NIH Office of Intramural Research
Office of Human Subjects Research Protections

IRB MEMBER UPDATE

Winter Edition DECEMBER 2022

Photo by Rodion Kutsaiev on Unsplash

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IRB MEMBER ANNUAL SURVEY

We have sent out the IRB Member Annual Survey to you all via email on December 9, 2022. Please take 5 minutes to respond to this survey if you have not already done so. These surveys are important in helping us figure out what processes are working well and where there is room for improvement.

- **IRB Member Survey link**
- **RCRC Member Survey link**
- Both surveys should be completed by **December 31, 2022**

Go Live Update

We will be going live on Tuesday, January 17, 2023, inside the NIH firewall. As you know, two issues impacted our timeline. Below it is explained how they have been addressed.

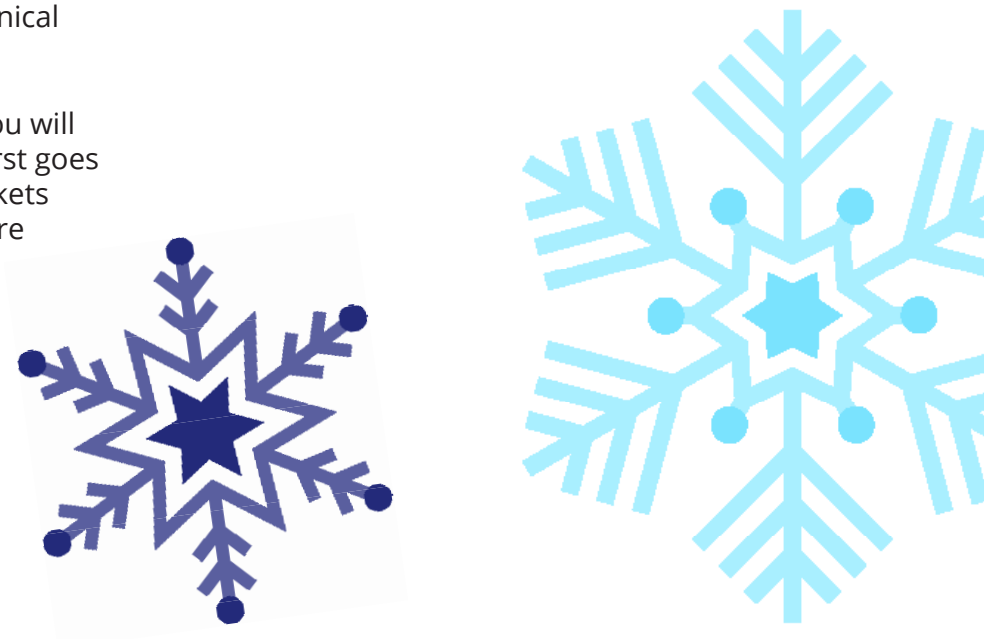
As part of the implementation process for any new software system at NIH, an in-depth security scan is performed by the NIH Information Security team. Through this process, security issues were brought to light. Many of these issues have been addressed by Huron. For those that haven't, a plan to mitigate these issues was presented by Huron and accepted by the Clinical Center and OD ISSO. We are permitted to go live INSIDE the fire wall in January. This will only impact the ability of external users (our unaffiliated IRB members and non-NIH sites) to access the system. Huron is currently working to address the issues keeping us from going outside the firewall. Once this is complete, our goal is to go outside the firewall in Spring 2023.

The second issue is the readiness of the system to be able to transmit data to the Clinical Center and to NCI through an API. Huron resolved this issue, and the Clinical Center and NCI are receiving data as needed. This is a mission critical function for clinical research operations at the NIH.

Note that for unaffiliated members, you will not have access to PROTECT when it first goes live. The IRBO will be sending you packets of review materials for meetings you are attending via email.

