Children's Hospital and Health System™

HUMAN RESEARCH REVIEW BOARD
STATEMENT OF VOLUNTEER CONSENT FOR RESEARCH STUDY

TITLE OF STUDY: International Registry for Vascular Anomalies Associated With Coagulopathy

PRINCIPAL INVESTIGATOR: Kelly Duffy, PhD

PHONE NUMBER: (414) 456-4078

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FULL STREET ADDRESS: Department of Dermatology, 8701 Watertown Plank Road, MFRC 4067, Milwaukee, WI 53226

CO-INVESTIGATORS: Ulrich Broeckel, MD
Beth Drolet, MD
Howard Jacob, PhD
Michael Kelly, MD, PhD
Richard Noel, MD, PhD
Paula North, MD, PhD

NAME OF SUBJECT: _____ MEDICAL RECORD NUMBER: _____

WE INVITE YOU TO TAKE PART IN THIS RESEARCH STUDY. TAKING PART IN THIS RESEARCH STUDY IS YOUR DECISION. YOU DO NOT HAVE TO PARTICIPATE. YOU MAY STOP OR DECIDE TO LEAVE THE STUDY AT ANY TIME. IF YOU STOP OR LEAVE THE STUDY, YOU WILL NOT BE PENALIZED. YOU WILL STILL RECEIVE ANY TREATMENTS, HELP OR BENEFITS COMING TO YOU. YOU WILL NOT BENEFIT OR BE HELPED FROM BEING IN THIS RESEARCH STUDY. THE INFORMATION IN THIS FORM EXPLAINS WHAT WILL HAPPEN TO YOU IN THE STUDY. THE RESEARCHERS MAY BE REVIEWING THIS FORM WITH YOU AND CAN ANSWER ANY QUESTIONS YOU MAY HAVE. THIS FORM ALSO TELLS YOU ABOUT THE RISKS, DISCOMFORTS AND OTHER INFORMATION ABOUT THE STUDY. MEDICAL LANGUAGE IS HARD TO UNDERSTAND FOR MOST PEOPLE. IF THERE IS ANYTHING THAT YOU DO NOT UNDERSTAND OR ARE UNSURE ABOUT, PLEASE ASK QUESTIONS. YOU SHOULD ONLY AGREE TO TAKE PART IN THIS RESEARCH STUDY AND SIGN THE CONSENT FORM IF YOU UNDERSTAND WHAT WILL HAPPEN TO YOU, WHAT THE RISKS ARE, AND THAT YOUR QUESTIONS HAVE BEEN ANSWERED.

A. WHAT IS THE PROBLEM?

You are being asked to participate in this research study because you have been identified with having a ***vascular disorder*** (blood vessel abnormality) that involves the skin and ***coagulopathy*** which is a bleeding disorder involving conditions of blood clots in which bleeding is prolonged and excessive.

This study asks for your consent to collect medical information and a small sample of tissue and/or a blood sample to study your genes. All cells contain genes. Genes provide instructions for the body to display traits such as eye color. Everyone's genes are a little different. Information about these differences among people can help doctors understand how to best identify and develop better ways to treat this vascular disorder.

B. WHAT IS THE PURPOSE OF THIS RESEARCH STUDY?

This research registry is designed to help clinicians and basic scientists identify and understand the cause of vascular disorders associated with coagulopathy, which may help lead to treatment and prevention. The registry also serves as an educational resource for families who are interested in learning about this disorder.

About 30 subjects will take part in this study. Study subjects will be recruited from other physicians and also through the world wide web.

Financial support for this research project is from the Children's Research Institute.

C. WHAT IS INVOLVED IN THE RESEARCH STUDY?

If you agree to be in this study, the following will happen:

1. Informed consent and permission to use or disclose your health information for research purposes will be obtained by Dr. Duffy, the principal investigator, or her research team. You will be contacted by phone by one of the people stated above to review this consent form with you. You will receive a copy of this consent form.
2. Permission to ask for and receive your health information from others including doctors and medical personnel.
3. You will be asked to fill out a medical questionnaire which will provide investigators with important family and medical history. You may ask health care professionals responsible for your care to assist in completing this questionnaire. The questionnaire will take approximately 15 to 30 minutes to complete.
4. A buccal swab will be obtained from you; this involves rubbing the inside of your cheek and removing cells to perform a genetic test called "Genomewide Association" (GWA).
5. You have the option of submitting your tissue sample from a biopsy. The tissue will be used for histopathological analysis and examination, and tissue culture. A small amount of left over tissue from the malformation, if is surgically removed, will be taken that is not needed for diagnosis or treatment. The portion of your tissue that is donated for research is part of what your doctor would ordinarily remove in order to treat and/or diagnose your condition. Optionally, if your child has a biopsy at an outside institution

and there is tissue sample remaining after standard of care treatment is performed, you may choose to submit it to us for further analysis, examination and tissue culture.

