RESEARCH SUBJECT INFORMATION AND CONSENT FORM

PROTOCOL TITLE: A Registry of Patients with Primary Immune Deficiency Disorders
Version 1.04

SPONSOR: National Institute of Allergy and Infectious Diseases
Bethesda, Maryland
United States

PRINCIPAL INVESTIGATOR: Ramsay L. Fuleihan M.D
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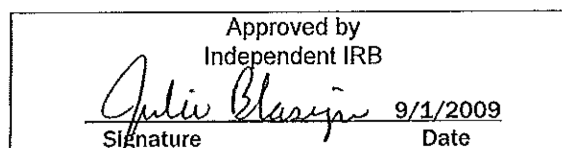
STUDY RELATED PHONE NUMBERS: Ramsay L .Fuleihan M.D.
866-939-7568
443-632-2556
773-327-1701

24 HOUR TELEPHONE AFTER HOURS NUMBER: 443-847-4330

INTRODUCTION:
You are being asked to participate in a research study because you have been diagnosed with a primary immunodeficiency disease. This study will include patients participating in the study at different physicians' offices. This consent form may contain words that you do not understand. Please ask the study doctor or the study staff to explain any words or information that you do not clearly understand. You may take home an unsigned copy of this consent form to think about or discuss with family or friends before making your decision.

<u>In this consent form, "you" always refers to the subject.</u> If you are a parent/legal guardian, please remember that "<u>you</u>" refers to the study subject.

You (or your child/legal dependent) have been invited to be part of a research study. Before you decide (or permit your child/legal dependent) to participate in this research study, you should read this form carefully. This form, called a consent form, explains the study. Please ask as many questions as needed so that you can decide whether you want to participate in this study (or agree



to the participation of your child/legal dependent in this study). Please read this form carefully and ask the study doctor or study staff about anything in this form that you have questions about or do not understand. Do not sign this form unless you are satisfied with the answers to your questions.

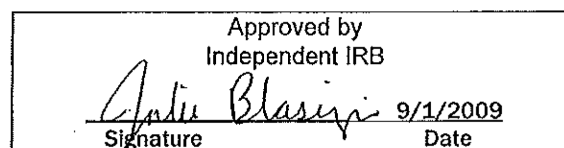
It is necessary that if you are a parent or legal guardian of a study participant that is not legally permitted to consent to be in a research study on his/her own behalf, then it is necessary that you sign this Informed Consent Form. In addition, if your child/legal dependent is 13 to the age of Legal Consent, the child will be asked to sign the "Assent Signature Section" of this consent form and be given the chance to indicate whether or not he/she wants to participate in this research study.

PURPOSE OF THE REGISTRY:
The purpose of this study is to build a National Registry of people with primary immune deficiency diseases, also known as inherited diseases of the immune system. A "Registry" is a list of clinical and laboratory information from people who have a certain condition in common. Primary immunodeficiency diseases are so rare that doctors and scientists at any single location do not have enough affected patients to understand the entire range of their problems or how to treat them best. By putting information about patients from many places into a single Registry we hope to gain knowledge about the rate of occurrence, causes, natural history, and outcomes of primary immunodeficiencies. There are many individual diseases included in the group of primary immunodeficiencies. The original Registry focused on a few of the more widely known examples including patients with severe combined immunodeficiency (SCID), X-linked agammaglobulinemia (XLA), common variable immune deficiency (CVID), DiGeorge syndrome (DGS), hyper IgM syndrome (HIGM), Wiskott Aldrich syndrome (WAS) and chronic granulomatous disease (CGD). The Registry has been enlarged to also include more than 100 other primary immune deficiency diseases. This is considered a research study because data is being collected about people with primary immunodeficiency diseases

DESCRIPTION OF THE REGISTRY:
The United States Immunodeficiency Network (USIDNET) Consortium, a National Institutes of Health (NIH)-funded group of investigators working in association with the Immune Deficiency Foundation (IDF) to conduct a study in which a patient Registry is being developed. The Immune Deficiency Foundation is the national patient organization dedicated to improving the diagnosis, treatment and quality of life of persons with primary immunodeficiency diseases through advocacy, education, and research. The IDF provides administrative support for USIDNET and developed the initial Registry of patients with Primary Immunodeficiency that has grown to become the current Registry. The National Institute of Allergy and Infectious Diseases (NIAID) at the National Institutes of Health (NIH) in Bethesda, Maryland, have supported the Registry since its beginning.

A Registry, or list of subjects and information about them, will help physicians understand how many people have each of the primary immunodeficiency diseases. The information collected from many patients will be put together with the goal of improving how doctors diagnose and treat these conditions.

