# Return of Individual Research Results

The purpose of this information sheet is to provide research teams guidance on returning individual research results to study participants. This guidance is intended to apply to clinical and non-clinical research, and speaks to the specifics of genomic testing. Please note that non-investigational results that are obtained during the course of standard-of-care are not considered to be research results.

**INDIVIDUAL RESEARCH RESULTS:**
Information that is linked to the identity of a research participant and pertains to that participant and the results related to their involvement in the research study. The information may be:

- Collected at the beginning of a study to determine if a person meets inclusion and exclusion criteria for the research. These are often referred to as “baseline findings”.
- Generated about a participant during the progress of the research. These are often referred to as “in-study findings”.
- Discovered during the research and is beyond the aims of the research, but the research result has potential health or reproductive importance (often called “incidental findings”).

**RETURN OF RESULTS:**
SACRHP considers "return of individual results” to include the return of results to the participants directly, their Legally Authorized Representative (LAR) should the participants be incapacitated adults, or the parents or guardians of pediatric participants. While the results might also be provided to the participants’ health care provider, the return of results solely to the provider is not considered a return of individual results to the participant.

In addition to returning research results directly to participants/ LAR/ parents or guardians, research results may also be placed in the medical record of which the participant will have access.

For certain types of research, such as genome sequencing, it may be appropriate to return "individual" results to family members of the original study participant. Whether appropriate to return these results must be heavily fact-dependent and weighed against legal and ethical implications.

**DECISION-MAKING FRAMEWORK:**
The table below provides guidance as to which results should be offered to research participants and the recommended timing, depending on the study purpose and the result-return plan. Definitions of these terms are available below the table:

| RESULT | TIMING | |
|---|---|---|
| Clinically actionable, valid, and urgent | As soon as possible | Researchers should return these results as soon as possible as there is a clear medical benefit. Declining to return the result could harm the participant (even though the harm does not arise directly from research activities). |
| Clinically actionable, valid, and non-urgent | As soon as possible | Researchers have the discretion to offer these results to participants unless the return of those results is not feasible. |
| Other results | Researcher discretion | Researchers have the discretion to choose to offer other results to participants. Examples: non-actionable genetic results, clinical test results in the normal range, investigational or unknown results. |

- Clinically actionable: A result that has medical or personal decision-making utility, notably when additional diagnostic or preventive measures are needed or when alternative treatment is available.
- Valid: Analytically and clinically valid results. Analytic validity pertains to how accurately and reliably the test measures a certain criterion, such as a genotype of interest. Clinical validity indicates the accuracy at predicting a clinical outcome.
- Urgent: An urgent result is any result that requires immediate follow-up, typically by a healthcare professional. This result could have been anticipated due to the research and condition under study, or it may be unanticipated and/or related to a previously undiagnosed condition.
- Feasible: The individual results can be returned without compromising the research. Feasibility must consider multiple factors including bias, the resources available to communicate the results effectively, and other challenges such as cost.

A result's reliability and analytic/clinical validity must be considered when deciding whether to return a research result. Results lacking analytical validity may be inaccurate and misleading; a lack of clinical validity renders an unclear research result, raising questions about how to return the research result, and if it should be returned at all.

The reliability and validity of a test or diagnosis conducted using devices or assays is usually demonstrated by regulatory approval from the Food and Drug Administration (FDA) or certification under the Clinical Laboratory Improvement Amendment (CLIA) from the Centers for Medicare and Medicaid Services (CMS). However, there is often justification to return research results that were obtained from a non-CLIA certified lab/ non-FDA approved research test, and this should be considered on a case-by-case basis with consideration given to the context of the study and priorities of the study population. Urgent results may be re-run in a regulatory compliant and clinically reliable manner with the results returned to the participant ASAP.

Results that are unvalidated, unreliable, and not actionable carry the least justification for returning to participants. Careful consideration must be given prior to returning such results. Researchers are generally discouraged from returning:

- Results that may be misinterpreted
- Results with limited benefit to participants that may lead to significant burden (cost or complexity) to return

- Results without established clinical validity for a serious/life-threatening or sensitive health condition
- Results for which there are serious questions regarding validity and/or reliability

**INFORMED CONSENT**
Regulations overseeing research require that the consent form state "whether clinically relevant research results, including individual research results, will be disclosed to participants and if so, under what conditions." ((45 CFR 46.116(c)(8)). The DF/HCC consent form template provides instructional text as to what language should be included under different scenarios. Consent forms should ensure that the following is included:

- An explanation of which results will be returned, whether the results are clinically actionable and if results will be returned only in specific circumstances. If there is no reasonable expectation of the return of results, this should be clearly stated along with an explanation as to why.
- A statement indicating that participants have the option of declining to receive the results, and an explanation of any circumstances (if any) in which they will not have this option.

Participants may require assistance in understand and deciding whether they want to receive the results, and resources should be available to facilitate this discussion. It is important to note that even if a participant consented to receiving results at the beginning of the study, they must be given the opportunity to decline or accept results when the results become available.

**COMMUNICATION OF RESULTS:**
The research results should be communicated to participants in a purposeful way that facilitates understanding of the meaning and limitations of the results. This communication should address whether the results are clinically actionable and what is known or unknown about the meaning of the result. It is important to ensure that adequate resources are in place to refer participants for further consultation (such as a genomic counselor) or follow-up care. Participants should be made aware of all available resources.

Participants may not understand that research results can have significantly greater uncertainties than clinical results. Therefore, for research results prone to misinterpretation or misuse, it is crucial to disclose this uncertainty. For example, if an investigational, unvalidated test returns a result indicating the presence of a gene susceptible to cancer, it is important to emphasize this uncertainty and refer the participant to the appropriate follow up care where the results can be validated.

**COMMUNICATION METHODS:**
There are a variety of communication methods for returning research results, and the communication approach should be decided on a case-by-case basis to align with the participant population and context of the research. Consideration should be given to the study design and objectives, characteristics of the participant population, types of research results, expertise of the investigators as it relates to the results, resources, and infrastructure. This may include, but is not limited to, an in-person meeting, confidential letter, phone/ video conference, or placing the result in the medical record with a note that it may be discussed with the study doctor and PCP. If you have questions about the different methods for returning research results, please contact OHRS.

**REFERENCES**:

- https://mrctcenter.org/return-of-individual-results/how-to-return-irr/roadmap-by-role/
- https://www.hhs.gov/ohrp/sachrp-committee/recommendations/attachment-b-return-individual-research-results/index.html