

January 26, 1999

TO: Division of Human Subject Protections, OPRR

FROM: Director, Division of Human Subject Protections, OPRR

SUBJECT: Engagement of Institutions in Research

Department of Health and Human Services (HHS) regulations at 45 CFR 46.103(a) require that each institution "engaged" in human subjects research provide OPRR with a satisfactory Assurance to comply with the regulations, unless the research is exempt under 45 CFR 46.101(b).

An institution becomes "engaged" in human subjects research when its employees or agents¹ (i) intervene or interact with living individuals for research purposes; or (ii) obtain individually identifiable private information for research purposes [45 CFR 46.102(d),(f)].

An institution is automatically considered to be "engaged" in human subjects research whenever it receives a direct HHS award to support such research. In such cases, the awardee institution bears ultimate responsibility for protecting human subjects under the award.

Examples

- (A) Institutions would be considered "engaged" in human subjects research (and would need an Assurance) if their nonexempt involvement includes the following:
- (1) Institutions whose employees or agents intervene with living individuals by performing invasive or noninvasive procedures for research purposes (e.g., drawing blood; collecting other biological samples; dispensing drugs; administering other treatments; employing medical technologies; utilizing physical sensors; utilizing other measurement procedures).

Agents include all individuals performing institutionally designated activities or exercising institutionally delegated authority or responsibility.
 - (2) Institutions whose employees or agents intervene with living individuals by manipulating the environment for research purposes (e.g., controlling environmental light, sound, or temperature; presenting sensory stimuli; orchestrating environmental events or social interactions; making voice, digital, or image recordings).

- (3) Institutions whose employees or agents interact with living individuals for research purposes (e.g., engaging in protocol-dictated communication or interpersonal contact; conducting research interviews; obtaining informed consent). (See Example (B)(3) below for certain informational activities that do not constitute "engagement" in research and do not require an Assurance.)
- (4) Institutions whose employees or agents release individually identifiable private information, or permit investigators to obtain individually identifiable private information, without subjects' explicit written permission (e.g., releasing patient names to investigators for solicitation as research subjects; permitting investigators to record private information from medical records in individually identifiable form). (However, see Example (B)(5) regarding release of such information with subjects' prior, written permission, and Example (B)(6) regarding release of such information to State Health Departments.)
- (5) Institutions whose employees or agents obtain, receive, or possess private information that is individually identifiable (either directly or indirectly through coding systems) for research purposes (e.g., obtaining private information from medical records in an individually identifiable form). (However, see Examples (B)(7) and B(8) for certain activities involving the release of information and/or specimens to investigators in non-identifiable form.)
- (6) Institutions whose employees or agents obtain, receive, or possess private information that is individually identifiable (either directly or indirectly through coding systems) for the purpose of maintaining "statistical centers" for multi-site collaborative research. Where institutional activities involve no interaction or intervention with subjects, and the principal risk associated with institutional activities is limited to the potential harm resulting from breach of confidentiality, the Institutional Review Board (IRB) need not review each collaborative protocol. However, the IRB should determine and document that the statistical center has sufficient mechanisms in place to ensure that (i) the privacy of subjects and the confidentiality of data are adequately maintained, given the sensitivity of the data involved; (ii) each collaborating institution holds an applicable OPRR-approved Assurance; (iii) each protocol is reviewed and approved by the IRB at the collaborating institution prior to the enrollment of subjects; and (iv) informed consent is obtained from each subject in compliance with HHS regulations.
- (7) Institutions whose employees or agents maintain "operations centers" or coordinating centers" for multi-site collaborative research. Where institutional activities involve no interaction or intervention with subjects, the IRB need not review each collaborative protocol. However, the IRB

should determine and document that the operations or coordinating center has sufficient mechanisms in place to ensure that (i) management, data analysis, and Data Safety and Monitoring (DSM) systems are adequate, given the nature of the research involved; (ii) sample protocols and informed consent documents are developed and distributed to each collaborating institution; (iii) each collaborating institution holds an applicable OPRR-approved Assurance; (iv) each protocol is reviewed and approved by the IRB at the collaborating institution prior to the enrollment of subjects; (v) any substantive modification by the collaborating institution of sample consent information related to risks or alternative procedures is appropriately justified; and (vi) informed consent is obtained from each subject in compliance with HHS regulations.

