

## Partners Human Research Committee

### Returning Individual Results and Incidental Findings to Participants in Genetic Research

#### Points to Consider

*This guidance document can be used to help investigators consider the issues involved in return of individual genetic research results or incidental findings to subjects. It can be used both to evaluate older or ongoing studies where a significant result is found as well as when designing a new study that may or may not anticipate returning results. We remind you that procedures for returning genetic research results to participants must be approved by the IRB.*

*Considering whether return of research results/incidental findings is appropriate for a specific case often involves review of multiple factors. Also, it may be hard to generalize a review to other subjects or studies - most will be reviewed on a case-by-case basis.*

*Please contact Dr. Elizabeth Hohmann, Chair and Director of the PHS Human Research Committee, if you would like to discuss a specific study in more detail.*

#### GENERAL CONSIDERATIONS

##### **1) Basic criteria for evaluating whether a research result should be returned to subjects**

- a) The findings are scientifically and analytically valid and can be reproduced in a CLIA-approved lab in a second sample from the same subject.
- b) The results are of “high medical importance”, i.e. there are significant implications for the subjects’ health or reproductive issues.
- c) Treatment or amelioration of the condition is available; or reproductive genetic counseling may be important.

*There may be situations where less rigorously-validated information is reasonably returned to subjects, with appropriate caveats from an experienced clinician.*

##### **2) Consent form (reviewing a consent form for an existing study)**

- a) What does the consent form say about return of genetic research results (RORR)?
  - i) Is it silent on RORR?
  - ii) Does it state that no results will ever be returned to subjects?
  - iii) Is there language in the CF that describes RORR and the circumstances under which results will be returned?
    - (1) Is receiving genetic research results optional (with check-box)?
  - iv) At the least, is re-contact for other reasons allowed?

##### **3) Is the result an “individual research result” or an “incidental finding”?**

- a) Individual research result = a result related to the condition under study or the aims of the research
- b) Incidental finding = a finding not related to the condition under study or the aims of the research
  - i) Returning an Incidental finding to subjects may be more anxiety-producing, as these results aren’t expected. This is especially true for healthy controls.
- c) Note: There is no duty to search for individual research results or incidental findings. Currently, there are no national standards for returning research results.

## **SIGNIFICANCE AND VALIDATION**

### **1) Who will determine whether the finding is of “high medical importance”?**

- a) The PI? The PI with the IRB? Expert consultants? A committee charged with this responsibility?
- b) What criteria will be used to define “high medical importance”; e.g. penetrance of the mutation, national consensus on the importance of the finding, etc.?

### **2) What actions are available to treat, prevent, or ameliorate the condition?**

- a) For example; drugs, lifestyle changes, reproductive counseling.
- b) You may consider the availability and cost of treatment.

### **3) Can the finding be reproduced in a CLIA certified lab?**

- a) Samples have to be re-tested in a CLIA approved lab to confirm research findings. The PHS Lab for Molecular Medicine is approved to perform clinical-level sequencing.
- b) Will the initial finding be reproduced in a CLIA lab before notifying the subject or after? In general, a new sample from the subject will need to be analyzed clinically, depending on the type of sample. What if the cost of testing is significant – who will pay?

## **PRACTICAL CONSIDERATIONS/LOGISTICS**

### **4) What type of study is it?**

- a) Multi-center clinical trial? Individual study? Local disease-specific repository? Department/hospital wide repository? Secondary use of samples from any of the above?
- b) Does the study include children or adults with impaired decision-making?
  - i) Studies that include vulnerable populations, especially children, need to consider the type of result that will be returned. Generally, incidental findings that reflect adult-onset diseases are not disclosed to children/parents.
- c) How does the study type affect return of results?

