NOTICE TO GUARDIANS OF THE CHILD TO BE STUDIED

Dear Parents,

We kindly ask you to read this notice and consider your child's participation in the FINT1DAS study, which aims to identify children who are developing type 1 diabetes.

Study name: Finnish Type 1 Diabetes Autoantibody Screening (FINT1DAS)

Information about type 1 diabetes In type 1 diabetes, the insulin production of the pancreas gradually declines and ends. The typical symptoms of diabetes, such as increased thirst, large amounts of urine, weight loss, and fatigue, are caused by this deficiency of the insulin hormone from the pancreas. Insulin replacement therapy is initiated for the patient, which alleviates the symptoms. The treatment also requires careful blood sugar monitoring and adjusting physical activity and meals to insulin doses.

How does type 1 diabetes develop? The exact cause of type 1 diabetes is unknown, but it is known that before symptoms appear, autoantibodies targeting the insulin-producing cells of the pancreas appear in the bloodstream. These autoantibodies can be measured from a blood sample and reflect cell damage in the pancreas even before diabetes symptoms appear. Autoantibodies typically develop in very young children, and the appearance of autoantibodies strongly predict the progression of the disease towards the need for insulin therapy. Thus, the development of type 1 diabetes can be identified early, before the onset of diabetes symptoms, by measuring autoantibodies related to type 1 diabetes from a blood sample. Early diagnosis can prevent severe metabolic disorder, diabetic ketoacidosis, which develops if the diagnosis is delayed.

What is the goal of the FINT1DAS study? The goal of the FINT1DAS study is to identify children aged 2 and 6 years, representing the entire population, who are developing type 1 diabetes. Identification is based on measuring autoantibodies related to the development of type 1 diabetes from a blood sample. The aim is to determine the proportion of all 2- and 6-year-old children who have autoantibodies related to the development of type 1 diabetes and find out the proportion of families participating in the screening from all invited families. If a child is found to have autoantibodies related to the development of type 1 diabetes, they will be invited to the FINT1DAS follow-up study, for which separate consent will be requested, and which aims to monitor the child's glucose metabolism and provide guidance to families. The goal of the FINT1DAS project is also to report to the Ministry of Social Affairs and Health on the progress and results of the FINT1DAS study with a view to future nationwide autoantibody screening for Finnish children.

Who can participate in the FINT1DAS study? All children living in Oulu or Turku who turn 2 or 6 years old in 2025-2026 and who have not been diagnosed with type 1 diabetes can participate in the study. A hereditary predisposition to the disease is not a prerequisite for participation in the study.

Autoantibodies measured in the FINT1DAS study As type 1 diabetes develops, white blood cells produce so-called autoantibodies that target the body's own structures, in this case, the insulin-producing cells of the pancreas. Four different autoantibodies are analysed from the child's blood sample:

- IAA (Insulin Auto-Antibodies)
- GADA (Glutamic Acid Decarboxylase Antibodies)
- IA-2A (Islet Antigen 2 Antibodies)
- ZnT8A (Zinc Transporter 8 Antibodies)

What do we know about the significance of autoantibodies? The presence of one type of autoantibody is associated with an increased risk of diabetes. If the same single autoantibody is present in repeated measurements, the risk of developing type 1 diabetes within 10 years is about 15%. If two or more types of autoantibodies are repeatedly detected in the child's sample, the child's risk of developing the disease is significantly increased – about 70% will develop type 1 diabetes within 10 years. If autoantibodies are not repeatedly detected, the risk of developing the disease is similar to the average population risk. The general risk of developing type 1 diabetes in Finnish children is 0.9% by the age of 15. Since autoantibodies are known to develop most often before school age, the risk of developing the disease is significantly lower than 0.9% if no autoantibodies are detected by the age of 6. If autoantibodies related to the development of type 1 diabetes are found in your child's sample, he/she may also have the opportunity to participate in a treatment study aimed at preventing the development of diabetes, which will be informed separately and for which separate consent will be requested.

Course of the FINT1DAS study Participation in the study requires written consent from the guardians, which is included with this notice in two copies that you can bring to the sample collection. The consent form also asks for information about the child's family members and whether they have type 1 diabetes. We want to find out whether families with type 1 diabetes participate in the FINT1DAS screening as often as other families. This is important because the project aims to provide information about the prevalence of autoantibody positivity in the entire child population. Background information on the presence of type 1 diabetes in the child's father, mother, or full siblings is important because type 1 diabetes in the father and siblings is associated with a higher risk of the child developing the disease and a faster disease progression than type 1 diabetes in the mother. A blood sample will be taken from the child's arm at the FINT1DAS research center, where you can book a suitable time at Vello booking system (https:/pro.vello.fi/fint1das) or by calling our research center's phone number (Turku, tel. 050 433 5853 and Oulu, tel. 050 408 7109). If you prefer, the sample can also be taken at another laboratory in your welfare area. In this case, we ask you to first call our research center, after which you will receive a return envelope for sending the consent form. Once we have received the consent, we will send you the necessary laboratory referral. The sample should ideally be taken no earlier than 3 months before or no later than 3 months after the child turns 2 years or 6 years old.

The blood sample is used to measure the four autoantibodies related to the development of type 1 diabetes (IAA, GADA, IA-2A, and ZnT8A). All families are informed by letter about the screening result and given additional information about type 1 diabetes. Children whose samples show autoantibodies are called for a new sample collection to confirm the result, and the family is informed of the possibility to participate in follow-up at the FINT1DAS research center, where the child's glucose metabolism is monitored in addition to autoantibodies. For this, we request new written consent. During follow-up visits, the child's results and their significance are discussed, and you will receive more information about type 1 diabetes and its early detection.

