Sheet 8: ANSWERS TO QUESTIONS FREQUENTLY ASKED OF NIH'S OFFICE OF HUMAN SUBJECTS RESEARCH (OHSR)

The following questions address issues related to research conducted by employees of NIH's Intramural Research Program (IRP).

1. WHAT IS THE NIH IRP'S HUMAN RESEARCH PROTECTION PROGRAM (HRPP)?

The IRP's HRPP is a system of policies and procedures to protect the rights and safeguard the welfare of human research subjects. The HRPP is made up of NIH ICs, NIH officials, NIH IRBs, researchers and staff who conduct and support research involving human subjects.

2. WHAT IS THE OFFICE OF HUMAN SUBJECTS RESEARCH?

The Office of Human Subjects Research (OHSR) is an office within the Office of the Deputy Director for Intramural Research (DDIR), National Institutes of Health (NIH). The OHSR was established in 1991 to help investigators in NIH's Intramural Research Program (IRP) understand and comply with ethical guidelines and regulatory requirements regarding research involving human subjects. You may contact OHSR by calling 301-402-3444 or by FAX 301-402-3443, or by referring to the OHSR website at **http://ohsr.od.nih.gov**. OHSR is located in Building 10, Room 2C 146.

3. WHAT IS THE OFFICE FOR HUMAN RESEARCH PROTECTIONS (OHRP) AND HOW DOES IT DIFFER FROM THE OHSR?

The OHRP (formerly the Office for Protection from Research Risks) is an administrative unit within the Department of Health and Human Services (DHHS), organizationally located in the Office of Public Health and Science, under the direction of the Assistant Secretary for Health. OHRP's responsibilities include implementation of the DHHS Regulations for the Protection of Human Subjects (45 CFR 46), and the provision of guidance on ethical issues in biomedical and behavioral research. A major difference between the OHSR and the OHRP is that the OHSR's activities are limited to the IRP, NIH, while the OHRP has oversight and educational responsibilities wherever DHHS funds are used to conduct research involving human subjects.

4. WHAT IS 45 CFR 46?

The Public Health Service Act of 1974 requires DHHS to issue regulations for the protection of human subjects. 45 CFR 46 refers to Title 45, Part 46 of the Code of Federal Regulations, Protection of Human Subjects. These regulations, which were most recently updated in June, 2005, govern human subjects research conducted by all federal agencies (e.g., Departments of Defense, Justice, etc.). Copies of the regulations are available from OHSR (301-402-3444), or the OHSR website at **http://ohsr.od.nih.gov**.

5. WHAT ARE THE MAJOR REQUIREMENTS OF 45 CFR 46?

The regulations require institutions conducting research involving human subjects to establish Institutional Review Boards (IRBs). IRBs review research prospectively from the vantage point of protecting the rights and safeguarding the welfare of human research subjects. 45 CFR 46 also requires that each institution engaged in human subjects research

provide to the OHRP a detailed written assurance (a Federal Wide Assurance {FWA}) specifying how it will comply with the law's requirements.

6. WHAT IS THE BELMONT REPORT AND HOW IS IT RELEVANT TO RESEARCH INVOLVING HUMAN SUBJECTS?

The Belmont Report - Ethical Principles and Guidelines for the Protection of Human Subjects of Research sets forth fundamental principles that form the foundation for rules governing all government funded research on human subjects.

7. WHAT ETHICAL PRINCIPLES GUIDE THE PROTECTION OF HUMAN SUBJECTS?

Three basic principles of ethics set forth in The Belmont Report are particularly relevant to the protection of human subjects in biomedical and behavioral research:

(a) Respect for persons: recognition of the personal dignity and autonomy of persons and the need for special protection for persons with diminished autonomy, such as children or prisoners;

(b) Beneficence: obligation to protect persons from harm by maximizing anticipated benefits and minimizing possible risks;

(c) Justice: fairness in distribution of the benefits and burdens of research.

These ethical principles are embodied in 45 CFR 46, which mandates institutional research review and approval mechanisms designed to promote the protection of human research subjects.

8. WHAT IS THE NIH's FEDERAL WIDE ASSURANCE (FWA)?

The NIH FWA is the IRP's written assurance to OHRP that the institution will abide by the ethical principles set forth in The Belmont Report and by the Federal regulations that protect human subjects. The NIH official responsible for implementing the FWA is the Deputy Director for Intramural Research. Dr. Michael Gottesman is currently the DDIR. The FWA applies to all research involving human subjects conducted by IRP investigators, or in which IRP personnel collaborate, regardless of the site.

9. WHAT ARE THE CONSEQUENCES IF AN IRP INVESTIGATOR FAILS TO COMPLY WITH THE REQUIREMENTS OF THE NIH FWA?

Failure to comply with the requirements of the FWA can lead to loss of research privileges for an individual, a laboratory, or an entire research program.

10. WHAT IS NIH INTRAMURAL POLICY ON THE RESEARCH USE OF HUMAN SPECIMENS/DATA?

The question of whether the research use of human specimens/data constitutes "research involving human subjects" is a determination that must be made by either an NIH IRB or OHSR. All NIH intramural research involving human specimens requires approval either by an NIH IRB or OHSR.

11. WHAT IS AN "EXEMPTION" FROM THE REQUIREMENTS OF THE NIH FWA AND WHAT DOES AN INVESTIGATOR NEED TO DO TO GET AN EXEMPTION?

