

PROCEDURES FOR PROTECTION OF HUMAN SUBJECTS IN RESEARCH SUPPORTED BY USAID

1. Introduction and Purpose

Along with many other Federal Agencies, USAID has adopted the Common Federal Policy for Protection of Human Subjects (referred to herein as the Policy - see 22 CFR Part 225). The Policy sets standards for the protection of human research subjects which must be followed when research activities supported by USAID involve human subjects. The Policy, at 22 CFR 225.101(a), permits each agency to adopt procedural modifications as may be appropriate from an administrative standpoint. In conformity with the Policy, safeguarding the rights and welfare of human subjects involved in research supported by USAID is the primary responsibility of the organization to which support is awarded. No work may be initiated for the support of research involving human subjects unless the research is approved as outlined in these procedures.

While the Policy sets forth detailed guidance, it allows for some latitude in adaptation to the specific situation of each Agency. The purpose of these procedures is to describe how the Policy is implemented and interpreted by USAID. It is intended especially to help Cognizant Technical Officers (CTOs), Technical Advisors (TAs) and Mission staff to understand and apply the Policy when supporting research involving human subjects. CTO's, TAs and Mission staff are the first line of action in determining applicability of the Policy to a particular research project and for assuring that those organizations receiving USAID funds for research are adhering to requirements set forth in the Policy. USAID's Cognizant Human Subjects Officer (CHSO or successor) assists with guidance, oversight and interpretation of the Policy. The CHSO, located in USAID/Washington, is appointed by the Assistant Administrator for the Bureau for Global Programs, Field Support and Research (AA/G). Ultimate authority for decisions regarding human subjects' protection rests with the USAID AA/G or her/his designee. (For more information refer to the Policy itself.)

2. Background and Principles

(a) Human subjects considerations are essential in the design and implementation of research projects. USAID strongly supports vigorous efforts to protect human subjects as provided for by the Policy. The Policy itself is primarily oriented towards experimental biomedical research, but some other types of research are included (see section 5 below for application of the Policy to various other types of research and for exemptions).

(b) In considering human subjects research it is essential to recognize the following three pillars of protection:

- (1) Review by a properly constituted ethical committee or Institutional Review Board (IRB)
- (2) A meaningful assessment of risk/benefit by the IRB
- (3) A meaningful informed consent procedure

(c) The Policy recognizes that foreign countries may often present special situations and it provides mechanisms to help deal with these {see 22 CFR section 225.101(h)}. As provided for in the Policy, USAID will accept legitimate foreign procedural systems, for example an institution which complies with the guidelines of the World Medical Assembly Declaration, as long as they are determined to provide protection "at least equivalent" to the Policy. Substantive application of the "three pillars" should generally satisfy this requirement. As noted in 22 CFR section 225.101(g), the Policy does not affect any laws or regulations in foreign countries regarding protection of human research subjects, and overseas research activities, in addition to adhering to the Policy, must also conform to legal and other requirements governing research with human subjects in the country where they are conducted.

(d) USAID's implementation of the Policy seeks to avoid undue burden that might be imposed by its application, while seeking to protect human subjects. It emphasizes practicality, flexibility and common sense. Because USAID conducts no research itself directly, no need is foreseen for an USAID IRB per se to review research proposals. For research other than experimental biomedical research, generally the primary issue is protection of privacy rather than direct physical harm. This guidance takes that into account.

3. Applicability in Various Research Settings

Whether procedures for protection of human subjects must adhere to the Policy or whether some alternative may be applied depends on where the research will be conducted.

(a) Research in the U.S. - When research takes place in the U.S. it must conform to all aspects of the Policy. In cases where all or part of the research is subcontracted to another institution, the prime recipient is responsible for complying in detail with the Policy. Recipient institutions may be of two categories: (i) Many U.S.-based institutions will have an ongoing Department of Health and Human Services (HHS) "multiple project assurances" (MPAs), indicating they have an HHS-approved system for human subjects' protection in place which can be applied to USAID-supported research by reference, or (ii) If no MPA exists, the institution must provide an acceptable "assurance" to USAID describing how it will comply with the Policy (see section 8 below).

(b) Research in Foreign Countries - There are generally three mechanisms by which USAID supports research in foreign countries:

(1) The recipient is a U.S.-based institution, with the research carried out in another country. In this situation, the primary recipient will be responsible for complying or assuring compliance in detail with the Policy as described above including either an HHS or USAID approved assurance governing the research. As part of its institution building mandate, USAID encourages, but does not require the host-country collaborators of U.S.-based institutions to use an in-country IRB.

(2) The recipient is an international organization or institution (e.g. WHO, UNICEF, UNDP, and certain non U.S.- based PVOs/NGOs).

