What to look for in reviewing return of secondary genomics plans

Does the research perform genomic analysis that will create data suitable for interrogation to identify secondary findings?

Analysis that can be interrogated:

- Whole Genome/Exome sequencing

Analysis that cannot be interrogated:

- Single Nucleotide Polymorphism (SNP) analysis
- Transcriptional arrays
- RNA sequencing
- Targeted sequencing of limited numbers of genes
- Microbiome/virome sequencing

Is the nature of the study and relationship of the investigator to the participant such that there is a reasonable expectation to return secondary findings?

Examples of studies that would be expected to return secondary findings:

- Longitudinal studies of rare disorders where the goal is to perform deep phenotyping as well as analysis of exome and/or genome data.
- A study that does not regularly perform large-scale sequencing, but occasionally does so for select participants, would have an obligation to those specific participants.
- A study that focuses on the health of particular community and meaningfully engages community members in the development and implementation of the research, also known as community-based participatory research.

Examples of studies not expected to return secondary findings

- A protocol looking at genetic factors relating to host-susceptibility for COVID-19, where even though there is an extensive health history taken, the participants are being seen only once and do not expect to receive any clinical care or information from the research team.
- A study that obtains consent and samples up front for genetic analysis, but explicitly does not plan to do that analysis for many years and does not have ongoing interactions with the participants.
- A large-scale population health study where participants regularly fill out health related questionnaires, but where there is minimal direct engagement except in select cases where participants are recruited for specific sub-studies.

What should be in the protocol?

- Clear identification as to whether or not secondary findings will be returned to study participants. If no findings will be returned, a justification must be provided and determined to be adequate by the IRB.

If secondary findings will be returned, the protocol should include the following information:

- What secondary findings will be sought and returned. The minimum acceptable is the ACMG list current at the time the analysis is performed.
- That the analysis will be conducted in a CLIA certified laboratory. If the initial analysis is performed in a CLIA certified lab, no additional sample collection or analysis is necessary. If the initial analysis is not in a CLIA certified lab, the protocol should address the collection of a second sample for analysis in a CLIA certified lab at no cost to the participant.
- A description of the anticipated timing of the analysis and participant notification. In particular, if it is known that this will not happen for an extended period, this should be stated.
- Whether the analysis for secondary findings will be performed once or repeated periodically. Once is acceptable.
- How the findings will be returned to participants including:
    - Method of notification of need for additional sample collection, if applicable
    - Whether results will be discussed in person, via telephone or telehealth
    - Whether genetic counselors will be involved. In general, unless the investigator has sufficient expertise, a genetic counselor should be present.
- To whom the secondary findings will be returned. Findings should be only returned to the participant themselves or the LAR unless there is a valid release of medical information request authorizing release to another person.

What should be in the consent?

If there is no intent to analyze for and return secondary findings in a study that is performing genomic analysis, the consent should state this. Otherwise, the following information should be in the consent.

- A statement informing that secondary genomic findings will be returned to participants.
- What secondary findings will be looked for and disclosed. It is not necessary to list specific genes. A generic statement such as "genes that are important for your health" is acceptable.
- A statement of the expectation that research participants must keep the NIH investigators informed of current contact information in order to receive their results and how to do so.
- Participants should be informed that they will not receive a negative report, unless the intention of the investigator is to provide such a report to all participants regardless of the presence of secondary findings.
- A description of expected time frame for the analysis and return of any findings relative to the time the sample is collected.
- A description of the process by which participants will be informed of secondary findings, including how they will be contacted, whether an additional sample will be collected (if applicable), and how the information will be provided to the participant.
- The participant should be informed that they may choose not to receive the information and that choice will be respected.
- A statement that the result will only be returned to the research participant or LAR. If they wish to have the result provided to another individual, they must provide a valid release of medical information request authorizing the disclosure.