The Registry includes information on age, sex, race or ethnic group, and lab tests that were used to diagnose and monitor the condition. The Registry also may include treatments that have been



used for your condition and medical problems that you may have had. This information will help doctors learn how to better diagnose and treat these diseases. It will also help doctors and scientists learn about some of the problems that seem to be bothersome for patients with a particular primary immunodeficiency.

Doctors and scientists who want to use the information in the Registry will need to submit a written application to a Registry scientific review panel. The panel will be composed of the Steering Committee of the USIDNET or their designees. Upon approval of a proposal by the scientific reviewers, the Registry Administrator will extract the requested data without providing any information that would reveal the identity of the individual patients in the Registry. In some cases, studies may be proposed to try out new diagnostic tests, or even to use new treatments. For this type of study a patient in the Registry would have to be notified and given the option to be matched up with the scientists or doctors conducting the study. Notification might come through your doctor, or if you wish, directly to you from the Registry Administrator. In either case it is strongly suggested that you discuss any new study with your doctor before agreeing to participate in it. Your identity will not be revealed to anyone wishing to have access to the medical information contained in the Registry or to anyone wishing to contact patients about other potential studies.

PARTICIPATION:
If you agree to participate in this study you will be asked to sign this Informed Consent Form. Your information will then be added to the Registry. The Registry information would include specific medical information on your condition, your sex, race, year of birth, state where you were born, state where you live, your doctor's name, and your doctor's address. Each time you return to your doctor additional information may be added to update the Registry, until we lose contact with you or you decide to stop participating in the Registry. This way the Registry can develop a picture over time of the course of your illness and your response to various treatments and procedures.

This study will enroll an unlimited amount of volunteers of all ages. Your participation in this study is ongoing, unless and until the "Registry" is closed or if at any time you choose to withdraw your participation in the study.

You may select one of three ways to join the Registry.
Under OPTION ONE, your identity will not be revealed. A code number will be assigned to your information, but only your doctor will know it. Your study doctor may update your information to include changes in your condition or treatment. The Registry Steering Committee may direct the Registry staff to send reports containing information about your disease to your doctor. The Registry committee may also permit information about proposals to study new tests or treatments to be sent to your doctor. Your doctor will be able to share this information with you. You cannot be contacted directly by the Registry staff because the Registry will not have your identifying information.

Under OPTION TWO, your name, full date of birth and mailing and/or email address will be recorded by the Registry Administrator, but kept in a database that is separate from any information about your condition. Your specific medical information will be assigned a code number when it is included in the Registry. The only link between your name and the medical information in the Registry will be the code number. Your doctor may periodically update your

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Independent IRB
Julie Blasingim 9/1/2009
Signature Date

Initials: ____________
Date: ____________

information to include changes in your condition or treatment as well as changes in your name or contact information. Investigators reviewing your medical information contained in the Registry database will not have access to your identifying information.

Under **OPTION TWO-A**, communication between the Registry staff and you will be carried out by the Registry staff. They will send all information to your doctor and he/she will then transmit that information to you. The only circumstance where the Registry staff might contact you directly would be in the case that you have moved and/or ended contact with your original doctor or your original doctor has retired or for some other reason can no longer be contacted by the Registry staff.

Under **OPTION TWO-B**, the Registry Administrator may get in touch with you directly to inform you about research results based on information gathered about your disease. The Registry staff may also ask you to clarify items that might be confusing about your personal information in the Registry or they might ask if you wish to update or add to your information in the Registry. The Registry staff may also send you notices about new research studies being planned that you may be eligible to join if you wish. Your doctor would also receive these notices at the same time so that you may discuss the new studies together.

Your identity will not be revealed to other investigators, but you will be provided with contact information to reach them if you decide you wish to receive additional information about a proposed study.

Under **OPTION ONE**, it will not be possible for the Registry staff to contact you, remove your information from the Registry or for the Registry staff to provide you with a copy of your personal information contained in the Registry. The Registry staff will not be able to determine which information is yours. Currently there is information from more than 2060 individuals with primary immunodeficiency diseases in the Registry. The number of patients is continually increasing as patients agree to participate in the Registry.

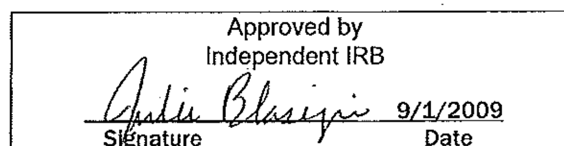
Under **OPTION TWO**, you can remove your information from the Registry. You can remove either your identifying information or all your information. The Registry staff will also be able to provide you with a copy of the information about you contained in the Registry. If you decide to stop being part of the registry or would like a copy of your Registry record, you should contact your doctor or Dr. Ramsay L. Fuleihan of the Immune Deficiency Foundation at telephone number 1-866-939-7568.