6. Approximately a teaspoon of blood sample may be obtained from you. In no case will the amount of blood taken exceed the guideline of *the lesser of 3 ml/kg or 50 ml.* You will go to your local laboratory to get this done.

We expect you to be involved in this study until you have the genetic testing performed.

D. WHAT ARE THE RISKS TO YOU IN THIS RESEARCH STUDY?
As part of the study you will undergo laboratory tests requiring a buccal swab collection and/or blood test, and the option of submitting a tissue sample.

The risks of a buccal swab sampling are possible discomfort, potential for irritation which may cause slight bleeding, and very small risk of infection. Risks relating to taking blood may cause some pain, bleeding or bruising at the spot of venipuncture. Rarely, taking blood may cause fainting or infection. However these risks are very rare. Should they happen, they are self-limiting and they don't require treatment.

There is no risk related to submitting the tissue sample. Obtaining biopsies is at the discretion and choice of the patient and their family. Submission of a tissue sample is not required for study enrollment. A tissue sample will be submitted only if the patient/patient family has chosen for a biopsy to be performed and elects for our study to receive a tissue sample of the biopsy.

If you have questions about risks of being in the study, please contact Dr. Duffy or her research team at 414-456-4078.

E. WHAT IF PROBLEMS OCCUR DURING THE STUDY OR WITH TREATMENT?
Your health is more important than following the research plan. If any changes are needed to protect your health, we will talk with you about them before they are made. We will also tell you if any new information becomes available that may change your willingness to stay in this study.

In the event that this research activity results in an injury, care for such injuries will be billed in the ordinary manner to you or your insurance company. Insurance companies may refuse to pay for injuries sustained while participating in a research study or while receiving a treatment that is considered experimental. If you think that you have suffered a research-related injury, let the study physician(s) know right away.

You do not waive any legal rights by participating in this study or by signing this form.

F. WHAT ARE THE POSSIBLE BENEFITS TO YOU IN THIS RESEARCH STUDY?
The information which is obtained may be useful scientifically and possibly helpful to others. The benefit to you/ your child, which may be expected from participating in this study, includes learning more information about the possible cause of vascular anomalies associated with

coagulopathy. If you agree to participate in this study, there may or may not be direct medical benefit to you. We hope the information learned from this study will benefit other patients with this rare medical condition in the future.

G. WHAT ARE THE FINANCIAL RISKS TO YOU IN THIS RESEARCH STUDY?
You (and/or your insurance company) will not be expected to pay for any of the procedures or tests that are required as part of your participation in this research study. All the procedures described above are paid for by other funds which may include internal funding or sponsorship from outside sources.

You or your insurance company will still be responsible for the cost of your usual ongoing medical care, including non-research related procedures and medications that your study doctor or regular doctor requires during this study as part of your usual medical care. If you have any questions, please ask the study doctor or a member of the study staff.

H. WILL YOU BE PAID FOR TAKING PART IN THE RESEARCH STUDY?
You will not receive any compensation for taking part in this study.

I. DO YOU HAVE TO PARTICIPATE IN THIS RESEARCH STUDY?
You do not have to participate in this study. You are free to withdraw at any time. Your decision to withdraw will not change the quality of care that you receive from the medical staff. However, if you decide to stop participating in the study, we encourage you to talk to the researcher and your regular doctor first.

Your genetic material will be labeled with a code so that no one will know it came from you. Your genetic material may be stored in the laboratory for up to 20 years. During that time, only Drs. Duffy, Drolet, Jacob, Broeckel, Kelly, Noel, North and personnel working in collaboration with them will have access to this material. You may withdraw from the study at any time. You may request that your genetic material be destroyed or that all personal identification be removed from the stored samples. If you so desire, you will have access to clinically relevant information after the study is completed and the results are analyzed. The information will be made available to no one else without your written permission. However, you may request that it be made available to relatives, personal physician, insurance companies, etc.

J. WHAT IF YOU HAVE MORE QUESTIONS?
For questions about the study or a research-related injury, contact the researcher, Dr. Duffy, or her research team at 414-456-4078.

