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TO: Division of Human Subject Protections, OPRR

FROM: Director, Division of Human Subject Protections, OPRR

SUBJECT: IRB Knowledge of Local Research Context

Department of Health and Human Services (DHHS) regulations at 45 CFR 46.103(d) require that the adequacy of Institutional Review Boards (IRBs) be evaluated in light of the anticipated scope of the institution's research activities, the types of subject populations likely to be involved, . . . and the size and complexity of the institution.

The regulations further require at 45 CFR 46.107(a) that IRBs be (i) sufficiently qualified through . . . the diversity of the members, including consideration of race, gender, and cultural backgrounds and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel; and (ii) able to ascertain the acceptability of proposed research in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice.

IRBs must also be capable of ensuring that (i) selection of subjects is equitable; (ii) privacy of subjects is protected and confidentiality of data is maintained; (iii) informed consent is sought in language understandable to the subject and under conditions that minimize the possibility of coercion or undue influence; and (iv) appropriate safeguards protect the rights and welfare of vulnerable subjects [45 CFR 46.111(a)(3),(a)(4),(a)(7),(b), and 46.116].

Institutions have a profound responsibility to ensure that all IRBs designated under an OPRR-approved Assurance possess sufficient knowledge of the local research context to satisfy these requirements. This responsibility endures regardless of the IRB's geographic location relative to the institution and the research. It is particularly critical where the research involves greater than minimal risk to subjects or vulnerable categories of subjects.

(A) OPRR considers the following standards when evaluating the adequacy of IRBs designated under an institutional Assurance, particularly when the IRBs are geographically removed from the local research context. These standards reflect minimum levels of adequacy. More stringent standards may be required, depending upon the nature of the proposed research or the relevant research context.

(1) Where the research involves minimal risk to subjects, the IRB should demonstrate that it has obtained necessary information about the local research context through written materials or discussions with appropriate consultants.

(2) Where the research involves greater than minimal risk to subjects but (i) the local research context involves no intervention or interaction with subjects and (ii) the principal risk associated with the local research context is limited to the potential harm resulting from a breach of confidentiality, the IRB should (i) demonstrate that it has obtained necessary information1 about the local research context through written materials or discussions with

appropriate consultants; and (ii) determine and specifically document that provisions to protect the privacy of subjects and maintain the confidentiality of data are adequate.

(3) Where the research involves greater than minimal risk to subjects and item (A)(2) does not apply, the IRB should demonstrate that it has obtained necessary information1 about the local research context through one or more of the following mechanisms, or through other mechanisms deemed appropriate by OPRR for the proposed research and the local research context.

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1 Necessary information under DHHS regulations includes all of the following:

- the anticipated scope of the institution's research activities;
- the types of subject populations likely to be involved;
- the size and complexity of the institution;
- institutional commitments and regulations;
- applicable law;
- standards of professional conduct and practice;
- method for equitable selection of subjects;
- method for protection of privacy of subjects;
- method for maintenance of confidentiality of data;
- language(s) understood by prospective subjects;
- method for minimizing the possibility of coercion or undue influence in seeking consent; and
- safeguards to protect the rights and welfare of vulnerable subjects.

(a) Personal knowledge of the local research context on the part of one or more IRB members, such knowledge having been obtained through extended, direct experience with the research institution, its subject populations, and its surrounding community.

(b) Participation (either physically or through audiovisual or telephone conference) by one or more appropriate consultants in convened meetings of the IRB. Such consultant(s) should have personal knowledge of the local research context, such knowledge having been obtained through extended, direct experience with the research institution, its subject populations, and its surrounding community.

(c) Prior written review of the proposed research by one or more appropriate consultants (see (b) above), in conjunction with participation (either physically or through audiovisual or telephone conference) by the consultant(s) in convened meetings of the IRB, when such participation is deemed warranted either by the consultant(s) or by any member of the IRB.

(d) Systematic, reciprocal, and documented interchange between the IRB and elements of the local research context. Such interchange should include (i) periodic visits to the research site, occurring several times per year, by one or more IRB members in order to obtain and maintain knowledge of the local research context, including the research institution, its subject populations, and its surrounding community; (ii) periodic discussion with appropriate consultants knowledgeable about the local research context; (iii) regular interaction with one or more designated institutional liaisons; and (iv) review of relevant written materials.

(B) The following standards apply where an institution holding an OPRR-approved Assurance wishes to avoid duplication of effort, in accordance with DHHS regulations at 45 CFR 46.114, by relying upon the IRB review of another Assurance-holding institution:

(1) The review arrangement must be approved in writing by OPRR and by appropriate officials of the institutions involved.

(2) The institution relying upon another institution's IRB has a responsibility to ensure that the particular characteristics of its local research context are considered, either (i) through knowledge of its local research context by the reviewing IRB (see (A) above); or (ii) through subsequent review by appropriate designated institutional officials, such as the Chairperson and/or other members of its local IRB.

(C) Regardless of the IRB's geographic location, each institution holding an OPRR-approved Assurance is expected to maintain a unified system of protections applicable to all human subjects research covered under the Assurance.

(1) Each institution remains responsible for safeguarding the rights and welfare of human subjects within its local research context.

(2) Each institution remains responsible for educating the members of its research community in order to establish and maintain a culture of compliance with Federal regulations and institutional policies relevant to the protection of human subjects.

(3) Each institution remains responsible for implementation, within its local research context, of appropriate oversight mechanisms in order to ensure compliance with the determinations of the reviewing IRB.

(4) Where institutions holding an OPRR-approved Assurance engage a separate entity to perform human subject protection activities, OPRR must review and approve those portions of the contract and/or other clarifying documentation detailing responsibilities and implementation mechanisms relevant to such activities.

(a) Such documentation must specify mechanisms to ensure that all institutional responsibilities under the Assurance are fulfilled (e.g., procedures for retention and accessibility of records in accordance with DHHS regulations at 45 CFR 46.115; procedures for prompt reporting to the IRB of proposed changes in approved research and for prompt reporting to OPRR of unanticipated problems in accordance with DHHS regulations at 45 CFR 46.103(b)(4), (5)).

(b) No arrangement may contain disincentives, impediments, or conflicts of interest that may hamper the exercise of the IRB's function or objectivity (e.g., procedures or fee schedules that could discourage prompt reporting to the IRB of proposed changes or unanticipated problems or that could impede the IRB's flexibility to take prompt, objective action where necessary to protect human subjects).

(c) In order to avoid real or perceived conflicts of interest, (i) no IRB member may hold an equity interest (e.g., partnership, stock, or profit-sharing) in the organization providing IRB review; (ii) no IRB member may be paid more than reasonable compensation or receive more than reasonable benefits for IRB-related activities; and (iii) no IRB member may receive compensation or benefits under arrangements that could impede or discourage objective decision-making on behalf of human subjects.

Assurance Coordinators within the Division of Human Subject Protections (DHSP) retain the authority to evaluate the adequacy of IRBs consistent with the above standards. Assurance Coordinators may require more stringent standards where warranted based upon the nature of the proposed research or the relevant research context. Assurance Coordinators should approve less stringent standards only in extraordinary circumstances and with concurrence by the Chief of the Assurance Branch or the DHSP Director.

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