Restrictions/Research Participant Responsibilities

- As a research participant you will be asked to complete the study procedures for this study, follow the instructions listed in this informed consent form, and notify the study doctor if any information regarding your health or availability to participate in this study changes.

POTENTIAL RISKS AND DISCOMFORTS:

Since taking part in this study involves only sending medical data to the Registry, there are no physical risks for you to participate. While we will not reveal your identity to the doctors or scientists using the Registry database, it is possible that someone could figure out who you are. Under OPTION TWO, your identity will be kept separately from your Registry information. It



is possible that your identity could be revealed even if it is held separately from your medical information. If USIDNET learns that your identity has been revealed, you will be told. Although procedures have been put into place that are designed to keep your identity confidential, there is a remote possibility that information from your participation in this study would adversely affect you or your family in some way, such as obtaining a job or health insurance.

UNKNOWN/UNFORESEEABLE RISKS:
In addition to the risks listed above, there may be some unknown or infrequent and unforeseeable risks associated with your participation in this study.

NEW FINDINGS:
You will be informed in a timely manner both verbally and in writing of any new information, findings or changes to the way the research will be performed that might influence your willingness to continue your participation in this study.

POTENTIAL BENEFITS:
There may be no direct benefits to you from being part of the Registry. It is possible that future studies of new treatments may be available to Registry participants, and enrollment may be offered to you either through your doctor or directly because your information is in the Registry.

Participation may help doctors and scientists to better understand these medical conditions, and may lead to better treatments. Information in the registry may also advance medical knowledge in general, so others may benefit.

COSTS:
There are no costs for you to be involved in this study. There will be no tests for this study since the Registry will contain medical information obtained as part of your regular medical care.

PAYMENT:
You will not receive any payment for being part of this study. If a hospital or doctor's office requests payment for copying and/or mailing your records to the Registry, the Registry can reimburse those expenses up to a maximum total of $25.00 upon presentation of an original bill from that hospital or doctor's office. You will receive payment within two weeks of submitting the medical records. USIDNET can also provide a pre-paid Mailer to send documents to the USIDNET office. Contact the USIDNET Project Manager at **866-939-7568** for these pre-paid mailers.

ALTERNATIVES TO PARTICIPATION:
The alternative is not to be part of the Registry and to not participate in this study.

CONFIDENTIALITY:
The identity of individuals who are part of the Registry will not be made public in publications based on Registry information. The identity of individuals providing information obtained will be kept confidential to the extent permitted by law. If required by law or regulation, your identity may be revealed to government agencies (such as the U.S. Food and Drug Administration (FDA) or the Department of Health and Human Services (DHHS)); individuals who are involved

Approved by
Independent IRB
Signature 9/1/2009 Date

Initials: ____________
Date: ____________

in the study, or authorized to monitor or audit the study; or the Independent Investigational Review Board (the committee that oversees research in humans for participating physicians who do not have a local IRB to provide such oversight).

The study sponsor will keep your identity confidential and, except for the disclosures described above, will not disclose your study records to other parties unless disclosure is required by law. Absolute confidentiality cannot be guaranteed. However, the Sponsor and its consultants will only use your information for purposes of the study and will not disclose your study records, unless disclosure is required by law. If reports or articles are written about the study, you will not be identified by name in them. You have the right to review your records at any time. You must contact the study doctor to request this information. This authorization does not expire (expires in 50 years in California and Washington). However, you have the right to cancel this authorization at any time. You can do this by giving written notice to the Principal Investigator informing him that you are canceling your authorization to use and disclose medical information. The contact information is listed on page 1 of this document. If you cancel this authorization to use and disclose your medical information, the information that has already been collected in your study records may continue to be used and disclosed (by "Sponsor" and its consultants) as described above, however, no new information will be obtained or added.

____________________ ____________

Patient's Signature Date

COMPENSATION/TREATMENT FOR INJURY:

There is no money to pay for injuries or treatment from being part of this study. If you believe that you have suffered an injury related to this study, you should contact your doctoror Dr. Ramsay L. Fuleihan of the Immune Deficiency Foundation at telephone number 866-939-7568.

You **do not** waive any of your legal rights by signing this consent form.

SOURCE OF FUNDING:

Funding for this registry will be provided by the National Institute of Allergy and Infectious Diseases (NIAID) and the National Institute of Child Health and Human Development (NICHD).

