

**DIVISION OF HUMAN SUBJECT PROTECTIONS
OFFICE FOR PROTECTION FROM RESEARCH RISKS
NATIONAL INSTITUTES OF HEALTH
DEPARTMENT OF HEALTH AND HUMAN SERVICES**

The INDIAN HEALTH SERVICE

MULTIPLE PROJECT ASSURANCE (MPA)

FOR COMPLIANCE WITH DHHS REGULATIONS

FOR THE PROTECTION OF HUMAN SUBJECTS

(45 CFR 46)

AS AMENDED

GLOSSARY

- Affiliate Institution** - an institution which is legally separate from the signatory institution(s) to an Assurance but has a formal affiliation with the signatory institution(s) through an OPRR-approved Inter-Institutional Amendment or Assurance
- Assurance** - a document negotiated with and approved by OPRR which assures institutional compliance with 45 CFR 46
- Component** - any institution which is legally inseparable from the signatory institution(s)
- Cooperative Project Assurance (CPA)** - an Assurance designed to accommodate CPRP multi-protocol, multi-site research specifically recognized by OPRR
- Cooperative Protocol Research Programs (CPRP)** - DHHS multi-site, multi-protocol clinical trials in differing subject areas where data are pooled across institutions and which are explicitly recognized by OPRR as suited for CPAs (e.g., cooperative oncology trials of the National Cancer Institute)
- Federal** - departments and agencies of the Federal government that are a party to the Federal Policy (see 56FR28003)
- Federal Policy (56FR28003)** - minimum Federal standards for the protection of human research subjects, effective August 19, 1991 (see FR Volume 56, No. 117, Tuesday, June 18, 1991), and contained in 45 CFR 46 as Subpart A - also known as the Common Rule
- 45 CFR 46 (DHHS Regulations)** - Title 45 of the Code of Federal Regulations, Part 46, which consists of Subpart A (the Federal Policy for the Protection of Human Subjects) and Subparts B, C, and D which apply to fetuses, pregnant women and in-vitro fertilization of human ova; prisoners; and children respectively
- Inter-Institutional Amendment (IIA)** - a limited form of assurance to comply with 45 CFR 46 which is prepared by certain MPA affiliates (see Affiliate Institution). IIAs apply only when the affiliate regularly serves as a performance site for research conducted by a signatory institution(s)
- Multiple Project Assurance (MPA)** - a DHHS Assurance which applies during fixed and renewable periods to a broad spectrum of unrelated research activities
- Noninstitutional Investigator Agreement (NIA)** - an OPRR-authorized document entered into between a signatory institution and a non-institutional affiliate investigator (e.g., private practitioner) which assures compliance with 45 CFR 46 for a specified activity (e.g., cooperative oncology group trials)

- Headquarters Division of Medical Systems Research & Development (DMSRD), and Area Research & Publication Committee (ARPC) - the IHS offices whose functions include those of an "office of research administration," that is: providing a central focus for researchers, IRB, and administrators in processing protocols; arranging IRB reviews; keeping records; doing internal audits; and reporting and communicating pertinent information about human subject research--the Director, DMSRD providing research administration for the Headquarters IHS, the ARPC Chair for its Area
- Performance Site - any location where human subjects are involved in research for which an MPA, NIA, IIA, SPA, or CPA Assurance is required
- Primary Signatory Institution - where applicable, the signatory institution of two or more which is chosen to assume the function of the "office of research administration" for all signatory institutions
- Signatory Institution - an institution which OPRR finds eligible to enter into an Assurance and which has signed the Assurance
- Single Project Assurance- (SPA) - an Assurance document which is submitted to OPRR, upon request, for a specific DHHS research activity at a performance site where an MPA, IIA, NIA or CPA does not apply

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The INDIAN HEALTH SERVICE

Multiple Project Assurance of Compliance with DHHS Regulations for Protection of Human Research Subjects

The Indian Health Service (IHS), hereby gives assurance, as specified below, that it will comply with the Department of Health and Human Services (DHHS) regulations for the protection of human research subjects, 45 CFR Part 46, as amended to include provisions of the Federal Policy for the Protection of Human Subjects (56FR28003) as Subpart A, and as may be further amended during the approval period for this Assurance.

PART 1 - PRINCIPLES, POLICIES, AND APPLICABILITY

I. Ethical Principles

- A. The IHS is guided by the ethical principles regarding all research involving humans as subjects, as set forth in the report of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (entitled: Ethical Principles and Guidelines for the Protection of Human Subjects of Research [the "Belmont Report"]), regardless of whether the research is subject to Federal regulation or with whom conducted or source of support (i.e., sponsorship).
- B. All institutional and non-institutional performance sites for the IHS, domestic or foreign, will be obligated by the IHS to conform to ethical principles which are at least equivalent to those of the IHS, as cited in the previous paragraph or as may be determined by the DHHS Secretary.

II. IHS Policy

- A. All requirements of Title 45, Part 46, of the Code of Federal Regulations (45 CFR 46) will be met for all applicable DHHS-supported research, and all other human subject research regardless of sponsorship, except as otherwise noted in this Assurance. Federal (all departments and agencies bound by the Federal Policy) funds for which this Assurance applies may not be expended for research involving human subjects unless the requirements of this Assurance have been satisfied.
- B. Except for those categories specifically exempted or waived under 45 CFR 46 § 101(b)(1-6) or 101(i), all research covered by this Assurance will be reviewed and approved by an Institutional Review Board (IRB) which has been established under a Multiple Project Assurance (MPA) with the Office for Protection from Research

Risks (OPRR) (see this MPA, Section 1.II.G). The involvement of human subjects in research covered by this Assurance will not be permitted until an appropriate IRB has reviewed and approved the research protocol and informed consent has been obtained from the subject or the subject's legal representative (see § 46.111, 46.116, and 46.117).

