious children may need some sedative medication. In these cases, a doctor will be available throughout the examination. For small infants it is sometimes enough to feed them and wrap them in a special pillow we can provide for the examination. During the MRI examination, older children have the opportunity to talk to the staff through a microphone if they want help or have questions. It is good if you as a guardian / guardian are available in the waiting room during the MRI examination period. You are welcome to ask us additional questions about this.

What happens to the child's data and test materials?

To carry out the study, information about your child will be collected and registered. Patient information that includes Swedish national personal numbers and clinical data is stored according to research guidelines in a special electronic database. Only persons responsible for the study will have access to this. All data results will be processed so that unauthorized persons cannot identify individual participants. The study is conducted in line with the EU Data Protection Regulation (GDPR). Personal information is retrieved from the child's medical record in the Jönköping County Region or the Child Heart Center in Lund. The institution responsible for handling of personal data according to the Personal Data Act is Region Jönköping County and Region Skåne, respectively. If you have questions about this, you can contact the Personal Data Representative at the University Hospital, 221 85 Lund. The samples taken and to be analyzed in the study are stored anonymised and coded in a so-

called biobank for a maximum of fifteen years and stored in a way so that only participating researchers can identify the samples. Samples are stored so that quality, traceability and safety are met. The name of the biobank is Laboratory Medicine's combination bank (Reg. No. 868). The overseeing body for the biobank is Region Jönköping County. Some of your child's so-called Guthrie card tests are retrieved from the screening laboratory's biobank in Stockholm and more information is available on their website (link: https://www.karolinska.se/for-vardgivare/kliniker-och-enheter-a-o/kliniker-och-enheter-a-o/funktion-karolinska-universitetslaboratoriet/centrum-for-medfodda-metabola-sjukdomar/pku-biobank/). If you agree to your child participating in the study, you have the right to withdraw at any later point in time. The samples and personal data will then be discarded or de-identified and deleted. The samples will only be used in the manner that you have given consent to and researchers have the right to submit complaints to the Data Inspector. In order to be able to track samples in the event of a changed consent, certain information about saved samples (biobank data) may be stored in the Swedish Biobank Register. More general information about the biobank in the Jönköping County region is available online via the 1177 care guide online (link: www.1177.se/Jonkopings-lan/Regler-och-rattigheter/Biobankslagen/). If there is a need for additional future research that is not yet planned, the Ethics Review Board will decide whether you should be consulted again. All research results will only be published without identifiable personal data at future scientific meetings and journals.

Voluntary participation

Participation is completely voluntary and you can choose to cancel participation at any time. If you choose not to participate or cancel your participation, you do not need to state why, nor will it affect your child's care or treatment. If you regret your participation and want to make changes to it, you should contact the person responsible for the study (see below). For further information, you can also contact Elin Friberg, research nurse at the children’s heart center in Lund (tel. 046 178472) or Petru Liuba, associate professor at the childrern’s heart center in Lund (tel. 046 178267).

Responsible for the study

Henning Clausen; leading paediatric cardiologist, the children's heart service in Jönköping
e-mail: henning.clausen@rjl.se, tel: 010 242 22 02

Consent to participate in the study

I have received verbal and written information about the study and have also had the opportunity to ask questions. I may keep the written information.

☐ I agree that my child participates in the study: "Improving care for children with congenital heart disease by cardiovascular biomarker profiling and advanced non-invasive cardiac imaging techniques."

☐ I agree that information about my child is processed in the manner described in the information about the study.

☐ I agree that my child's samples are stored in a biobank in the manner described in the information about the study.

☐ I agree that part of my child's Guthrie card test (approx. 30 µl) that has been saved in a biobank at Karolinska University Hospital is handed out and used in the manner described in the information about this study.

☐ I agree that part of my child's cardiovascular tissue (approx. 5 grams) should be taken in connection with the heart operation in Lund and should be saved in a Swedish biobank. In the case my child's cardiovascular tissue is already stored in a Swedish biobank, some should be handed out (approx. 5 grams). The samples should be used as described in the information on this study.

Child's full name & Swedish national personal number:

_____

Guardian / parent:

1. Signature & print your full name

_____

2. Signature & print your full name

_____

Date: _____