VOLUNTARY PARTICIPATION:

Your participation in this study is voluntary. You may decide not to participate or you may leave the study at any time (or withdraw your child/legal dependent). Your decision will not result in any penalty or loss of benefits to which you are entitled or affect the availability of your future medical care.

Approved by
Independent IRB
Julie Blasingim 9/1/2009
Signature Date

Initials: __________
Date: __________

Your study doctor, local institution, or sponsor may remove your (your child/legal dependent's) information from the Registry at any time without your consent and may also remove the child/legal dependent's information from the registry at any time if they indicate that they do not wish to participate in the study.

If you change your mind after you sign this consent form, every effort will be made to remove your information from the Registry. If your information has not yet been entered in to the Registry database, your information will not be submitted. Under **OPTION ONE** it will not be possible to remove your information from the Registry after submission. Under **OPTION TWO** your information can be removed from the Registry. Under **OPTION TWO**, you may also decide to change to **OPTION ONE** by having your identifying information permanently removed.

CONTACT PERSON(S):
If you have any questions, at any time, about this research please contact your doctoror Dr. Ramsay L Fuleihan of the Immune Deficiency Foundation at telephone number 866-939-7568 or 443-632-2556. If you still have questions, you can also call the U.S. government office, Office for Human Research Protection (OHRP) which oversees this type of research at telephone number 866-447-4777.

If you have any questions regarding your rights as a research participant, please contact Kim Lerner, Chair of the Independent Investigational Review Board, Inc. at toll free 1-(877) 888-iirb (4472) during regular working hours. You can also contact the Independent Investigational Review Board, Inc. if you would like to report problems in a research study, express concerns, ask questions, request information, or provide input. The Independent Investigational Review Board is a committee established for the purpose of protecting the rights of participants in a research study. For more information about your rights and role as a research participant you can visit the Research Participant section of the IIRB, Inc. website at www.iirb.com.

IIRB is not able to answer specific questions about appointment times, etc. but you may contact IIRB if the Registry staff cannot be reached or if you wish to talk to someone other than the Registry staff.

Do not sign this consent form unless you have had a chance to ask questions and have received satisfactory answers to all of your questions.
If you agree to be in this study, a signed and dated copy of this consent form will be given to you.

Approved by
Independent IRB
Signature 9/1/2009 Date

Initials: ____________
Date: ____________

CONSENT:
The subject/legally authorized representative and the study doctor/designee must each SIGN, DATE and TIME this authorization consent form.

1. I agree to participate (allow my child/legal dependent to participate) in the USIDNET Registry under the supervision of the Steering Committee of the USIDNET Consortium.
2. The nature and purpose of the Registry has been explained to me. This explanation included a description of the risks of participating. I have been able to ask all my questions about the registry. All the questions I asked were answered.
3. I have read, this entire consent form in a language I understand well and all blanks or statements that require completion were completed before I signed.
4. I authorize the release of my (my child/legal dependent's) medical records for research or regulatory purposes to the sponsor, the FDA, DHHS agencies, governmental agencies in other countries, and the IIRB®.
5. By signing this consent form, I have not given up any of my/my child's/legal dependent's legal rights.
6. I wish to participate following the conditions outlined below (choose one only of the three choices by inserting your initials in the correct box):

OPTION ONE in which no record of my personal identity is kept by USIDNET.

______________ Initials

or

OPTION TWO in which my identity will be kept in a separate location by USIDNET and will be linked to my Registry information by an assigned code number.

Plus

Under OPTION TWO-A all communication between the Registry and me will be sent thru my original physician, unless my physician cannot be located or does not know my current contact information.

______________ Initials

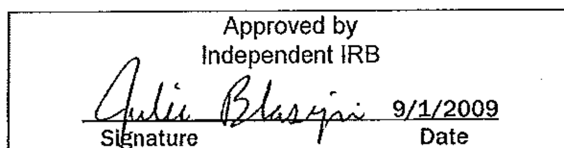
or

OPTION TWO in which my identity will be kept in a separate location by USIDNET and will be linked to my Registry information by an assigned code number.

Plus

Under OPTION TWO-B communication between the Registry and me can be directly by the Registry staff with all communications also sent to my physician.

