Office for Human Research Protections
Department of Health and Human Services

Guidance on Extension of an FWA to Cover Collaborating Individual Investigators and Introduction of the Individual Investigator Agreement

Date: January 31, 2005

Scope: This document describes a permissible mechanism under which an institution holding an Office for Human Research Protections (OHRP)-approved Federalwide Assurance (FWA) (hereafter referred to as the ***assured institution***) may extend – for one or more research protocols – the applicability of its FWA to cover two types of collaborating individual investigators: collaborating **independent** investigators and collaborating **institutional** investigators.

This mechanism would be permitted for **any Department of Health and Human Services (HHS) conducted or supported human subjects research when the research is being conducted under the direction and supervision of a principal investigator from the assured institution**. This mechanism provides an alternative to establishing additional FWAs for numerous institutions that do not hold FWAs (hereafter referred to as ***non-assured institutions***) and do not routinely conduct human subjects research.

Any non-assured institution may choose to submit an assurance to OHRP for approval rather than agree to the use of this mechanism that extends another institution's FWA to cover a collaborating institutional investigator employed by the non-assured institution. Please note that if HHS-conducted or -supported human subjects research activities routinely occur at a non-assured institution, the institution should obtain an OHRP-approved FWA because this guidance does not apply. Also, **if the non-assured institution is the primary awardee for an HHS-supported award providing support for non-exempt human subjects research, the institution must obtain its own OHRP-approved FWA.** If an institution is uncertain about the need for its own FWA, it should consult with OHRP.

This document also introduces a new sample agreement called the Individual Investigator Agreement, which allows for the flexibility offered in this guidance and which will replace all prior sample investigator agreements developed by OHRP.

Target Audience: This document primarily is intended to assist institutional review board (IRB) administrators, research administrators, IRB chairpersons and members, investigators, institutional officials, and funding agencies that may be responsible for review or oversight of human subjects research conducted or supported by HHS.

REGULATORY BACKGROUND

HHS regulations at 45 CFR 46.103(a) require that each institution engaged in HHS-conducted or -supported human subjects research provide written assurance, satisfactory to HHS, that it will comply with the requirements of the HHS regulations for the protection of human subjects, unless the research is exempt under 45 CFR 46.101(b). HHS regulations at 45 CFR 46.103(b)

require that each institution engaged in HHS-conducted or -supported human subjects research certify to the HHS funding agency that the research has been approved by an IRB designated in the assurance.

TWO TYPES OF COLLABORATING INDIVIDUAL INVESTIGATORS

OHRP notes that some human subjects research conducted by an assured institution may involve the following two types of collaborating individual investigators:

(1) A collaborating **independent** investigator is:
   (a) not otherwise an employee or agent of the assured institution;
   (b) conducting collaborative research activities outside the facilities of the **assured** institution; and
   (c) not acting as an employee of **any** institution with respect to his or her involvement in the research being conducted by the assured institution.

(2) A collaborating **institutional** investigator is:
   (a) not otherwise an employee or agent of the **assured** institution;
   (b) conducting collaborative research activities outside the facilities of the **assured** institution;
   (c) acting as an employee or agent of a **non-assured** institution with respect to his or her involvement in the research being conducted by the **assured** institution; and
   (d) employed by, or acting as an agent of, a ***non-assured institution*** that does not routinely conduct human subjects research.

Prior to January 31, 2005, the effective date of this guidance document, assurance options for collaborating **independent** investigators included (1) the Unaffiliated Investigator Agreement (UIA), for collaborating independent investigators engaged in research activities in collaboration with FWA institutions and who are not acting as employees of any institution with respect to the research activities; (2) the Non-Institutional Investigator Agreement (NIA), for collaborating independent investigators solely involved in Cooperative Protocol Research Programs; and (3) the Agreement for Independent Investigators (AII), for collaborating independent investigators involved in any other HHS-conducted or -supported human subjects research not covered by a UIA or NIA. Now, the Individual Investigator Agreement, or another similar agreement developed by an assured institution, will be the sole assurance option for collaborating **independent** investigators.

Prior to this guidance, OHRP had not established a routine formal mechanism for an assured institution to extend the applicability of its FWA to cover collaborating **institutional** investigators.

INTRODUCTION OF THE INDIVIDUAL INVESTIGATOR AGREEMENT

Effective January 31, 2005, OHRP has replaced the UIA, NIA, and AII with the sample Individual Investigator Agreement, which will provide greater flexibility and simplicity.

Previously executed AIIs, NIAs, and UIAs may remain in effect until all applicable research that has already been initiated is completed or until the previous agreement has been replaced by an new Individual Investigator Agreement or other written agreement developed by an assured institution.

The new sample Individual Investigator Agreement may be used by an assured institution to extend – for one or more research protocols – the applicability of its FWA to cover either collaborating **independent** investigators or collaborating **institutional** investigators.