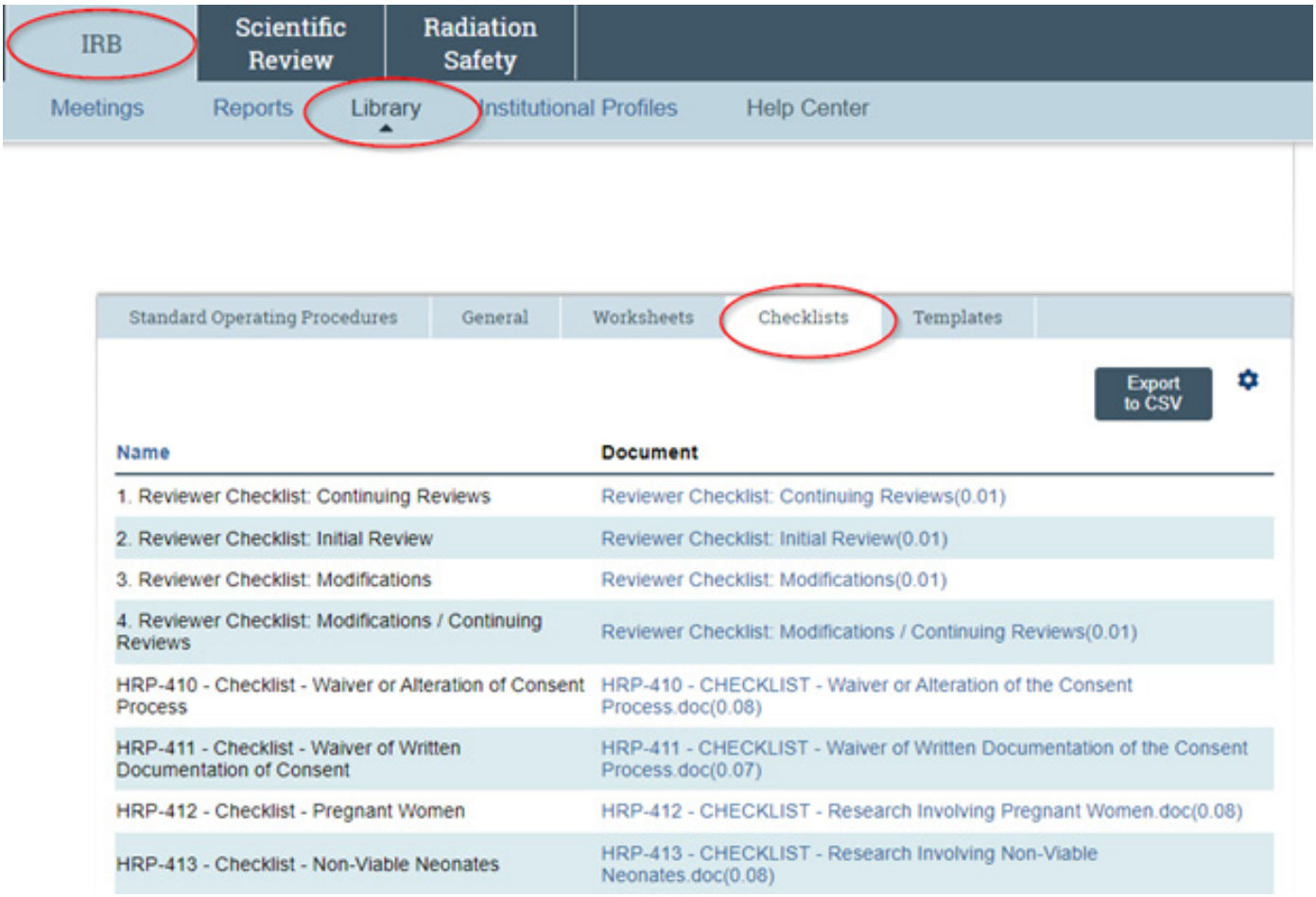
IRB Member Trainings

IRB members received the opportunity to attend one of two PROTECT IRB Member training sessions on Oct 28th and Nov 7th. Both sessions were identical, and members can view the recordings of the session along with the slides on the **Share Point site**. This Share Point site is also behind the NIH firewall so cannot be accessed by unaffiliated IRB members. You will have to sign in and then scroll down to the section titled *IRB Staff Training Materials* and then click on the folder titled *IRB Reviewer Materials*. If you are having trouble logging in, please place a ticket with the iRIS Help Desk. Unaffiliated members, if you would like a copy of the presentation emailed to you, please let us know.



