SUBJECT INFORMATION and CONSENT FORM

The International Pyridoxine-Dependent Epilepsy Registry

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Invitation

We are inviting you to participate in a research project called "The International Pyridoxine-Dependent Epilepsy Registry". A registry is a way to collect, store and analyze similar medical information from a group of individuals with the same or similar condition. All information collected is de-identified prior to use in order to protect patient privacy and confidentiality. This a multi-centre registry with participating centres from Canada, the United States, and Europe.

Throughout this document

"you" refers to "you", "your child" or "your ward"; "we" means the physicians and other staff conducting the study.

What is the purpose of this study?

We are collecting medical data from people to generate more solid evidence and gain greater insight into the development of the disease and effect of treatments.This information will be put into a database which we can then use to better understand this rare disease, improve patient care and achieve the best health outcomes for the individuals with this condition.

Why are we asking you to participate?

We are asking you to participate in our research as you have been diagnosed with a confirmed Pyridoxine dependent epilepsy (PDE) due to antiquitin (*ATQ)* deficiency. PDE is a rare form of epilepsy characterized by seizures that begin in infancy or, in some cases, before birth. Researchers recently discovered that PDE is caused by a defect in a gene (*ATQ*) that affects the body's ability to break down a substance called lysine, an important protein building block. The chemicals that accumulate in the body because of this defect are thought to be toxic to brain cells and therefore responsible for the developmental delays experienced by 75-80% of PDE patients.

What kind of medical data will be collected?

With your permission, your doctor or a study coordinator will collect information about your symptoms due to PDE, including specifics about your seizures, PDE effects on development, and treatments you are taking to treat your PDE and its effect. We also want to collect clinical data about previous clinical and laboratory test results or findings in blood, urine and spinal fluid which may be associated with these conditions. Lastly, for a subset of patients, we are interested

in learning about your quality of life, participation in social activities and general behavior. Therefore, we will ask you to fill out online questionnaires found on KLIK (ww.hetklikt.nl). Your doctor will provide you with log in codes.

The following information will be collected:

- Diagnosis
- Month and Year of birth for age determination
- Symptoms of the disease (seizures, developmental delay, etc)
- De-identified clinical and laboratory data including related test results (for example: EEG, MRI images and data, behavior tests, lab tests,blood/urine test results)
- Questionnaires:
    - WHO Disability Assessment Schedule (WHODAS) 2.0
        - 36 Questions
        - 5-20 minutes of your time
    - Community Integration Questionnaire
        - 15 Questions
        - 15 minutes of your time

Will genetic data be collected?
We also want to collect information about the gene test that was done in your blood to confirm the diagnosis of PDE due to ATQ deficiency

Are there any risks or discomforts from being in the study?
There are no physical risks or discomforts because the study only involves collecting data normally gathered during a routine office visit. All information obtained for the registry will come from a chart review, no extra testing is involved.

There is a small risk of being identified due to the rarity of the disease. Every effort will be made to protect your identity and confidentiality.

Can I choose NOT to participate in this project? Yes.
Participating in the research is completely voluntary.

Will participating or NOT participating in this study negatively affect my clinical care? No.

Will I receive any direct benefits from participating?
There is no direct benefit to your participation in this research study.

Are there other benefits from me participating?
Sharing of your de-identified data and information will help to better understand the individual variability of your condition. This will allow us to better inform affected individuals about their potential outcome for the future. We also think that it is important to understand the nature of the disease to find better treatments.

How will my information be used?
We are asking for permission to include your de-identified information in the PDE registry. The registry database includes information collected from clinical visits and patient charts. At each centre the patient and their designated parent are being asked to provide consent to participate in the study. Usually this consent is discussed during a clinic visit. If you decide to consent, medical information will be entered into the PDE research database. This will occur each time your child visits your doctor's clinic until 2026. Information from previous clinic visits if required will be collected by reviewing your child's medical chart.The purpose of this database is to share the information about the natural course of the disease and treament options with scientists and other practitioners/researchers, while protecting your privacy.