There are six categories of research which, although they involve human subjects, are exempt from the requirements of the NIH FWA. One example of exempt research is the study or collection of existing records (e.g., pathological specimens, blood samples), if these sources are publicly available or if the information is recorded by the investigator so that subjects cannot be identified, directly or through identifiers linked to the subject. Other exemptions include some types of research involving taste-testing of food, some surveys, interviews, use of educational tests and observation of public behavior. The rationale behind the six categories of exemption is that, although the research involves human subjects, it generally does not pose physical, social, or ethical risks to human subjects. Only the OHSR is authorized to make determinations about exemptions. If an investigator thinks a planned research activity is exempt, he/she should fill out the OHSR form "Request for Review of Research Activity Involving Human Subjects", and send it to the OHSR (phone 301-402-3444, FAX 301-402-3443). OHSR will respond in writing. Researchers must obtain exemptions from OHSR before they start their investigations.

12. HOW MANY INSTITUTIONAL REVIEW BOARDS (IRBs) DOES THE NIH HAVE?

As of November 2006, the NIH has IRBs in the following Institutes: NCI (2 IRBs); NIAID; the Combined Neurosciences (CNS) IRB (NINDS/NIDCD/NIA/NIAAA/NIMH/NEI); NIDDK/NIAMS; NHLBI; NIDR; NICHD; NIDA, NIEHS and NHGRI.

13. WHAT IS THE PRIMARY RESPONSIBILITY OF IRBs?

The primary responsibility of IRBs is **to protect the rights and safeguard the welfare of human subjects of research**. Committee membership is diverse with expertise in science, ethics, and other non-scientific areas, fostering a comprehensive approach to the protection of human subjects.

14. HOW DOES THE IRB PROTECT THE RIGHTS AND WELFARE OF HUMAN RESEARCH SUBJECTS?

IRBs are responsible for prospective review of all research involving human subjects. They evaluate proposed research activities using the following criteria: **(1)** the design of the study is consistent with sound scientific principles and ethical norms; **(2)** the protocol meets the NIH criteria necessary for approval; **(3)** the necessary elements of informed consent have been fulfilled, and **(4)** additional appropriate safeguards have been provided if potentially vulnerable subjects (e.g., children, prisoners, fetuses) are to be studied. NIH IRBs follow the IRB review criteria found attached to Information Sheet 3.

In addition, IRBs conduct continuing review of each approved research protocol or activity at least yearly, although an IRB may request earlier evaluations or updates if it determines

that the research presents significant physical, social, or ethical risks to subjects. The IRB may modify, suspend, or terminate approval of research that has been associated with serious harm to subjects or is not being conducted in accord with the NIH FWA or the IRB's decisions, stipulations and requirements, or the NIH IRB Standard Operating Procedures.

15. WHAT IS A "RESEARCH PROTOCOL"?

A research protocol is a written description of, and scientific rationale for, a proposed research activity. Protocols are submitted to the IRB and include a discussion of the human subject protection issues that are relevant to the study. At a minimum this discussion should address the risks to subjects; all procedures which are experimental; the anticipated benefits to subjects, if any; the anticipated number of subjects; the proposed consent document and consent process to be used; and appropriate additional safeguards if potentially vulnerable subjects are to be enrolled. Potentially vulnerable subjects may include the elderly, prisoners, children, cognitively impaired individuals, or people who are economically or educationally disadvantaged. More information on how to prepare a research protocol may be obtained from Laboratory, Branch, and Section Chiefs, the OHSR (see Information Sheet No. 5), or the Clinical Center's publication **"Protomechanics"**, which is available on request from the Clinical Center's Office of Communications (301-496-2563) and at the Clinical Center's Website (http://www.cc.nih.gov/ccc/protomechanics/index.html).

16. WHAT DOES NIH CONSIDER "COLLABORATIVE" HUMAN SUBJECTS RESEARCH AND WHAT DOES NIH REQUIRE WHEN IRP INVESTIGATORS COLLABORATE IN HUMAN SUBJECTS RESEARCH?

In the IRP, collaboration exists if the NIH PI expects "something in return" as a result of having participated in a research activity. "Something in return" could include data, authorship on a publication, samples, or even patent rights. The NIH views authorship as *prima facie* evidence of collaboration. Collaborative activities may include but are not limited to: the collection of specimens, visits to institutions to perform research activities or clinical work, exchange of information containing personal identifiers, preliminary data-collection activities involving human subjects, and substantive intellectual contributions to research techniques, protocol design, or interpretation of data. Even remote participation--such as supplying important reagents, performing tests, or analyzing data--may constitute collaboration. Investigators should contact their IRB Chair or the OHSR for guidance in cases where it is unclear whether or not collaboration exists. The question of whether a collaboration is human subjects research is a determination that must be made by either an NIH IRB or OHSR. All NIH intramural research involving human subjects requires approval either by an NIH IRB or OHSR.

HOW TO GET MORE INFORMATION ABOUT RESEARCH INVOLVING HUMANS.

Ask your Laboratory, Section or Branch Chief, the Clinical Director of your Institute, the Chair of the IRB in your Institute, or call the OHSR (301-402-3444), or visit the OHSR website at **http://ohsr.od.nih.gov**. OHSR is located in Building 10, Room 2C 146.