

Under 14 years of age: Parental Permission only
14 years of age-17 years of age: Assent and Parental Permission Form

The Ohio State University Parental Permission For Child's Participation in Research

Study Title: Genetics, Molecular Diagnostics, and Mechanisms of Juvenile Cobalamin Deficiency

Principal Investigator: Stephan Tanner, PhD

Sponsor:

- **This is a parental permission form for research participation.** It contains important information about this study and what to expect if you permit your child to participate. Please consider the information carefully. Feel free to discuss the study with your friends and family and to ask questions before making your decision whether or not to permit your child to participate.
- **Your child's participation is voluntary.** You or your child may refuse participation in this study. If your child takes part in the study, you or your child may decide to leave the study at any time. No matter what decision you make, there will be no penalty to your child and neither you nor your child will lose any of your usual benefits. Your decision will not affect your future relationship with The Ohio State University. If you or your child is a student or employee at Ohio State, your decision will not affect your grades or employment status.
- **Your child may or may not benefit as a result of participating in this study.** Also, as explained below, your child's participation may result in unintended or harmful effects for him or her that may be minor or may be serious depending on the nature of the research.
- **You and your child will be provided with any new information that develops during the study that may affect your decision whether or not to continue to participate.** If you permit your child to participate, you will be asked to sign this form and will receive a copy of the signed form. You are being asked to consider permitting your child to participate in this study for the reasons explained below.

1. Why is this study being done?

This study is being done to better understand the genetic causes of juvenile cobalamin (vitamin B12) deficiency (JCD).

2. How many people will take part in this study?

Approximately 500 people will take part in this study.

3. What will happen if my child takes part in this study?

Upon enrollment in this study, you and your child will be asked to provide demographic and family history information. We will also request that your child's primary care physician provide information about your child's diagnosis of juvenile cobalamin deficiency (JCD). You may choose to provide contact information for your child's health care provider, so that we may follow-up with results of this study.

As a participant in this study, your child will be asked to provide a blood or cheek cell sample. If your child chooses to donate blood, a small needle will be inserted into a vein in his/her arm and about 4 tablespoons of blood will be taken. If your child is not able to meet with us at Ohio State University Medical Center to have blood drawn, a blood kit will be sent to your child via FedEx. Your child will then need to have blood drawn by a certified phlebotomist at their physician's office. The specimen will need to be packaged and sent to us using a provided postage-paid FedEx envelope. Your child will not be required to pay for shipping of the sample, however, you or your child may need to pay a small fee for blood drawing (usually \$10-\$20).

If your child is uncomfortable providing a blood sample, your child can provide a cheek cell sample by donating a saliva sample, buccal swab sample, or mouthwash sample. Donating saliva involves spitting into a small cup until the desired amount is obtained (typically about 2 tablespoons, which takes approximately 1 minute). Donating a buccal swab sample involves rubbing a soft brush on the inside of the cheek, and donating a mouthwash sample involves rinsing the mouth with a mouthwash (like Scope) and spitting it back into a collection cup. These samples can be collected at OSUMC or at home with a provided kit, and sent back to us at our expense. You and your child will need to let us know which option is preferred.

Your child's sample will be sent to a laboratory at The Ohio State University, where DNA/RNA (genetic material) will be removed from the cells. His/her genetic code will be analyzed for changes in certain genes (called GIF, AMN, CUBN). Changes in these genes have been associated with juvenile cobalamin (vitamin B12) deficiency (JCD). The sample will also be used for research to identify other genes that may be associated with JCD. Samples will be destroyed 3 years after the completion of this study.

If your child turns 18 years old during the study, we will try to recontact him/her so that he/she can decide whether or not to continue to be in the study. If your child decides to continue to be in the study, he/she will be asked to sign a new (adult) consent form. If your child decides he/she does not want to be in the study, we will destroy any samples (such as blood or saliva) and information that we had previously obtained. If we are unable to find your child, his/her sample and information will continue to be used until the study is complete.

You and your child have the option to receive genetic test results from this study. If you would like to be contacted by a genetic counselor with your child's test results, you must specify this on the consent form (#13). You will have time to discuss questions or concerns with the counselor over the phone, or in person, if you prefer. You, and/or other family members will also be given the option to participate in this research study.

4. How long will my child be in the study?

Participation in this study involves a one-time donation of a blood or cheek cell sample, which should only take a few minutes. However, the DNA/RNA extracted from your child's sample will be used in research over the next several years, and may not be discarded for up to 3 years after study completion. We estimate that research will be complete in the year 2012, so samples will be kept until 2015. Future use of the data or specimens will be restricted to this study and not used for other, unspecified research projects.

You have the choice whether or not to receive your child's test results from this study. Results should take approximately 2-6 months.

5. Can my child stop being in the study?

Your child may leave the study at any time. If you or your child decides to stop participation in the study, there will be no penalty and neither you nor your child will lose any benefits to which you are otherwise entitled. Your decision will not affect your future relationship with The Ohio State University.

6. What risks, side effects or discomforts can my child expect from being in the study?

Your child may experience some physical discomfort associated with getting blood drawn. There is a chance your child will experience some slight bruising at the site of needle insertion and there is a small chance of infection. There are no known risks to cheek cell collection.

Participation in this study could provide additional evidence to support a diagnosis of inherited juvenile cobalamin deficiency in your child. If your family members also participate in this research, testing could help identify who else in your family may have inherited a predisposition to JCD. There is the potential that non-paternity can be revealed through genetic testing.