Part of the blood sample taken from the child is stored at the research center and may be used in the future to study other factors influencing the development of type 1 diabetes, such as microbes, environmental chemicals, and dietary factors. In possible future studies, the data and samples collected from your child may need to be used without identifiable information in international research collaborations outside the EU area in projects developing more efficient autoantibody measurement methods or diabetes research requiring the special expertise of a foreign laboratory. You will be informed in more detail about any future studies, and separate consent will be requested for them later.

Potential benefits and risks of participating in the study The study can help detect the potential development of diabetes at a very early stage, which is crucial to prevent ketoacidosis (severe metabolic disorder of the body). If autoantibodies are detected in the child's screening sample, we will inform the family and invite the child to the FINT1DAS follow-up, where a new blood sample will confirm the presence of autoantibodies and regular monitoring of glucose metabolism will begin. During follow-up visits, the family will receive up-to-date information on the child's glucose metabolism results, allowing early identification of diabetes requiring insulin therapy, thus avoiding intensive care for ketoacidosis, and starting insulin therapy usually with small doses according to individual needs. Taking a blood sample may cause temporary needle pain, which can be alleviated with numbing cream. Sometimes a bruise may remain from the blood sampling. If autoantibodies are detected in the child's screening sample, it may cause concern about the increased risk of developing type 1 diabetes, which we aim to alleviate through discussions with the family. All participants in the study are covered by the hospital's patient insurance.

Voluntary participation Participation in the study is voluntary. You can withdraw from the study at any time without giving a specific reason. If your child withdraws from the study, the data and samples collected up to the point of withdrawal can be used as part of the study material. If you withdraw your consent, the data collected up to that point can still be used in research, but the analysis of the samples will no longer be possible. Participation in the study, refusal to participate, or withdrawal from the study will not affect the care your child needs now or in the future.

Study costs and funding Participation in the FINT1DAS study is free of charge for you. You will not be paid for participating in the study. The study is funded by grants from, among others, Sanofi and the university hospitals of Oulu and Turku.

Confidentiality and data protection In the study, the identities of the child and guardians are known only to the local research staff, all of whom are bound by confidentiality. All collected data and samples are handled in a coded manner so that individual people cannot be identified. Only the necessary personal data for the purpose of the study are stored in the local research register, and no identifying personal data is disclosed outside the center. The collected samples are stored coded at the Oulu research center, where autoantibody analyses are performed. The combined research register stores the research data collected from the child only in coded form, in a secure environment on the University of Oulu server. Research data or samples are handled with potential research collaborators only in coded form, without personal identifiers. The FINT1DAS study's data protection statement can be read on the study's website dipp.fi and is also available at the research centers.

Study implementers The FINT1DAS study is conducted at two research centers, in Turku and Oulu. The principal investigator and person responsible for the study is Professor Riitta Veijola at Oulu University Hospital and the University of Oulu. She is a member of Sanofi's scientific advisory board. In Turku, the study is led by Professor Jorma Toppari at Turku University Hospital and the University of Turku. He is a member of Diamyd Medical's data and safety monitoring board in the DIAGNODE clinical trial. The mentioned university hospitals also act as joint controllers of the research register. The FINT1DAS study has received a favorable opinion from the Regional Medical Research Ethics Committee of The Wellbeing Services County of North Ostrobothnia. Research permission for the FINT1DAS study has been granted from both university hospitals. We are happy to provide more information personally.

On behalf of the research team,
Riitta Veijola, Professor, Chief Physician, University of Oulu and Oulu University Hospital Children's Clinic
Jorma Toppari, Professor, Chief Physician, University of Turku and Turku University Hospital Children's Clinic

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CONSENT TO PARTICIPATE IN THE STUDY *(This consent form remains with the family)*

Finnish Type 1 Diabetes Autoantibody Screening (FINT1DAS)

I/We have read the attached notice regarding the diabetes study. I/We consent to the testing of our child's blood sample for autoantibodies related to type 1 diabetes. We will be informed of the results and any further actions by phone or letter approximately two months after the sample is taken. Part of the blood sample will be stored for research on other factors influencing the development of diabetes.
We give permission for the collection of necessary information about our child for the research database. Information, such as a possible diagnosis of type 1 diabetes, may be requested from the healthcare facilities where our child's patient records are kept or from health registers such as those of KELA and THL. For this purpose, the doctor may record our child's personal identification number and use it to obtain information. We have the right to know from where information about our child has been obtained. The FINT1DAS research staff may contact us even after the follow-up has ended.

Please enter the child's details:

_____

Child's first name Last name Personal identification number (ddmmyy-id)

I/We consent to our child's participation in the screening phase of the FINT1DAS study.
Check your preferred option:

YES ☐

NO ☐

_____

Date Mother's/Guardian's signature and printed name

Mother's address: _____ Mother's postal code and city: _____

Mother's phone number: _____ Mother's email address: _____

_____

Date Father's/Guardian's signature and printed name

Father's address: _____ Father's postal code and city: _____

Father's phone number: _____ Father's email address: _____

We hope that both guardians will sign the consent, but one signature is sufficient.

_____

Date Signature and printed name of the person receiving the consent

This signed consent form and notice remain with the family. The other signed consent form and inquiry remain with the research group.