Also, the research study has been reviewed and approved by the Human Research Review Board, whose purpose is to see that the rights and welfare of research participants are adequately protected, and that risks are balanced by potential benefits. A member of this committee is available to speak to you if you have any questions or complaints at 414-266-7454.

You will get a copy of this form. You may also request a copy of the protocol (full study plan). A copy of the signed consent, and/or assent and HIPAA Authorization will be kept in your medical record.

K. WILL INFORMATION BE CONFIDENTIAL?

Children's Hospital of Wisconsin / Children's Health System, its researchers and their designees will maintain the privacy and confidentiality of your personal and health information to the extent permitted by law. Efforts will be made to keep your personal information confidential. We cannot guarantee absolute confidentiality. Your personal information may be disclosed if required by law. Also, scientific data from this study, without identifiable information, may be presented at meetings and published so that it may be useful to others, as long as it is not identifiable with you. Some organizations that may inspect and/or copy your research records for purposes of quality assurance and data analysis include groups such as Human Research Review Board, Children's Hospital of Wisconsin, and Children's Research Institute.

A new Federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

Be aware that this new Federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

L. PERMISSION TO PROCEED

The signing of this consent does not release your doctors from their responsibility for your proper medical care at all times.

The proposed research study and consent has been explained to you by:

_____	_____
Name Of Principal Investigator or Designee	**Signature Of Principal or Designee**

When you sign this form, you agree that you have read the above description of this research. You also agree that you have had a chance to discuss the research study with a member of the research team; that your questions have been answered, and that you want to take part in this research.

Signature of Subject or Authorized Representative	**Date**
Signature of Subject or Authorized Representative	**Date**

Concerning <u>your participation</u> in this study, you consent to the following (please initial one):

_____ Your participation in this study <u>may be shared</u> with your primary care doctor.

_____ Your participation in this study <u>may not be shared</u> with your primary care doctor.

ASSENT OF MINOR:

The above has been explained to me and I agree to participate.

Signature of Minor	**Date**

WAIVER OF MINOR'S ASSENT:

"In my opinion, this child is not capable of assent due to being 6 years of age or under."

Signature of Principal Investigator or Designee	**Date**

CONSENT FOR GENETIC / TISSUE BANKING

TITLE: International Registry for Vascular Anomalies Associated With Coagulopathy

PRINCIPAL INVESTIGATOR: Kelly Duffy, PhD

Your genetic and/or tissue material will be labeled with a code so that no one will know it came from you. Your genetic and/or tissue material may be stored in the Children's Hospital of Wisconsin laboratory for up to 20 years. During that time, only Drs. Duffy, Drolet, Jacob, Broeckel, Kelly, Noel, North and personnel working in collaboration will have access to this material.

You may withdraw from the study at any time. You may request verbally or in writing that your genetic and/or tissue material be destroyed or that all personal identification be removed from the stored samples.

If you so desire, you will have access to clinically relevant information after the study is completed and the results are analyzed. Your written permission is required in order to give this information to anyone. However, you may request that it be made available to relatives, personal physician, insurance companies, etc.

You will need to re-consent for storing your samples when you become an adult (at the age of 18). After you turn 18 years old, the researchers will not be able to use your stored samples for research unless they obtain your consent. If we are unable to contact you for re-consent your stored tissue samples will automatically be destroyed.

Concerning possible use of your stored genetic and/or tissue material for future scientific studies, you consent to the following (please initial one):

_____ a. Your genetic and/or tissue material will not be used for any purposes other than this study.

_____ b. Your stored genetic and/or tissue material may be used for future research. If you agree, this genetic and/or tissue will be kept and may be used in research to learn more about vascular anomalies associated with coagulopathy provided that your confidentiality is maintained.

CONSENT FOR CONTINUED PARTICIPATION IN RESEARCH
(when subject turns 18)

TITLE: International Registry for Vascular Anomalies Associated With Coagulopathy

PRINCIPAL INVESTIGATOR: Kelly Duffy, PhD

You are currently taking part in a research study. Permission for you to take part in this research study was given by one of your parents and/or guardian. Now that you have reached the age of majority (18 years old), we are asking for your consent for continued participation in this research study. The age of majority means you are considered adult enough to sign legal contracts and consents for yourself. We are now giving you a copy of the original consent document to review.

Blood or tissue samples may have already been sent for research testing as part of this study. Researchers will not be able to use your stored samples unless they obtain your consent.