Information will be entered via an internet link to a secure webpage that uses the same kind of secure internet connections that banks use. Only authorized people who work with the database and your doctor will be able to access the information about you. Your identifiable information will not be shared with anyone outside the database. Only approved projects conducted by scientiests, researchers and clinicians who are participants of this project, will be given de-identified information for their future studies and upon their request and only after approval is granted by a review committee and an ethics board.

How will my information be protected?
Protecting the security and privacy of your data is extremely important to us. Your name and other confidential data are not stored in the database. We are implementing a system in which a computer program assigns a unique code to each new patient being entered into the database. The attending physician will see the code and will be able to assign that code to your chart. The project coordinator will also be aware of the code with respect to the physician and the patient data being consented. Aside from the physician, your name will never be known to anyone associated with PDE Registry database and no record of your name will ever be entered to any element of the online dataset. If the physician wants to update a patient's dataset, he or she can access the database by entering his or her own name, and the unique code. Your name will never appear on the dataset and the only record of your name will be on the written consent form, which will be kept in the secured office of the Principal Investigator or in the office of the co-investigator who is collecting and entering the data with your informed consent. The consent form will be stored in a locked filing cabinet in the office of your physician and only he/she or an assigned research coordinator will have the key. Neither the consent form nor any of the information on the consent form will be kept elsewhere and in particular it will not be kept on an electronic file.

We do want to have one level of connection between the database and you and that would be your physician. Should our research put us in a position that we would like to request updated information or should you be a candidate for a potential new treatment, we would like to be able to contact your physician. Your physician will then have an opportunity to contact you and allow you to make a decision to proceed with our request.

Is the database where my data are stored secure?
The database itself is located in a secure network and the physical harddrives are located in a secure medical building. Any acess to the stored data will be given by the project leader only after she determines the appropriateness or necessity of the request. Only de-identified

information will be realeased to those scientists or clinicians who participate in this project and who requested this for the research purposes and whose intent of using such data was approved by the project leaders.

Who can access the database?
Only the Principal Investigators or their appointed designees as well as the Institutional Review Board will be granted direct access to your original medical and research records. Investigators from other participating centers will not have access to your original records.

Who can give your medical information to the REDCap® database?
All the information about you that is shared with the REDCap® database will come directly from your physician or other attending medical professional. After you sign the consent form your doctor will enroll you in the REDCap® and will enter your health information.

How long will my information be stored?
A database of this type becomes more useful as more patient data are included. Therefore, we are asking permission to retain your data for for a minimum of 10 years. If there continues to be no financial support after this additional period, then the match lists in the registries will be destroyed. This means that your now anonymized data may be used but there will be no link to any of your personal identifying information.

Can I stop participating in the study at any time in the future? Yes.
You can decide to stop participating in the study at any time by writing or calling your/your child's doctor. There is no penalty for withdrawing and you will not lose any benefits to which you are otherwise entitled. If you decide to stop participating, all information that was already included in the database will continue to be used, but no new information will be added to the database for research purposes.

Are there any extra costs to participate? No.

Will I be paid or given anything extra for participating? No

Will your physician be paid for sharing your health information with the database? Your physician will not receive payment from the REDCap® Database for his or her sharing your consented health information.

Will my taking part in this study be kept confidential? Your confidentiality will be respected. However, research records and health or other source records identifying you may be inspected in the presence of the Investigator or his or her designate for the purpose of monitoring the research. No information or records that disclose your identity will be published without your consent, nor will any information or records that disclose your identity be removed or released without your consent unless required by law.
You will be assigned a unique study number as a subject in this study. Only this number will be used on any research-related information collected about you during the course of this study, so that your identity [i.e. your name or any other information that could identify you] as a subject in

this study will be kept confidential. Information that contains your identity will remain only with the Principal Investigator and/or designate. The list that matches your name to the unique study number that is used on your research-related information will not be removed or released without your consent unless required by law.