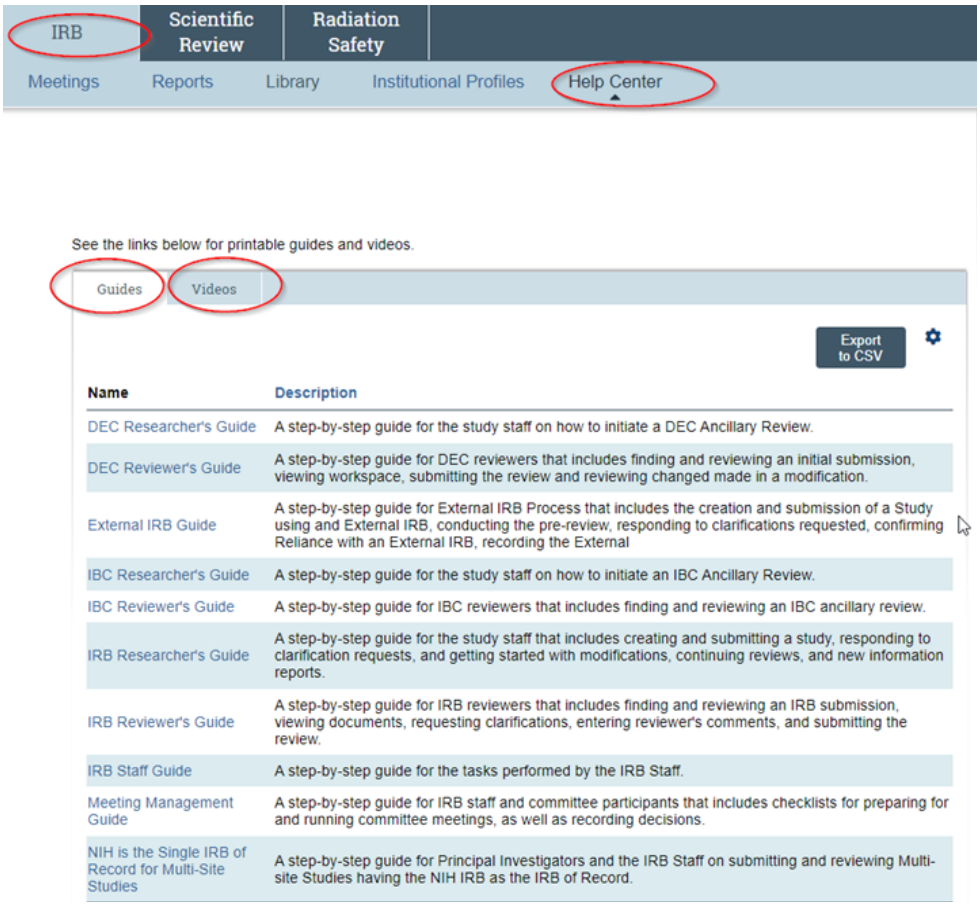
IRB Member Process Change Reviewer Checklist

In our new PROTECT system, IRB members will complete and upload reviewer checklists as part of their reviews. These checklists are located in the PROTECT system as shown on the screenshot below. Reviewers download the checklist, complete it, save, and upload into PROTECT in their review.



IRB Member Training Guides/Training Videos

IRB members can access user training guides and training videos, which are located in the PROTECT system as shown on the screenshot below. These were created by Huron for NIH and should be reviewed and utilized alongside your reviews in the beginning, so you know what steps to follow.



Training Environment (or "Sandbox")

We have configured a training environment for PROTECT users to log into with their NIH credentials. This site is not accessible currently to unaffiliated IRB members. In this environment, users can log in, tour the workspace and navigation, and see how the system works. As IRB members, you will not see assignments or reviews in your inbox because there is not much test data in the system, but if you would like to look and see what the environment is like, you may use the **sandbox** environment to do so.

Visit our eIRB Project website!

We have a page on our OHSRP website devoted to the eIRB Refresh Project. Progress updates and testing and training opportunities can be found here. Please visit anytime to see what's new! **eIRB Refresh Project Page**

Questions & Comments

We have created an eIRB Project Mailbox for the community to send us general questions and comments. This is monitored by our eIRB Project Manager, Meredith Mullan, and our eIRB Change Management Lead, Sue Tindall. Send your questions here and one of us will respond to you. (**OHSRPeIRBProject@od.nih.gov**)

New ICF Review Process Updates

OHSRP is developing a new program, tentatively called the **Informed Consent Enhancement Program**, with the goal of improving the informed consent process across the IRP, as well as reducing the number of Reportable New Information reports (formerly REFs) submitted to the IRB.

The program will have three components:

- Review of the Informed Consent Document – improving readability prior to IRB review and approval
- Education (Coming in 2023) – educating study teams about their protocol-specific, IRB-approved consent process, and how to handle unexpected situations related to the consent process as they arise
- Observation (Coming in 2023) – For newly-approved IRs, observation by OHSRP of the informed consent discussion that takes place between the study team and the potential participant. We have just begun piloting the enhanced review of informed consent documents submitted at the time of IR. Chris Witwer, Policy Analyst in the office of Policy and Accreditation, is working alongside IRB Analysts to provide readability feedback to study teams during pre-review. Feedback incorporates lessons and tools from OHSRP's *How to Write an Effective Consent Form: A Workshop for Investigators, Protocol Navigators and Research Staff*, presented by Peg Sanders and Chris Witwer.

