Marshfield Clinic

Guidance on Returning Research Results to Subjects

1. SCOPE

1.1. System Wide

2. DEFINITIONS & EXPLANATIONS OF TERMS

2.1. Anticipated finding: The planned outcome of the experiment or research activity.

2.2. Clinical research: Patient-oriented research

2.3. Clinical significance: A measure of the practical relevance and importance of a research finding to patients and/or health care providers

2.4. Clinical validity: A measure of the reproducibility of a research finding

2.5. Clinically actionable: A research result that in the professional opinion of the investigator requires that the subject (patient) undergo further testing, treatment or observation.

2.6. Incidental finding: A finding that is made in the course of the research activity, but is not related to the specific aims of the research.

2.7. Impracticable: Infeasible

2.8. Research result: Outcome of a research activity

2.9. Aggregate: Summary measures of the research results, reflecting the entire cohort of relevant participants (or a subsection thereof).

2.10. Individual: results derived from a single research subject

3. RESOURCE GUIDE BODY

This document is intended to provide investigators and Marshfield Clinic Research Foundation Institutional Review Board (MCRF IRB) members with guidance on when it is appropriate to return research results to subjects.

3.1. Background – Clinical Care vs. Research

a. Health care providers engaged in clinical care at Marshfield Clinic have an ethical obligation to act in the best interests of their patients. This obligation is reflected in the Clinic's mission statement ("To serve patients through accessible high quality health care, research, and education"). Consequently, all diagnostic tests and procedures, and attempts at therapeutic intervention should be undertaken in an effort to help the individual patient. In most instances, the clinical approach to a given patient follows the accepted "standard of care," thought to offer the highest probability of a satisfactory outcome.

b. Clinical research generally seeks to compare two or more interventions, at least one of which is unproven. Consequently, it is impossible to predict which intervention is "best" for the subject at the outset of his or her participation.

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c. The goal of patient care, which is to improve the health of the individual, differs fundamentally from that of human subjects research, which is to contribute to generalizable medical knowledge.

d. Despite the unavoidable uncertainty caused by reliance on the scientific method, clinical research protocols may at times offer the best remaining hope to patients whose diseases have proven refractory to the commonly accepted "standard" treatments, or for which no promising treatment currently exists. The boundaries between clinical care and research have therefore become blurred. Even though a given investigation may not be designed to directly benefit the subject, the potential exists in most clinical research studies for some (even minimal) benefit to the participant. The possibility of benefit to subjects also exists in research that traditionally may be considered non-clinical (e.g. genetic and observational, as well as translational research). Finally, unanticipated results detected by chance during the course of research activity ("incidental findings", or IFs) can potentially influence subject health and well-being.

3.2. Responsibilities of Investigators

a. Returning Results

- Traditionally, researchers at Marshfield Clinic have not been obligated to return research results to subjects. As implied above, however, the results of clinical or genetics research activity may be relevant to and influence the individual subject's health and well-being. MCRF IRB has concluded that the principles of respect for persons and beneficence set forth in the Belmont Report offer compelling reasons for investigators to offer certain research results to those individuals who choose to participate in research studies. This applies to both the aggregate and individual anticipated results that accrue as a result of the research activity, as well as to incidental findings.
- CLIA
  - In keeping with the Clinical Laboratory Improvement Act (CLIA) Subpart A,42 CFR 493.3, research laboratories that report patient specific results to a patient or physician for use in the diagnosis, prevention or treatment of any disease or impairment or for the assessment of the health of the individual must be CLIA-certified. Therefore, by law, research results from non- CLIA certified laboratories may not be returned to research subjects.
- In view of the potential importance of research related findings to the health and well-being of the individual, MCRF Office of Research Integrity & Protections (ORIP) has determined that as of July 1, 2010, each project submitted to MCRF IRB for approval will include a plan describing how the researchers will address the issue of returning research results to subjects.
  - Researchers must describe whether study subjects will be informed of relevant anticipated study-related results, as well as incidental findings, and if so, by what mechanism.
  - While some individuals, if offered the choice, might opt to not receive such information, MCRF IRB has concluded that researchers affiliated

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with Marshfield Clinic have a duty to inform research subjects of both anticipated results and incidental findings that may affect the participant's health, and which are actionable.

- Similarly, should the research reveal a finding that is matter of public health, the finding must be promptly reported to the appropriate authority.

b. Informed Consent

- As part of the process of obtaining informed consent prior to study enrollment, the subject should be informed of the research results that will be made available to him/her, in addition to those test results that will not be made available.
- This guidance encourages results to be released to subjects whenever possible and appropriate, and legal under CLIA. If the investigator concludes that it is infeasible to return any results, he or she must offer some plausible explanation as to why the specified result(s) will not be released to the subject. Possible reasons for not releasing results to subjects include:
  - It is impracticable to do so (e.g., it may be infeasible to locate subjects once a study is completed, due to delays in communication or other inefficiencies inherent to the research process, or arising from the multicenter nature of the research effort);
  - The clinical significance of the finding is not clear;
  - The finding is not considered "actionable";
  - The validity of the test employed is uncertain (e.g., the laboratory in which the test is conducted is not CLIA-certified).
- The rationale for not returning results to subjects should be explained both in the IRB application and in the consent form.
- The researcher should also define the process for determining whether a result/incidental finding is both significant and actionable. Note that in the case of research directed by investigators without relevant clinical experience, consultation with a clinician may be required to discuss, both, the clinical importance of a given finding and the possibility of appropriate intervention.
  - MCRF IRB supports the practice of providing results in an appropriate context/framework to facilitate comprehension of the risk, if any, that is implied by the result. As suggested, this should include consideration of the analytical validity of a given test (i.e., the technique used to obtain the information is well established and the results are reproducible). Limitations to the inferences that may be made based upon the data should be carefully explained to the subject.
  - In the case of genetic studies, the MCRF IRB recommends that no individual result be released without associated genetic counseling.
  - Incidental findings of non-paternity should not be revealed unless the information carries major health implications for the affected individual.

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- In addition to encouraging the return of individual test results, MCRF IRB urges researchers to make available to subjects a summary of the overall/aggregate research findings, along with an interpretation of their significance to advancement of medical science.
- In anticipation of releasing results and incidental findings to subjects, during the process of obtaining informed consent the researcher should carefully review the plan for conveying anticipated results to the subject. The researcher should ensure that the subject understands the concept of Incidental Findings. It should also be made clear to the subject that he/she will be informed of any actionable results or incidental findings that could influence his/her health and well-being.

c. Documentation

- The IRB application form(s) collect information relevant to the process of returning both anticipated and unanticipated findings (incidental findings) to subjects.
- In some cases an incidental finding may represent an Unanticipated Problem (UP). If it satisfies the reporting criteria for UPs, the appropriate report must be submitted for IRB review on a timely basis. See the institutional document, "Unanticipated Problems, Reporting and Review of," for more information.
- Finally, research-related or incidental findings that are of direct consequence to the subject's health and well-being may be recorded in the subject's Clinic medical record.

4. ADDITIONAL RESOURCES

4.1. References:

- FDA Guidance for Sponsors, Clinical Investigators, and IRBs: Data Retention When Subjects Withdraw from FDA-Regulated Clinical Trials
- OHRP Guidance on Withdrawal of Subjects from Research: Data Retention and Other Related Issues

4.2. Supporting documents available:

- None

5. DOCUMENT HISTORY

Version No.	Revision Description
1.0	New Document in Document Control transferred from Policy & Handbook Library - #3857.2 (no changes made)
2.0	

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3.0	

6. DOCUMENT PROPERTIES

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