DFCI IRB REQUIREMENTS RELATING TO RETURN OF RESEARCH RESULTS

This Information Sheet provides information to Investigators regarding the DFCI IRB requirements for DF/HCC research regarding the return of research results.

Summary of Requirements

Protocol

1. State whether or not results will be returned
2. If returning results, state that results will be analyzed in a CLIA certified laboratory and describe the plan for returning results

Consent

1. State whether or not results will be returned
2. If returning results, solicit participant preferences
3. State that results may be returned under extraordinary circumstances, regardless of participant preferences

A. Investigators Who Envision the Possibility of Offering Individual Results

1) Study protocol

a) In the study protocol, investigators should describe **a plan to use a CLIA-certified laboratory** for genomic analyses. Results may only be returned if the research samples have remained in a CLIA-certified environment at all times.

b) Investigators should **include an outline of their plan for identifying and returning individual genetic findings** in the protocol that they submit to the IRB for approval.

i. The outline should describe whether or not the research team plans to systematically analyze participants' genomic data against a particular list of "returnable" genes and/or variants, such as the list of genes published by the ACMG (http://www.acmg.net/docs/ACMG_Releases_Highly-Anticipated_Recommendations_on_Incidental_Findings_in_Clinical_Exome_and_Genome_Sequencing.pdf). If the team does not plan to utilize such a list, the outline should describe how the team will decide which variants, if identified in the genomic data, should be considered for return.

ii. The outline should describe the steps that the investigators will take if they identify a variant that they believe to be returnable, including (1) to whom the information will be provided (e.g., directly to the participant/proxy, or indirectly via the participant's physician); and, (2) how the information will be provided. Note that, in general, the IRB requires that results be returned to the participant's physician.

iii. The outline should describe how the investigators will involve clinicians with the appropriate genetics expertise (e.g., genetic counselors, medical geneticists) in the process of disclosing any germline genetic incidental findings to study participants.

iv. The outline should address the availability of resources to (1) locate and contact research participants; and, (2) provide information to all participants/their physicians.

2) Consent form

a) Investigators should **include a section in their research consent form that addresses the topic of return of individual genetic findings, solicits participants' preferences for whether or not they wish to receive results, and describes how any identified results will be returned**. Investigators may ask consenting participants a single global question regarding return of individual genetic findings. Alternately, investigators may identify a set of relevant categories of findings and ask participants to indicate their preferences regarding return within each category.

i. Investigators should also include in their consent forms a section where **participants can identify a proxy** whom they would like to receive results if the participant is unable to receive them.

b) Investigators should disclose to participants in the research informed consent form and process that, in **extraordinary circumstances** (as defined below), the information may be provided to the participant and/or his/her physician even if the participant has otherwise opted not to receive results.

i. The phrase "extraordinary circumstances" refers to rare cases in which a result is identified that entails an imminent and substantial threat to health that can be markedly reduced by an available intervention.

3) Returning incidental findings discovered during the course of research

a) When an incidental finding is discovered during the course of research that the investigator believes should be returned to the study participant, she or he should **seek approval from the IRB, or from a committee designated by the IRB.** This includes "extraordinary circumstances" (as defined above). Investigators should submit an Other Event to OHRS in order to seek this approval.

b) If both the IRB-approved protocol and consent clearly state that, if the specific variant under consideration is identified, the information will be returned to participants and/or their physicians, **case-by-case approval** by the IRB or designated committee is **not** needed. Note that, if only a single global question was asked in the consent form, IRB/committee approval is required. The IRB or designated committee may wish to identify categories of genetic alterations (e.g., research testing performed at a

clinical lab identifies a known pathogenic variant in a known gene) that should be exempt from the requirement for case-by-case approval by the IRB or designated committee.

B. Investigators Who Do Not Envision the Possibility of Offering Individual Results

Investigators who do not plan to offer individual results should be aware that, except in extraordinary circumstances as defined above, they will be unable to return any individual results from those analyses to participants or their physicians. Such investigators should take the following steps:

1) Study protocol

a) Include a section in the protocol that they submit to the IRB for approval that states that, except in extraordinary circumstances as defined above and as approved by the IRB, no individual findings will be returned to participants or their physicians.

2) Consent form

a) Include a section in the research consent form that clearly states that no findings will be returned except in extraordinary circumstances as defined above.

3) Returning incidental findings of extraordinary importance that are discovered during the course of research

a) Seek approval from the IRB, or from a committee designated by the IRB, to return findings that satisfy the definition of "extraordinary circumstances" outlined above. Investigators should submit an Other Event to OHRS in order to seek this approval. In deciding whether or not to grant this approval, the IRB or designated committee will determine whether the finding should first be confirmed in a CLIA-certified laboratory, and if so, how that confirmation will be performed, and how the results will be communicated to the research participants.