### **5) Benefit/risk to subjects and/or family**

- a) Does the ‘net’ benefit outweigh the risk of learning the result?
  - i) Possible risks include psycho-social risks associated with learning about a serious medical condition or reproductive impact of the finding.
- b) Are there health or reproductive implications for family members?
  - i) Are there any circumstances where a result should be returned to family members?
    - (1) Generally, researchers should not have to meet standards that are higher than those that are required clinically, and therefore researchers are not required to return results to family members. There is a great deal of discussion around this issue nationally.
    - (2) The proband may decide to inform family members, if desired
    - (3) If the proband is deceased and there is a perceived benefit to sharing results with family members, do not contact the family until this is discussed with the IRB

### **6) Timeliness/Age of subjects**

- a) When was the sample obtained? Months ago? Years ago? Does the condition under study make it unreasonable to contact subjects who donated samples years ago? Have the subjects “aged out” – has it been so long since the sample was donated that subjects are too old to benefit from this knowledge?

**7) Who found the result?**

- a) The PHS PI of the original study
- b) A secondary user at PHS or outside of PHS

**8) Who will return the result to the subject?**

- a) This person should be someone known to the subject from the primary study or as explained in the consent form, preferably a physician with training in interpreting genetic results or genetic counselor.
- b) What are the relevant qualifications/experience of the person who will return results?

**9) What is the process for returning the result?**

- a) Letter, phone call, etc. or some combination? What will happen if the subject can't be reached?
- b) Will the subject's clinician be notified? At what point – same time as the subject? After the subject? Generally it is difficult to reliably identify a subject's clinician. The IRB recommends notifying the subject first, and providing information for the clinician upon the subject's request.
- c) Will referrals to genetic counselors or other experts be available to subjects?

**10) Financial considerations**

- a) How expensive is re-testing to confirm the result and/or clinical testing once the subject has been notified? Who will bear the burden of paying for testing?

**OPTIONS FOR RETURNING GENETIC RESEARCH RESULTS AND LANGUAGE THAT CAN BE USED IN CONSENT FORMS**

- 1. **Studies that do not anticipate or have a plan for returning results, but do not want to exclude the possibility**
  - a. Include neutral language that doesn't exclude RORR

For example: replace “*You will never get the results of research performed on your sample*” with

“You should not expect to get personal results from this research. Researchers will study samples and information from many people; it will take many years before they know if the results have any meaning. There is a small chance that researchers could find something that might be important to your health. If this happens, we may contact you to find out if you would like to learn more. However, even if we find something important to your health, we cannot guarantee that you will be contacted”.

- 2. **Studies that do anticipate returning results**

- a. **Should RORR be optional or not?**

- i. **In general, the PHS IRB recommends that investigators do not make receiving results optional for subjects (see pros/cons below)**

- a. Receiving results is offered as an option

- o **Pros** – gives subjects a choice ‘up front’ and they will never know if there is a significant finding; there may be less anxiety involved

- **Cons** – what if a research finding is clearly important and treatable? What if the result could affect reproduction? Will you be comfortable honoring the subject’s option to not receive results?
- b. Receiving results is not optional
  - **Pros** – PI is not caught with a clearly important finding that can’t be returned to the subject. The subject can always refuse to learn the finding at the time he/she is contacted.
  - **Cons** – Lessens the subject’s autonomy – he/she may want to avoid the anxiety of knowing that something is significantly wrong.
  - Subjects should understand what they are signing up for – they may not wish to participate under these circumstances.

### 3. An example of RORR consent form language approved for use in a tissue repository

- ▶ You may receive a newsletter or other information that will tell you about the research discoveries from the Bank. This newsletter will not identify you or describe any of your personal results.
- ▶ Generally, we will not return individual results from research using your samples and data to you or your doctor. Research using your sample is just a stepping stone in learning about health and disease. Most of the findings that come from studying your sample will not be relevant to your personal health. However, in the future, this may change.
- ▶ It is important to remember that research results are not always meaningful and are not the same as clinical tests. While you should not expect to receive any results from your participation in this research, if experts from the Bank decide that research results from your sample are of high medical importance, we will attempt to contact you. In some situations, follow up testing might be needed in a certified clinical lab. You and your medical insurer may be responsible for the costs of these tests and any follow up care, including deductibles and co-payments.
- ▶ It is possible that you will never be contacted with individual research findings. This does not mean that you don’t have or won’t develop an important health problem.
- ▶ In the future, when research results are published, they may show that certain groups (for example, racial, ethnic, or men/women) have genes that are associated with increased risk of a disease. If this happens, you or others may learn that you are at increased risk of developing a disease or condition.