Some individuals have concerns regarding confidentiality of genetic testing and/or the potential for discrimination based on genetic test results. There are federal and state laws to protect your child from health insurance discrimination based on genetic information. This protection extends to all group health care plans (HMP, PPO, etc), but does not include private health insurance plans. There are no protections for life insurance or

disability discrimination. While discrimination related to genetic testing is possible, very few documented cases of any type of discrimination based on genetic information currently exist. All efforts will be made to keep your child's test results confidential; results will be released upon request only by you.

7. What benefits can my child expect from being in the study?

Participation in this study may be beneficial to your child as it may help to identify the genetic mutations that led to the development of JCD. A better understanding of these genetic changes will also assist researchers in developing a clinical genetic test. A clinical genetic test could be used to identify other individuals in your family at increased risk to inherit JCD, and would enable early treatment to prevent complications from this disease.

8. What other choices does my child have if he/she does not take part in the study?

You or your child may choose not to participate without penalty or loss of benefits to which you are otherwise entitled. If your child has a suspected diagnosis of JCD, your child will receive the usual treatment for JCD regardless of participation in this study. Other options for genetic testing for JCD do not currently exist. You may also elect to participate in this study without receiving results of your child's genetic testing (specify preference under #13).

9. Will my child's study-related information be kept private?

Efforts will be made to keep your child's study-related information confidential. However, there may be circumstances where this information must be released. For example, personal information regarding your child's participation in this study may be disclosed if required by state law. Also, your child's records may be reviewed by the following groups (as applicable to the research):

- Office for Human Research Protections or other federal, state, or international regulatory agencies;
- U.S. Food and Drug Administration;
- The Ohio State University Institutional Review Board or Office of Responsible Research Practices;
- The sponsor supporting the study, their agents or study monitors; and
- Your insurance company (if charges are billed to insurance).

If the study involves the use of your child's protected health information, you may also be asked to sign a separate Health Insurance Portability and Accountability Act (HIPAA) research authorization form.

10. What are the costs of taking part in this study?

You may be responsible for the cost of getting your child's blood drawn. This fee is typically \$10-\$20 depending on the physician office. You may request a cheek cell collection kit if you prefer, in order to avoid the phlebotomy fee. You will not be responsible for the cost of the cheek cell kit or blood kit, shipping of the sample, or cost of research genetic testing or counseling.

11. Will I or my child be paid for taking part in this study?

Neither you nor your child will be paid to participate in this study.

12. What happens if my child is injured because he/she took part in this study?

There is minimal risk involved with participation in this study, since it only requires a blood draw or donation of saliva. If your child suffers complications as a result, you should notify your doctor immediately, who will determine if you should obtain medical treatment.

The cost for this treatment will be billed to you or your child's medical or hospital insurance. The Ohio State University has no funds set aside for the payment of health care expenses for this study.

13. What are my child's rights if he/she takes part in this study?

If you and your child choose to participate in the study, you may discontinue participation at any time without penalty or loss of benefits. By signing this form, your child does not give up any personal legal rights your child may have as a participant in this study.

Research subjects who are minors when they enter the study will have the option of being re-consented once they reach adulthood or request that their specimen and associated data be discarded.

You and your child will be provided with any new information that develops during the course of the research that may affect your decision whether or not to continue participation in the study. You or your child may refuse to participate in this study without penalty or loss of benefits to which you are otherwise entitled.

An Institutional Review Board responsible for human subjects research at The Ohio State University reviewed this research project and found it to be acceptable, according to applicable state and federal regulations and University policies designed to protect the rights and welfare of participants in research.

You and your child may choose whether or not you want to receive the results of your child's genetic testing (see check boxes below). If you choose to receive genetic test results, they will be communicated to you by a genetic counselor in person, or by

telephone, when they become available. Research genetic test results should not be used for clinical management until they are confirmed in a CLIA-approved laboratory. Currently, clinical testing through a CLIA-approved laboratory is available through GeneDx. The cost of clinical confirmation testing will not be covered by the research study.

If you choose not to have your child’s test results released, they will be kept confidential in your child’s research chart at Ohio State University and stored in a password protected database.

Would you like to receive results of your child’s genetic testing once it is available?

Yes No _____ (initial and date)

If you would also like your child’s health care provider to be contacted with results, please provide his/her name, phone number and address of your child’s health care provider:

14. Who can answer my questions about the study?

For questions, concerns, or complaints about the study you may contact Amy Sturm at (614) 293-6694.

For questions about your child’s rights as a participant in this study or to discuss other study-related concerns or complaints with someone who is not part of the research team, you may contact Ms. Sandra Meadows in the Office of Responsible Research Practices at 1-800-678-6251.

If your child is injured as a result of participating in this study or for questions about a study-related injury, you may contact Amy Sturm at (614) 293-6694 or 1-888-329-1654 (toll free).

15. Signing the parental permission form

I have read (or someone has read to me) this form and I am aware that I am being asked to provide permission for my child to participate in a research study. I have had the opportunity to ask questions and have had them answered to my satisfaction. I voluntarily agree to permit my child to participate in this study.

I am not giving up any legal rights by signing this form. I will be given a copy of this signed form.

Printed name of subject

Printed name of person authorized to provide permission for subject

Signature of person authorized to provide permission for subject

Relationship to the subject

Date and time AM/PM

Investigator/Research Staff

I have explained the research to the participant or his/her representative before requesting the signature(s) above. There are no blanks in this document. A signed copy of this form has been given to the participant or his/her representative.

Printed name of person obtaining consent

Signature of person obtaining consent

Date and time AM/PM

Witness(es) - *May be left blank if not required by the IRB*

Printed name of witness

Signature of witness

Date and time AM/PM

Printed name of witness

Signature of witness

Date and time AM/PM