We hope that you will soon begin to see more readable consent documents during your reviews. One of our goals is to achieve as close to a 6th–8th grade reading level as possible (required template language excepted). If you have questions or feedback about this program, Chris would love to hear from you: **Chris.Witwer@nih.gov**

Returning Secondary Genomic Findings to Research Subjects

A new IRB guidance was released this fall regarding the return of secondary genomic findings to research subjects titled, **IRB Guidance for Return of Secondary Genomic Results in the NIH Intramural Program**. This document discusses the IRB's expectation regarding the return of clinically significant findings that can be generated by genomic research methodologies being used by researchers across the Intramural Research Program (IRP).

There was presentation of the topic in September by Sara Hull and Ben Berkman that is available on the NIH Videocast website titled, **NIH IRB Expectations for Returning Secondary Genomic Findings to Research Participants**. There is also a more operational guidance document in process, and more information will be sent out when it becomes available.

In the meantime, as of October 1, 2022, the NIH IRB expects new protocols to describe a plan for returning clinically actionable secondary genomic findings to research participants, unless there is a strong justification not to do so.

The most commonly acceptable reasons for not returning results will be:

1. the absence of a clinical relationship with participants or
2. the data being generated by the study are insufficient for conducting secondary analyses.

Protocols and consent forms should describe the plan for the return of secondary genomic results when the study involves **genomic sequencing as part of the primary research objectives**. In the protocol, this information is currently provided in the *Management of Results* section. For the consent, there is suggested language for Investigators in the **Consent Library** under the Genomic Sequencing section in the subsection titled *Secondary Findings*. Once the operational guidance is released, there may be additional changes.

Further information and resources are available on the IRBO Website on the **Secondary Genomic Findings page.**

Pregnant Partners of Research Subjects

Some protocols at NIH involve the collection of pregnancy outcome data on the *pregnant partners* of their research subjects. The Investigator may be interested in this data for various reasons; however, this involves the release of the private information of a person who has not signed a consent form or been through any consent process. This means they have not been informed of the potential risks of the unintended release of their information, an overview of confidentiality protections, and an explanation of a Certificate of Confidentiality and the Privacy Act. Remember that medical information at NIH is not protected under the Health Insurance Portability and Accountability Act (HIPAA), which is not common knowledge.

The stance of the NIH IRP is that *pregnant partners* of research subjects are also themselves considered research subjects. To collect pregnancy outcome data, the *pregnant partner* of a research

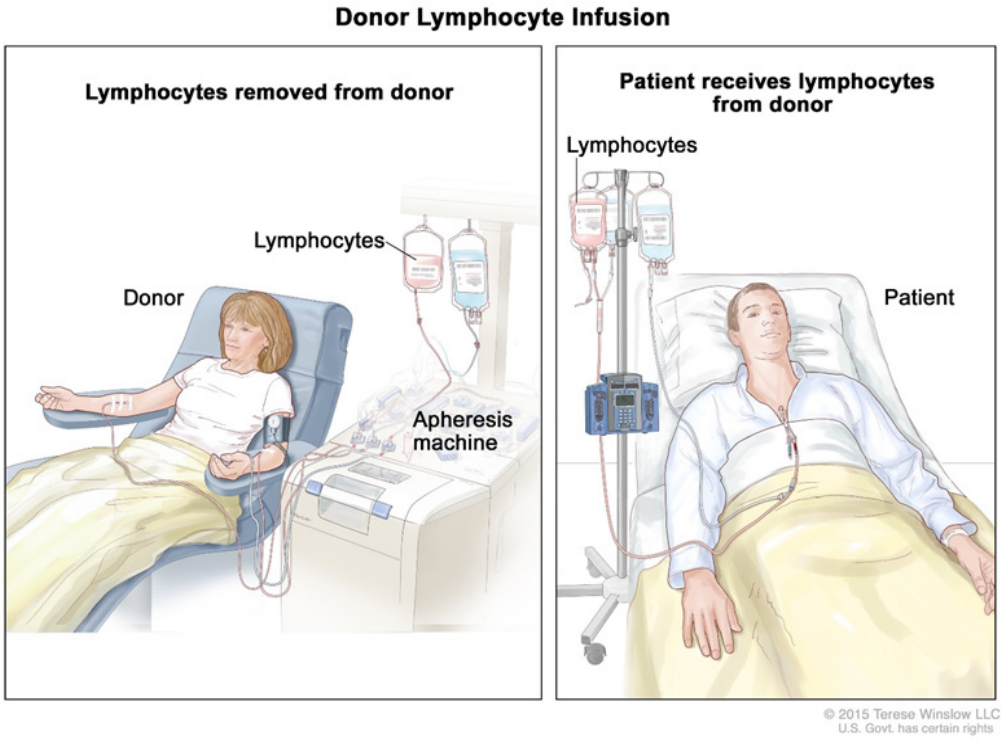
subject must be enrolled on a protocol. If a protocol is not specifically collecting pregnancy outcome data on someone not enrolled, then further no action needs to be taken.