- (8) Institutions receiving a direct HHS award to conduct human subjects research, even where all activities involving human subjects are carried out by a subcontractor or collaborator (e.g., a small business receives a HHS award to design a medical device at its own facility and contract with a medical clinic to test the device with human subjects; a foundation receives a HHS award on behalf of an affiliated institution that will actually conduct the human subjects research).
- (B) Institutions would not be considered "engaged" in human subjects research (and would not need an Assurance) if their involvement is limited to the following:
- (1) Institutions whose employees or agents act as consultants on research but at no time obtain, receive, or possess identifiable private information (e.g., a consultant analyzes data that cannot be linked to individual subjects, either directly or indirectly through coding systems, by any member of the research team).
 - (a) Should a consultant access or utilize individually identifiable private information while visiting the research team's institution, the consultant's activities become subject to the oversight of the research team's Institutional Review Board (IRB). However, the consultant's institution is not considered to be "engaged" in the research and would not need an Assurance.
 - (b) Should a consultant obtain "coded" data for analysis at the consultant's institution, the consultant's institution is considered "engaged" in human subjects research, and would need an Assurance, unless a written agreement unequivocally prohibits release of identifying codes to the consultant.

- (2) Institutions whose employees or agents (i) perform commercial services or the investigators (or perform other genuinely non-collaborative services meriting neither professional recognition nor publication privileges), and (ii) adhere to commonly recognized professional standards for maintaining privacy and confidentiality (e.g., an appropriately qualified laboratory performs analyses of blood samples for investigators solely on a commercial basis).
- (3) Institutions whose employees or agents (i) inform prospective subjects about the availability of research; (ii) provide prospective subjects with written information about research (which may include a copy of the relevant informed consent document and other IRB-approved materials) but do not obtain subjects' consent or act as authoritative representatives of the investigators; (iii) provide prospective subjects with information about contacting investigators for information or enrollment; or (iv) obtain and appropriately document prospective subjects' permission for investigators to contact them (e.g., a clinician provides patients with literature about a research study, including a copy of the informed consent document, and tells them how to contact the investigator if they want to enroll; a clinician provides investigators with contact information about potential subjects after receiving explicit permission from each potential subject).
- (4) Institutions (e.g., schools, nursing homes, businesses) that permit use of their facilities for intervention or interaction with subjects by research investigators (e.g., a school permits investigators to test students whose parents have provided written permission for their participation; a business permits investigators to solicit research volunteers at the worksite).
- (5) Institutions whose employees or agents release identifiable private information to investigators with the prior written permission of the subject (e.g., with written permission of the subject, a clinician releases the subject's medical record to investigators).
- (6) Institutions whose employees or agents release identifiable private information or specimens to a State or Local Health Department or its agent for legitimate public health purposes within the recognized authority of that Department. However, utilization of such information or specimens by Department investigators for research purposes would constitute engagement in research, and would require an Assurance from the Department.
- (7) Institutions whose employees or agents release information and/or specimens to investigators in non-identifiable (i.e., non-linkable) form, where such information/specimens have been obtained by the institution for purposes other than the investigators' research (e.g., nursing home

employees provide investigators with a data set containing medical record information, but the data set contains no direct or indirect identifiers through which the identity of individual subjects could be ascertained, either by the investigators or by nursing home personnel; a hospital pathology department releases excess tissue specimens and relevant medical record information to investigators, but these materials include no direct or indirect identifiers through which the identity of individual subjects could be ascertained, either by investigators or by hospital personnel, including the pathology department; consistent with applicable law or recognized authority, local hospitals or health departments permit State or Local Health Department investigators to access information for research purposes, but the investigators record no direct or indirect identifiers through which the identity of individual subjects could be ascertained, either by the investigators or by local hospital or health department personnel.)

- (8) Institutions whose employees or agents receive information or specimens for research from established repositories operating in accordance with (i) an applicable OPRR-approved Assurance; (ii) OPRR guidance (see <http://ohrp.osophs.dhhs.gov/humansubjects/guidance/reposit.htm>); and (iii) written agreements unequivocally prohibiting of release of identifying information to recipient investigators.
- (9) Institutions (or private practitioners) whose clinical staff provide protocol-related care and/or follow-up to subjects enrolled at distant sites by clinical trial investigators in OPRR-recognized Cooperative Protocol Research Programs (CPRPs). In such cases, (i) the CPRP clinical trial investigator (consistent with a registered investigator as defined in Section 14.1 of the NCI Investigator's Handbook) retains responsibility for oversight of protocol related activities; (ii) clinical staff may not accrue subjects or obtain informed consent for research participation; (iii) clinical staff may only provide data to the investigator in accord with the terms of informed consent; and (iv) the informed consent document should state that such data are to be provided by clinical staff as directed by the investigator.

Assurance Coordinators within the Division of Human Subject Protections (DHSP) retain the authority to determine whether institutions are "engaged" in human subjects research consistent with the above guidelines. The DHSP Director and the Assurance Branch Chief should be consulted should Coordinators require assistance in applying these guidelines to specific situations.

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Attachment

cc: Dr. Gary Ellis
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