The sample Individual Investigator Agreement may be found on the OHRP website at http://www.hhs.gov/ohrp/assurances/forms/unaflsup.rtf. Institutions also may develop their own agreements for individual investigators, provided the conditions below are met.

CONDITIONS FOR EXTENDING AN FWA TO COVER COLLABORATING INDIVIDUAL INVESTIGATORS

OHRP will permit an assured institution to extend its FWA to cover a collaborating **independent** or **institutional** investigator provided all of the following conditions are satisfied:

(1) The principal investigator at the assured institution directs and appropriately supervises all of the collaborative research activities to be performed by the collaborating individual investigator outside the assured institution.

(2) The extension of the coverage of the FWA is put in place by use of an appropriate written agreement, such as the sample Individual Investigator Agreement, for each collaborating individual investigator who will be engaged in the research being conducted by the assured institution. **The assured institution must maintain the Individual Investigator Agreement,** or other written agreement used by the assured institution, **on file and provide copies to OHRP upon request.**

(3) For collaborating **institutional** investigators, the appropriate authorities at the non-assured institution state in writing that the conduct of the research is permitted at their institution.

(4) The assured institution and the responsible IRB designated under the FWA approve the extension of the assurance through either the Individual Investigator Agreement or other written agreement used by the assured institution.

(5) The following documents are made available to the collaborating individual investigator: (a) *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research* (see http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.html) or other internationally recognized equivalent (see section B.1. of the Terms of the Federalwide Assurance (FWA) for International (Non-U.S.) Institutions on the OHRP website at http://www.hhs.gov/ohrp/assurances/assurances/filasurt.html#sectionb); (b) the HHS regulations for the protection of human subjects at 45 CFR part 46 (see

http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html) or other procedural standards designated by a non-U.S. institution under its FWA (see section B.3. of the Terms of the Federalwide Assurance (FWA) for International (Non-U.S.) Institutions on the OHRP website at http://www.hhs.gov/ohrp/assurances/assurances/filasurt.html#sectionb); (c) the FWA and applicable Terms of the FWA for the assured institution; and (d) the relevant institutional policies and procedures for the protection of human subjects of the assured institution.

(6) The collaborating individual investigator understands and accepts the responsibility to comply with the standards and requirements stipulated in the documents referenced in the preceding paragraph and to protect the rights and welfare of human subjects involved in research conducted under the Individual Investigator Agreement or other written agreement used by the assured institution..

(7) The collaborating individual investigator agrees to comply with all other applicable federal, international, state, and local laws, regulations, and policies that may provide additional protections for human subjects participating in research conducted under the Individual Investigator Agreement or other written agreement used by the assured institution.

(8) The collaborating individual investigator agrees to abide by all determinations of the Institutional Review Board (IRB)/Independent Ethics Committee (IEC) designated under the FWA of the assured institution and agrees to accept the final authority and decisions of the IRB/IEC, including but not limited to directives to terminate participation in designated research activities conducted under the Individual Investigator Agreement or other written agreement used by the assured institution.

(9) The collaborating individual investigator agrees to complete any educational training required by the assured institution and/or the IRB/IEC prior to initiating research covered under the Individual Investigator Agreement or other written agreement used by the assured institution.

(10) The collaborating individual investigator agrees not to enroll subjects in research under the Individual Investigator Agreement or other agreement used by the assured institution, prior to the research being reviewed and approved by the IRB/IEC.

(11) The collaborating individual investigator agrees to report promptly to the IRB/IEC any proposed changes in the research conducted under the Individual Investigator Agreement or other agreement used by the assured institution. The collaborating institutional investigator agrees not to initiate changes in the research without prior IRB/IEC review and approval, except where necessary to eliminate apparent immediate hazards to subjects.

(12) The collaborating individual investigator agrees to report immediately to the IRB/IEC any unanticipated problems involving risks to subjects or others in research

covered under the Individual Investigator Agreement or other agreement used by the assured institution.

(13) The collaborating individual investigator, when responsible for enrolling subjects, agrees to obtain, document, and maintain records of informed consent for each such subject or each subject's legally authorized representative as required under HHS regulations at 45 CFR part 46 (or any other international or national procedural standards selected in the FWA for the institution referenced above) and stipulated by the IRB/IEC.

(14) The collaborating individual investigator acknowledges and agrees to cooperate with the IRB/IEC's in its initial and continuing review, record keeping, reporting, and certification for the research covered by the Individual Investigator Agreement, or other agreement used by the assured institution. The collaborating institutional investigator agrees to provide all information requested by the IRB/IEC in a timely fashion.

If you have specific questions about how to apply this guidance, please contact OHRP by phone at (866) 447-4777 (toll-free within the U.S.), (301) 496-7005, or by e-mail at ohrp@hhs.gov.