WHO DO YOU CALL IF YOU HAVE QUESTIONS OR PROBLEMS?
For questions about the study or a research-related injury, contact the researcher Kelly Duffy, PhD, at (414) 456-4078. If additional questions arise, you can ask your doctor. Also, the research study has been reviewed and approved by the Human Research Review Board, whose purpose is to see that the rights and welfare of research participants are adequately protected, and that risks are balanced by potential benefits. A member of this committee is available to speak to you if you have any questions or complaints at 414-266-7454.

Copies of the previously signed informed consent / parental permission form and this consent form will be given to you and kept in your medical record.

By signing below, you agree to continue your participation in this research study.

Participant _____ Date _____

PI or Designee _____ Date _____

Children's Hospital and Health System™

HUMAN RESEARCH REVIEW BOARD
ASSENT *(ages 7-13)*

STUDY TITLE: **International Registry for Vascular Anomalies Associated With Coagulopathy**

INVESTIGATOR: Kelly Duffy, PhD

PHONE NUMBER: 414-456-4078

NAME OF SUBJECT: _____ MEDICAL RECORD NUMBER: _____

A. WHAT IS THE PROBLEM?

You are being invited to take part in this study because you have a rare disease that involves your skin plus blood problems called vascular anomaly linked with coagulopathy.

B. WHAT IS THE PURPOSE OF THIS RESEARCH STUDY?

The purpose of this study is to find out what causes the skin and blood problems. We will also ask if you can give some of your cheek cells, blood, and a piece of the skin that is not normal.

C. WHAT IS INVOLVED IN THE RESEARCH STUDY?

If you are going to be in the study a sample of your cheek cells and blood may be taken. You may also get a piece of the skin that isn't normal taken off by a doctor that is taking care of you. If you want, you may send us a piece of that skin so we can study it. When you turn 18 years old, we will ask you again if it is ok to be a part of our study.

D. WHAT ARE THE RISKS TO YOU IN THIS RESEARCH STUDY?

You may feel uncomfortable, have some pain, and maybe infection at the spot of your blood draw, but this does not happen all the time.

E. WHAT ARE THE POSSIBLE BENEFITS TO YOU IN THIS RESEARCH STUDY?

We will use your information along with other children who are in this study to find the reason why this disease happens. When we learn more about this disease, we will be able to tell you more about it in the future. Knowing more may also help us find a medicine to treat it.

F. WILL YOU BE PAID FOR TAKING PART IN THE RESEARCH STUDY?

You will not be paid to be part of the study.

G. DO YOU HAVE TO PARTICIPATE IN THIS RESEARCH STUDY?
You do not have to be in this study, and if you are in it you can stop at any time. If you have any questions please ask your doctor.

H. PERMISSION TO PROCEED
Your parents / guardian will receive a copy of this form. A copy of the signed consent, assent and HIPAA Authorization will be kept in your medical record.

Writing my name on this page means that the page was read (by me/to me) and that I agree to be in the study. I know what will happen to me. If I decide to quit the study, all I have to do is tell the person in charge.

_____

Childs Name

_____ _____

Child's Signature **Date**

Assent Form administered and explained in person by:

_____ _____

Principal Investigator or Designee **Date**

CHILDREN'S HOSPITAL & HEALTH SYSTEM, INC.
HUMAN RESEARCH REVIEW BOARD
PERMISSION TO USE OR DISCLOSE (RELEASE) HEALTH INFORMATION FOR RESEARCH PURPOSES

Patient's Name: _____ Date of Birth: _____

Principal Investigator: Kelly Duffy, PhD CHW / HRRC #'s 07/226

Name of Research Study: **International Registry for Vascular Anomalies Associated with Coagulopathy**

1. What is the purpose of this form?

You've been asked to allow your child to be part of the research study identified above. If you want your child to be part of this study, you must sign two forms: 1. an informed consent form explaining the study and 2. this form. Signing this form gives (a) your child's health care providers permission to disclose information to the researcher for the study; (b) your permission for the researcher to use your child's information to conduct the study; and (c) permission for the researcher to share your child's health information with others as needed to conduct the study.

2. What health information do the researchers want to use?

The researchers want to copy and use portions of your child's medical record, or information obtained as part of this study, that they will need for their research. If you agree to have your child participate in this study, the following information may be used and/or released:

- ☒ Past and present treatment of your child as an inpatient or in an outpatient, clinic or physician office setting.
- ☒ The history and diagnosis of your child's disease.
- ☒ Other medical conditions that may affect your child's treatment.
- ☒ Laboratory, radiology and pathology test results.
- ☐ HIV test results.
- ☐ Alcohol or drug treatment records.
- ☐ Mental health treatment records.
- ☐ Disability reports.
- ☐ Other research information including: _____

3. How will the researchers use my child's health information?

Your child's health information may be used for the following purposes:

- to decide whether your child is eligible to participate in this study;

- to monitor your child's health while in the study;
- to evaluate the results of the study procedures
- to seek payment for services not covered by your health insurance;
- as described in the Notice of Privacy Practices that will be provided to you.
- to make reports to companies sponsoring the study;
- to allow government and private reviewers to make sure the study complies with laws, policies and procedures.