Investigators who are interested in collecting pregnancy outcome data on a person who is not eligible to be enrolled on their protocol have a couple of options. The first option is to submit an amendment to the protocol that adds a new cohort to include these subjects; this cohort would require a new consent specific to their needs. The other option is to enroll the person on the *NIH Intramural Research Program's Pregnancy Registry Protocol for Subjects and Their Partners* (IRB 000268). The PI of this protocol is Gini (Virginia) Guptill, and she should be contacted by any interested PI.

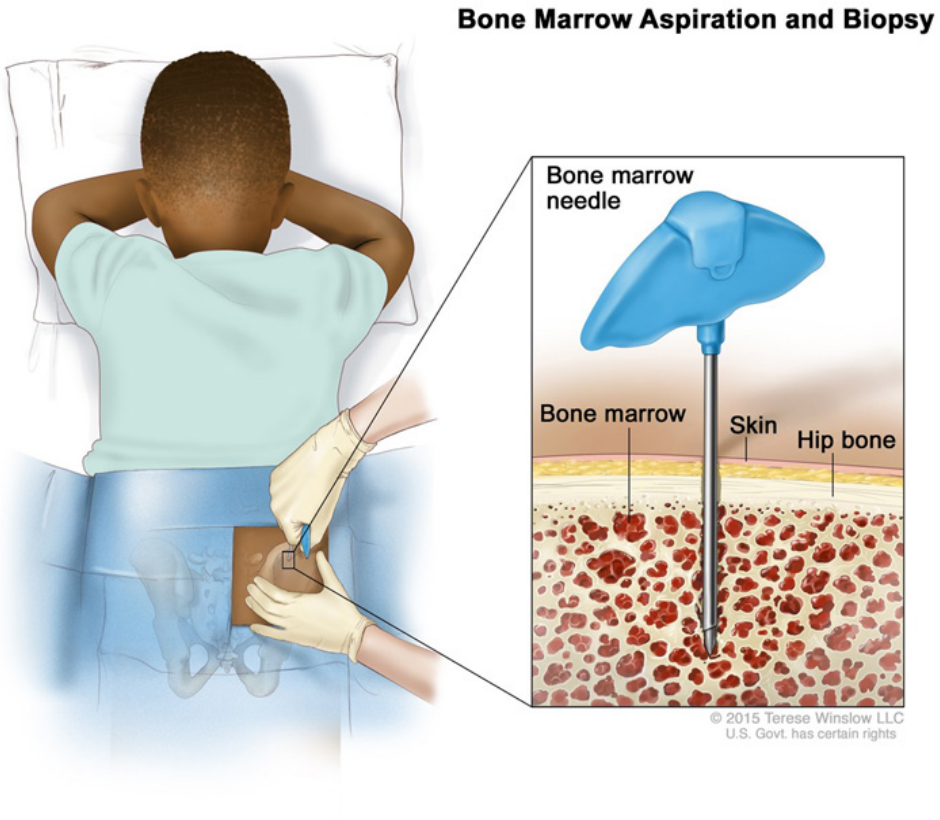
Healthy Donors for Bone Marrow or Stem Cell Transplant Protocols

Methods for Collection of Cellular Products

At the NIH, there are protocols that involve the donation of various cellular products through a process called apheresis. Apheresis is a medical procedure where blood is removed from the donor's body and filtered through a machine that only collects the part of the blood that the medical team wants and then returns everything else to the donor. The collected cell product can then be used for various types of cellular therapy protocols. Apheresis has the potential to be fairly risky and is considered greater than minimal risk. The following picture is an example of one type of apheresis and cellular therapy.