(3) The recipient is a host country government or non- government institution.

In the last two cases, for non-U.S.-based institutions, there are three ways acceptable standards can be applied:

(i) An acceptable assurance complying with the Policy can be developed directly with USAID.

(ii) Access can be made to appropriate U.S. or other internationally accepted bodies such as an HHS- approved or WHO/CIOMS-approved IRB/Ethical Committee {see section 4(a) below} either directly or through a collaborative arrangement.

(iii) An alternative human subjects system can be employed if it can be determined (by the AA/G or her/his designee) to be "at least equivalent" to the Policy {as delineated in section 4(b) below}.

4. Determination that Alternative Protection Procedures are "at Least Equivalent" to the Policy

(a) 22 CFR section 225.101(h) describes the use of alternative protection of human subjects systems when research is conducted outside the U.S. It specifically cites the example of "...a foreign institution which complies with guidelines consistent with the World Medical Assembly Declaration (Declaration of Helsinki amended 1989) issued either by sovereign states or by an organization whose function for the protection of human subjects is internationally recognized." Research supported through or adhering to the standards established by United Nations agencies is considered to qualify as affording such "at least equivalent" protection.

(b) To make a determination that another system provides "at least equivalent" protection, a justification memorandum is required for an individual or class of research activities which is cleared by the Agency's CHSO (designee or successor) and is signed by the AA/G (or designee.) Such a justification memorandum must describe how the alternative system provides the "three pillars" of protection described above under section 2(b)(1-3). An additional tool available for the determination of equivalency is a checklist of considerations which are common components of such systems (Available from the CHSO.) In assessing equivalency, the general concept should be whether protection under the system is for all practical purposes the same when viewed in toto and not whether any specific component (e.g. the precise make-up of the IRB equivalent) is identical. Each determination of "at least equivalent" protection, including the determination of a class of activities will be published in the Federal Register in accordance with 22 CFR 225.101(h).

5. Applicability to Various Types of Activities

As defined in the Policy {22 CFR section 225.102(d)} "Research means a systematic investigation, including research development, testing and evaluation designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program which is considered research for other purposes." The Policy applies only to research involving living human subjects (including samples derived from living subjects.) The following listed activities are guidelines for helping to assist in determining applicability of the Policy to a particular research activity. They are by no means intended to be totally inclusive. It is expected that questions will arise and when this occurs guidance should be sought from the CHSO.

(a) Experimental Biomedical Research - The Policy clearly applies to experimental biomedical research related to prevention, transmission, treatment, or curing of human diseases and to prevention of pregnancy; including vaccine and drug development; clinical trials of new drugs, devices, and vaccines; and experimental studies of disease transmission involving human subjects.

(b) Survey Research\Demographic Data Collection

(1) Survey research in which no individual identifiers are collected or in which the data collected are not highly sensitive is exempt {See 22 CFR section 225.101(b)(2) & (3)}. Research involving issues of privacy and confidentiality are not exempt, for example, surveys of high-risk sexual behavior and of HIV infection. Surveys generally considered exempt would include typical censuses, general

reproductive surveys such as the demographic and health surveys (DHS), and standard nutrition surveys.

- (2) Studies such as surveys involving anthropometry and the gathering of human material through defined "minimal risk" activities are treated as survey research and may be exempt as described in section 5(b)(1) above. Examples of "minimal risk" activities include collection of hair, nail clippings, external secretions, data via physical sensors applied to the surface of the body, etc.. In and of itself, collection of such materials would not require coverage. However, if such gathering of human material exceeds these defined "minimal risk" activities, such as collection of blood samples, then this research is not exempt. A listing of activities defined as "minimal risk" is available from the CHSO.
- (3) Anthropologic/ethnographic research is considered survey research as broadly defined and the same rules apply. Clearly, informed consent in this context is often unnecessary, impractical and may be waivable {See section 6(a) & (b) below}.

(c) Epidemiologic Research - Depending on methodology, epidemiologic studies may be classified as survey research and treated accordingly {22 CFR section 225.101(b)(2)}. As described above {section 5(b)(1)}, when no individual identifiers are collected or when data are not highly sensitive, this research is exempt. Epidemiologic studies include:

- (1) Standard Case-Control and Cohort Studies. Generally treat as survey research.
- (2) Surveillance. 22 CFR section 225.101(b)(4) exempts research involving existing publicly available data, records and specimens or if the investigator does not record data in an identifiable manner.
- (3) Other epidemiologic studies utilizing existing data or specimens. Generally exempt under 22 CFR section 225.101(b)(4).
- (4) Outbreak Investigations. Treat as survey research, but recognize the need for expedited procedures (See section 6(b) below).