4. Who is permitted to use or disclose my child's health information?

By signing this form, you give your permission for the organization(s) identified below to use or disclose your child's health information for purposes of the study.

X Members of the research team	☐ CHW-Fox Valley
X Children's Hospital & Health System, Inc.	☐ CHW-Kenosha
X Children's Hospital of Wisconsin, Inc.	☐ Children's Medical Group, Inc.
☒ Medical College of Wisconsin	☐ Surgicenter of Greater of Milwaukee
☐ Froedtert Memorial Lutheran Hospital	☐ The Blood Center of Wisconsin, Inc.
☐ Other (list)	

5. Who will be able to use my child's health information?

As part of the research, your child's health information may be given to the following groups. These groups may also review your child's original records to assure that the information is accurate:

☐ The sponsor of the study or organizations acting for the sponsor;

■ Human Research Review Board (HRRB) of Children's Hospital of Wisconsin, Inc. or other review boards that may be responsible for monitoring this study.

■ Children's Hospital & Health System, Inc., CHHS or government agencies as authorized or required by law;

☒ A Data Safety Monitoring Board or other body responsible for reviewing the safety of the study;

☒ Health care providers who are not involved in the study, but who may care for your child, if the health information created as part of the study is important to your child's treatment;

☒ Your child's health insurer, if necessary, in order to secure payment for treatment not paid for through the study;

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☐ Other: _____

6. How will information about my child be kept private?

All reasonable efforts will be made by the researcher and the groups listed in this form to protect the confidentiality of your child's health information. Your child's health information will not be given to others except as authorized or required by law. You should understand that some of the groups to whom your child's health information may be given may not be required by law to obtain your permission to share your child's health information with others.

7. What happens if I do not sign this permission form?

If you do not sign this permission form, your child will not be able to take part in this research study. If you sign this form, you must be given a copy of the signed form to take with you.

8. If I sign this form, will my child automatically be entered into the research study?

No, your child cannot be entered into any research study without further discussion and separate consent. After discussion, you may decide to have your child take part in the research study. At that time, you will be asked to sign a specific research consent form.

9. Can my child's health information be used for other research studies?

Your child's health information can only be used again if the Children's Hospital of Wisconsin Human Research Review Board gives its permission. That Board may (or may not) require that the researcher obtain your permission once again. The additional research can only be done if your child's health care information is kept private.

10. What happens if I want to withdraw my permission?

You can change your mind at any time and withdraw your permission. If you want to withdraw your permission, **you must do it in writing**. Beginning on the date you withdraw your permission, no new health information regarding your child will be used for research. However, researchers may continue to use the health information that was provided before you withdrew your permission.

If you sign this form and enter your child in the research study, but later change your mind and withdraw your permission, your child will be removed from the research study at that time. However, your child's regular medical care and any other benefits to which your child is entitled, will not be affected.

To withdraw your permission, please contact the person named below. He/she will make sure your written request to withdraw your permission is processed correctly:

Should either be Principal Investigator or Medical Records Department:
Kelly Duffy, PhD

Children's Hospital and Health System™

Address: Department of Dermatology, 8701 Watertown Plank Road, MFRC 4067, Milwaukee, WI 53226

Phone/Fax: 414-456-4078/414-456-6518

11. How long will this permission last?

Unless you withdraw your permission, this permission will last:

☐ Until the study is concluded;

☒ 20 years after the end of the study;

☐ Until _____(Date).

12. What are my rights regarding access to my child's health information?

You have the right to refuse to sign this permission form. You also have the right to review and/or copy records of your child's health information related to this study. You should understand that from time to time, it may be difficult for the researcher to give you immediate access to your child's health information related to the study. If your access is temporarily denied, you will be granted access as soon as possible and, at the very latest, at the end of the study. You do not have the right to review or copy other records kept by the researcher or others associated with the research study.

I agree that my child's health information may be used for the research purposes described in this form.

_____ Date: _____

Patient or Legal Representative

_____ _____

Print Name of Legal Representative Relationship to Patient

Witness: _____ Date: _____

_____

Print Name of Witness