______________ Initials


Approved by
Independent IRB
Signature 9/1/2009 Date

Consent and Assent Instructions:

Consent: Subjects legal age of consent and older must sign on the subject line below
For subjects under legal age of consent, consent is provided by the Legally Authorized Representative

Assent: Is not required for subjects 12 years and younger
Is required for subjects ages 13 through age of legal consent using the Assent Section below

Subject Name:____
Print Name

CONSENT SIGNATURE:

Subject:____
Signature (if no legally authorized representative is used)

Date:__________________________ Time:__________________________

Legally Authorized Representative:______________________________
(when applicable) Signature

Date:__________________________ Time:__________________________

____
Authority of Subject's Legally Authorized Representative or their Relationship to the Subject

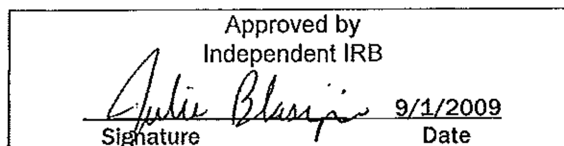
I have explained the nature, purposes, benefits, and risks of participation in the registry to the above subject/legally authorized representative. I have also offered to answer any questions the above subject/legally authorized representative might have with respect to the registry and have fully and completely answered all such questions.

____
Signature of Principal Investigator/Delegate/Person Conducting Informed Consent Discussion

____
Print Name of Person Conducting Informed Consent Discussion

Date:__________________________ Time:__________________________

Approved by
Independent IRB



9/1/2009
Signature Date

Initials: ____________
Date: ____________

ASSENT SIGNATURES, For Subjects Ages 13 through age of legal consent:

Assent:

This research study has been explained to me and I agree to be in this study.

Subject's Signature for Assent:______________________________________

Printed Name of Subject: ______________________________________

Date:__________________ Time:_________ Age (years):__________________

I confirm that I have explained the study to the extent that is compatible with the subject's ability to understand, and that the subject has agreed to be in the study.

Signature of Person Conducting Assent Discussion:____________________________

Date:______________________________________ Time:________________

Copy of consent form given to research participant on (date) _________ by (initials) _________

Independent Investigational Review Board, Inc.
Approved: 9/1/2009

Authorization for collaboration of USIDNET data with that of CIBMTR

USIDNET would like to collaborate the data of individuals with Primary Immune Deficiency Diseases (PIDD's) that are treated by bone marrow or stem cell transplantation, with that of the Center for International Blood and Marrow Transplant Research (CIBMTR). All bone marrow transplant must by law now be reported to a central database held by the Center for International Blood and Marrow Transplant Research (CIBMTR), which is, like the USIDNET Registry, a password-protected database with assigned code numbers rather than patient names. The data collected before transplantation in the USIDNET Registry are important for those doctors who perform the bone marrow /stem transplantation. During and after the stem cell transplantation, the transplant doctors will collect and submit clinical data, laboratory details and the status of the transplant to the CIBMTR Registry. Once the bone marrow transplantation procedure has been completed, patients will be followed by their immunologists to be completely informed about the details of their bone marrow transplantation, the data collected in the CIBMTR- Registry will then be transferred to the USIDNET National Registry.

CIBMTR data is used for approved research projects to determine best practices for transplants. USIDNET has worked with CIBMTR to harmonize data forms so that PID patient data does not have to be completely re-entered if a transplant is performed. If you (your child) have a transplant to treat your PID, would you direct the code numbers of the USIDNET Registry and the CIBMTR Registry to be linked?

☐ Yes

☐ No ____________________

Consent and Assent Instructions:

Consent: Subjects legal age of consent and older must sign on the subject line below

For subjects under legal age of consent, consent is provided by the Legally Authorized Representative

Assent: Is not required for subjects 12 years and younger

Is required for subjects ages 13 through age of legal consent using the Assent Section below

Subject Name:____

Print Name

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CONSENT SIGNATURE:

Subject:____

Signature (if no legally authorized representative is used)

Date:____________________________ Time:____________________________

Legally Authorized Representative:____

(when applicable) Signature

Date:____________________________ Time:____________________________

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Authority of Subject's Legally Authorized Representative or their Relationship to the Subject

I have explained the nature, purposes, benefits, and risks of participation in the registry to the above subject/legally authorized representative. I have also offered to answer any questions the above subject/legally authorized representative might have with respect to the registry and have fully and completely answered all such questions.

____

Signature of Principal Investigator/Delegate/Person Conducting Informed Consent Discussion

____

Print Name of Person Conducting Informed Consent Discussion

Date:____________________________ Time:____________________________

ASSENT SIGNATURES, For Subjects Ages 13 through age of legal consent:

Assent:

This research study has been explained to me and I agree to be in this study.

Subject's Signature for Assent:____

Printed Name of Subject: ____

Date:__________________ Time:_________ Age (years):____________________

I confirm that I have explained the study to the extent that is compatible with the subject's ability to understand, and that the subject has agreed to be in the study.

Signature of Person Conducting Assent Discussion:_______________________________

Date:_______________________________________ Time:_______________

Copy of consent form given to research participant on (date) _________ by (initials) _________