(d) Operational or Operations Research - Operational/operations research or service delivery research includes research on service delivery systems for the purpose of understanding how they function and how to improve efficiency and effectiveness. It includes making alterations in how services are provided among acceptable alternatives (e.g. comparing differences in clinic hours or evaluating the impact of adding new services.) It is generally exempt under 22 CFR section 225.101(b)(5) which exempts research on public benefit or service programs. Nevertheless, operations research in highly sensitive areas involving issues of privacy such as HIV prevention, may need special attention regarding matters

such as confidentiality and there may be instances where the formal protection procedures should be applied.

(e) Research on Diagnostic Tests - Research to develop or assess diagnostic tests on blood, urine, etc. is not well delineated in the Policy and spans several research categories.

(1) Research on existing specimens is generally exempt if sources are publicly available or subjects cannot be identified.

(2) Research on newly collected materials may be treated as survey research unless collection activities exceed "minimal risk."

(3) Research on existing standard of care diagnostic methods (eg. comparing two techniques for diagnosing Chlamydia, both of which are commonly used in programs) may be treated as operations research.

(4) Other diagnostic research may be considered experimental biomedical research.

(f) Education Research - Education research involving special subjects, such as children and mentally disabled individuals, is covered by the Policy. Much educational research is exempted under 22 CFR section 225.101(b)(1) including research in educational settings involving normal educational practices.

6. Balancing Protection with Burden

(a) Implementation of the Policy at USAID is intended to comprise the steps necessary for providing adequate protection of human research subjects, while avoiding imposition of undue burden to USAID staff and program personnel. Common sense, practicality, and flexibility are essential, especially in areas other than experimental biomedical research where there is no issue of causing physical harm. In the area of epidemiologic research, for example, informed consent may not be necessary nor practical and might pose a major impediment to conducting the research. 22 CFR sections 225.116 and 225.117 describe appropriate mechanisms for altering or waiving the informed consent procedure, which requires IRB approval. It might also well be reasonable in many instances of survey research for the informed consent procedure to consist simply of a legitimate statement that participation is voluntary and that information will be kept confidential. In unusual circumstances, where consent is required but written consent is inappropriate in a given culture or population, verbal consent may be appropriate, but it must be witnessed and documented in writing.

(b) Additional situations calling for practicality can be foreseen. For example, there may be instances where a number of surveys or other similar research activities are highly standardized or systematized. Review and approval of such research as a group by an IRB may be appropriate. Likewise, it may be

reasonable to approve outbreak investigations as a class in advance because of the emergency nature of such research.

7. Right of Access of USAID Officials to Records

To implement and monitor human subjects research activities properly, it is essential that USAID reserve the right to audit and inspect subjects and other relevant records and to prohibit research which presents unacceptable risks. Appropriate language to that effect must be included in contracts, grants and other support documents as well as in informed consent documents.

8. Implementation

(a) All research activities involving human subjects that are funded by USAID (central or Mission funds) must adhere to the standards set forth in the Policy, or have a system that provides "at least equivalent" protection which has been approved by the AA/G or designee. Compliance with USAID's human subjects procedures is the primary responsibility of the organization receiving USAID support. To help ensure observance of USAID's human subjects procedures by such recipients appropriate language will be included in funding documents when appropriate.

(b) Unless the research is conducted under application of an HHS-approved Multiple Project Assurance, or qualifies as affording "at least equivalent" protection as described in section 4 above, the recipient must provide USAID with a satisfactory written "assurance" that it will comply with the requirements set forth in the Policy. As described in 22 CFR section 225.103 (b) (1), the assurance must include: a statement of principles governing the institution's responsibilities, designation of one or more IRBs, a list of IRB members, written procedures which the IRB will follow, and written procedures for ensuring prompt reporting of unanticipated problems to the IRB. Assurances may be for a single research project or for multiple projects. USAID must accept the application of existing HHS-approved multiple project assurance in lieu of a separate assurance.

(c) Within USAID the CTO, TA or Mission personnel have the first line responsibility for implementation of procedures for the protection of human subjects including an initial determination of the applicability of the procedures. In addition, the CHSO (or successor) located at USAID/Washington, is available to provide additional guidance, oversight and interpretation. In some circumstances (for example if an assurance is especially complicated or if there is a specific concern about risk) it may be reasonable to call on expertise from outside of USAID such as the Office for Protection from Research Risks (OPRR) at the National Institutes of Health. Copies of the Policy, a list of those

procedures which qualify as "minimal risk" activities and other guidance are available upon request from the CHSO. Questions and concerns that arise regarding interpretation and applicability of the Policy should be directed to the CHSO, USAID/Washington.