Discussing Rare Disease Research Findings to Participants: General Guidance on Best Practices

We have prepared this document for clinical investigators in the Rare Disease Discovery Hub (the "Hub") who are considering inviting their patient(s) to participate in Hub research. You have identified a question regarding your patient's rare disease that can only be addressed or explored further in a research-based setting. All participants enrolled in the research activities of the Hub must be invited by a care-providing clinical investigator willing and able to keep them informed of findings from the research.

According to published reports, there is evidence that patient-participants may conflate research findings and clinical results, unless the difference is made very clear to them throughout the course of a research study. When a referring physician discloses research findings to their patient, the Discovery Hub suggests covering the following points with regard to genetic research findings:

1. **Differences between research and clinical care**

   The goal of research is to provide generalizable new knowledge through a process, which may not offer any benefit to the individual. Research laboratories are not subject to the same standards of validation or quality controls (ex., re-confirmation of sample identity) as are clinical laboratories. Clinical laboratories generally provide more rigorous testing methods and have standards for interpretation, such as clinically accredited training of personnel, and take strong measures to protect chain of custody. Research, on the other hand, may have an advantage in being able to attempt novel approaches to gain new understanding of a disease or variant. Research findings from the Hub have not been validated in a clinical setting (until / unless the referring physician has coordinated this, which frequently may not be possible), and thus research findings hold a non-negligible level of uncertainty. **Medical decisions should be based on results obtained from clinical testing, and it is advisable to replicate research-based testing in a clinical laboratory when possible.**

2. **Conclusions may be impossible or may change over time as new knowledge accumulates**

   The fields of the genomic sciences and rare diseases are still evolving. Even after clinical validation of a finding (if possible), it may be unclear what, if any, clinical recommendations should be made until a strong body of evidence (contributed by various sources i.e. population, computational, functional, segregation data) exists for or against a gene/variant-disease association. The research findings from this study may not contribute greatly to a body of evidence.

   In fact, there is a strong possibility that, through the course of our learning more about this variant over time, we may come to find out that our research findings today were mis-understood with respect to associating a variant as disease causing. Research findings, over time can prove to be contradictory and theories can change over time.

3. **Therapeutic misconception by the patient participant should be avoided during the discussion of research results.**

Finally, if you are unsure about the purpose or limitations of an experimental assay or the strength of evidence derived from its results, it is important to engage with the scientist performing the assay to learn more. The Hub steering committee is available to facilitate further discussion.