There is also another option for cell collection that is used for bone marrow transplants. In bone marrow transplants, you can give a patient a new immune system by harvesting a portion of a donor's bone marrow for infusion into the recipient patient. The bone marrow harvest involves inserting a needle into the donor's hip bone and taking out roughly 3 to 5 soda cans worth of bone marrow. Below is a picture of a diagnostic procedure called bone marrow biopsy which looks similar to a bone marrow harvest but they only collect about 2–3 teaspoons of bone marrow during that procedure. Here is a teaching video of a real bone marrow harvest, if you are interested. A bone marrow harvest is more invasive and carries more risk due to the volume of bone marrow being removed. Both procedures are considered to be greater than minimal risk.



So why is this relevant?

In some of these protocols, the person donating the cellular product is also the person who is going to receive the final cell therapy product, usually in some modified form. So, they are undergoing the risk of the collection along with receiving any potential direct benefits from the therapy. However, there are also protocols where the person donating is someone else like a **healthy volunteer**. In this case, the healthy volunteer bears the risks of the collection procedure but does not receive any direct benefit, even if the recipient of the therapy is a family member.

This is not a problem in healthy adults who have the capacity to consent to a greater than minimal risk procedure that is of no direct benefit to them. This is a problem with a healthy child who is a potential donor for someone else. For children, research involving greater than minimal risk and no prospect of direct benefit to an individual subject can be approved under §46.406 as long as it is likely to yield generalizable knowledge about the subject's disorder or condition and the risk represents a minor increase over minimal risk. Since the healthy child has no disorder and these collection procedures are greater than a minor increase over minimal risk, the collection would not be approvable under §46.406. The only option for approval would be to go through the §46.407 process and ask for approval by the Secretary of HHS.

What this means is that it is rightfully difficult for the IRB to approve the process of healthy children donating cellular products for research purposes. However, there is a type of therapy where the donation process may not be considered research.

Stem Cell or Bone Marrow Transplant

At NIH, there are a few Institutes that conduct protocols that include stem cell or bone marrow transplants. These protocols use apheresis to collect stem cells or a bone marrow harvest to collect bone marrow that is then used to transplant a healthy immune system into an affected recipient. It is not uncommon that the best donor candidate is a relative who is a child.

So, how can that child donate their stem cells or bone marrow to their family member if it is a greater than minimal risk procedure that is of no direct benefit to them? In this case, the collection of the bone marrow/stem cells is not considered a research procedure and is considered standard of care. This means that the procedure is outside the consideration of the IRB.

Why? This decision is based solely on the experience of the healthy donor. If the affected recipient has the possibility of receiving a standard of care transplant at another hospital, then the healthy child/adult would be allowed to donate. The experience of a healthy child or adult to donate for a transplant at NIH does not differ from the standard of care transplant donation process that occurs at other transplant centers. For example, the healthy donor undergoes the same clinical consent process that anyone at Johns Hopkins Hospital or University of Maryland Medical Center would experience.

Since the donation is standard of care, would a healthy donor for a stem cell or bone marrow transplant ever have to sign a protocol consent? Yes. If there will be research procedures that are beyond the standard of care collection, the research consent and assent documents would have to cover those activities. The research activities would also have to receive IRB approval. These activities are typically minimal risk and usually include the collection of identifiable data, blood collection, excess bone marrow sampling, excess apheresis sampling, and genetic testing.

IRB Member Tip Sheets and Education Sessions

This year we initiated IRB Member Tip Sheets and education sessions. Every month a tip sheet is sent out with the IRB meeting agendas that gives a brief overview of a topic commonly discussed by members at IRB meetings. This is followed by a brief presentation of the information during the IRB meetings for that month. The hope is that these tips sheets will provide a snapshot of the topic and include links to more detailed information.

There IRB Member Tip sheets are available on the IRB Member Review Resources page on the IRBO website. Here are the topics that were covered this year:

- Research with Economically or Socially Vulnerable Subjects
- Research Involving Pregnant Subjects
- IRB Member Review of Consent Forms
- COI-What IRB Members Need to Know
- IRB Review of Possible UPs
- Research Involving Children
- Reportable Event Review Process-IRB vs. RCRC
- Consent form considerations for Early Phase research
- Data and Safety Monitoring Plans
- Device Determinations
- Equitable Selection

Have a Tip Sheet topic to suggest? Feel free to email suggestions to the Compliance and Training Inbox at ohsrpcompliance@od.nih.gov or contact any of the members of Compliance and Training di