Your rights to privacy are legally protected by federal and provincial laws that require safeguards to insure that your privacy is respected and also give you the right of access to the information about you that has been provided to the sponsor and, if need be, an opportunity to correct any errors in this information. Further details about these laws are available on request to your study doctor.

By signing this form, you do not give up any of your legal rights and you do not release the study doctor or other participating institutions from their legal and professional duties.

Studies involving humans now routinely collect information on race,gender and ethnic origin as well as other characteristics of individuals because these characteristics may influence how people respond to different medications. Providing information on your race or gender or ethnic origin is voluntary.

Who gives the consent?

If you were consented to be enrolled in the study while you were a child, the consent would have been given by your parents / legal custody. We will inform you of any new information that might influence your decision to participate in the research project. You may be asked to sign a revised consent form if this occurs. Should you become 18 years of age during the study period you will be contacted by the clinic investigator and given the opportunity to provide your individual consent to continue your participation in this study.

Who can I contact for more information if I have questions during the study?

If you have any questions or desire further information about this study, you can contact the project director **Dr. Clara van Karnebeek** at **604-875-2628** or email: cvankarnebeek@cw.bc.ca

Who do I contact if I have questions about my rights as a subject during the study?

If you have any concerns or complaints about your rights as a research participant and/or your experiences while participating in this study, contact the Research Participant Complaint Line in the University of British Columbia Office of Research Ethics by e-mail at RSIL@ors.ubc.ca or by phone at 604-822-8598 (Toll Free: 1-877-822-8598).

Please take time to read the following information carefully and to discuss it with your family, friends, and doctor before you decide.

CONSENT TO PARTICIPATE

SUBJECT CONSENT TO PARTICIPATE:

- I have read (or have had it read to me) and understand the subject information and consent form.
- I have had sufficient time to consider the information provided and to ask for advice if necessary.
- I have had the opportunity to ask questions and have had satisfactory responses to my questions.
- I understand that my child's data will be used to increase the knowledge of PDE.
- I understand that all the data collected will be kept confidential and that the results will only be used for scientific objectives.
- I understand that my child's participation in this study is voluntary and that I am completely free to refuse to participate or to withdraw from this study at any time without changing in any way the quality of care that I receive.
- I understand that there is no guarantee that this study will provide any benefits to me.
- I understand that my child's coded data will be shared among the investigators listed on this study.
- I understand that I am not waiving any of my or my child's legal rights as a result of signing this consent form.
- I have read this form and I freely consent to participate in this study.
- I have been told that I will receive a dated and signed copy of this form.

Additional options. With your signature you consent to participate in the study as described above. Additionally you have the option to be contacted if you want to learn more about other research studies relevant to my child's medical condition and / or to be asked for feedback on your experiences as a participant in this study.

Option 1: Future Research Studies

☐ YES, I agree to be contacted in the future, by my child's physician who will be informed by the research team, to learn more about any future research studies that may be relevant to my family.

☐ NO, I DO NOT wish to be contacted about any future research study that may be relevant to my family.

Option 2: Future Contact Feedback

☐ YES, I agree to be contacted in the future, by my child's physician who will be informed by the research team, to provide feedback on my child's experiences as a research subject in this study.

☐ NO, I DO NOT agree to be contacted in the future to provide feedback on my child's experiences as a research subject in this study.

I CONSENT BY SIGNING BELOW TO PARTICIPATE IN THIS STUDY

By signing I hereby consent to participate in this study. _____ *Name of study participant*

_____
Name of Participant or Parent/Legal Guardian

_____
Signature of Participant or Parent/Legal Guardian Date: _____

_____
Name of Person who Obtained Consent

_____ Date: _____
Signature of Person who Obtained Consent

Note to Physician: After consent, can you please write the PDE Regisry REDCap® web-page generated patient data code here: _____