- C. The IHS assures that before human subjects are involved in nonexempt research covered by this Assurance, the IHS IRBs will give proper consideration to:
 - 1. the risks to the subjects; and
 - 2. the anticipated benefits to the subjects and others; and
 - 3. the importance of the knowledge that may reasonably be expected to result; and
 - 4. the informed consent process to be employed.

- D. Certification of IRB review and approval for all Federally-sponsored research involving human subjects will be submitted to the Division of Medical Systems Research Development (DMSRD) or the Area Research and Publication Committee (ARPC) for forwarding to the appropriate Federal department or agency. Compliance will occur within the time and in the manner prescribed for forwarding certifications of IRB review to DHHS or other Federal departments or agencies for which this Assurance applies. As required under § 46.119, the IRB will review and recommend approval for involvement of human subjects in Federal research activities for which there was no prior intent for such involvement, but will not permit such involvement until certification of the IRB's review and approval is received by the appropriate Federal department or agency.

- E. Institutions that are not direct signatories to this Assurance are not authorized to cite this Assurance. The IHS will ensure that such other institutions and investigators not bound by the provisions of this Assurance for DHHS-sponsored research will satisfactorily assure compliance with 45 CFR 46, as required (see this MPA, Sections 2.I.D. and 2.II.N.), as a prior condition for involvement in human subject research which is under the auspices of the IHS (see this MPA, Section 1.III.A.). Institutions that have entered into an Inter-Institutional Amendment (IIA) to this Assurance must submit a Single Project Assurance (SPA) to OPRR of DHHS for DHHS-sponsored research, on request, when that research is not conducted under the auspices of a signatory institution to this Assurance.

- F. The IHS will comply with the requirements set forth in § 46.114 regarding cooperative research projects. When research covered by this Assurance is conducted at or in cooperation with another entity, all provisions of this Assurance remain in effect for that research. The IHS may accept, for the purpose of meeting the IRB review requirements, the review by an IRB established under another DHHS MPA. Such acceptance must be (a) in writing, (b) approved and signed by Director of DMSRD, and (c) approved and signed by correlative officials of each of the other cooperating institutions. A copy of the signed understanding will serve as an addendum to this Assurance and will be forwarded to the OPRR of DHHS by the DMSRD for approval.

- G. The IHS will exercise appropriate administrative overview to ensure that the IHS's policies and procedures to protect the rights and welfare of human subjects are being effectively applied in compliance with this Assurance.

III. Applicability

- A. This Assurance applies to all research involving human subjects, and all other activities which even in part involve such research, regardless of sponsorship, if one or more of the following apply:
 - 1. the research is sponsored by the IHS; or
 - 2. the research is conducted by or under the direction or co-direction of any employee or agent of the IHS in connection with his or her institutional responsibilities; or
 - 3. the research uses any property or facility of the IHS; or
 - 4. the research involves the use of the IHS's non-public information to identify or contact human research subjects or prospective subjects.
- B. All human subject research which is exempt from IRB review under § 46.101(b)(1-6) or 46.101(i) will be conducted in accordance with:
 - 1. the Belmont Report; and
 - 2. the IHS's administrative procedures to ensure valid claims of exemption; and
 - 3. orderly accounting for such activities.
- C. Components of the IHS are bound by the provisions of this Assurance. Those components which can be expected to participate in human subject research sponsored by DHHS or other Federal departments or agencies for which this Assurance will apply are identified in Appendix A. Appendix A will be revised as changes occur and revisions forwarded to OPRR.
- D. This Assurance must be accepted by other Federal departments or agencies that are bound by the Federal Policy for the Protection of Human Subjects when appropriate for the research in question and therefore applies to all human subject research so sponsored. Research that is neither conducted nor supported by a Federal department or agency but is subject to regulation as defined in § 46.102(e) must be reviewed and approved, in compliance with §§ 46.101, 46.102, and 46.107 through 46.117.

PART 2 - RESPONSIBILITIES

I. The IHS

- A. The IHS acknowledges that it bears full responsibility for the performance of all research involving human subjects covered by this Assurance, including complying with Federal, state, Tribal, or local laws as they may relate to such research.
- B. The IHS will require appropriate additional safeguards in research that involves:
 - 1. fetuses, pregnant women, or human ova *in vitro* fertilization (see 45 CFR 46 Subpart B); or
 - 2. prisoners (see 45 CFR 46 Subpart C); or
 - 3. children (see 45 CFR 46 Subpart D); or
 - 4. cognitively impaired subjects; or
 - 5. other groups requiring special attention, e.g., subjects of genetic research, subjects of research involving radiation, third parties at risk by the research, or potentially vulnerable people.
- C. The IHS, including all its named components (see this MPA, Appendix A), acknowledges and accepts its responsibilities for protecting the rights and welfare of human subjects of research covered by this Assurance.
- D. The IHS is responsible for acquiring appropriate Assurances or Amendments, when requested, and certifications of IRB review and approval for federally sponsored research from all its standing affiliates (see this MPA, Appendix B) and Assurances or Agreements for all others, domestic or foreign, which may otherwise become affiliated on a limited basis in such research.
- E. The IHS is responsible for ensuring that no affiliates cooperating in the conduct of federally sponsored research for which this Assurance applies do so without an appropriate assurance of compliance and satisfaction of IRB certification requirements.
- F. In accordance with the compositional requirements of § 46.107, the IHS has established the IHS IRBs for the IHS components listed in Appendix A and the membership rosters in Appendix C. Certain research supported by the U.S. Department of Education will be reviewed in accordance with the requirements of Title 34 CFR Parts 350 and 356 which require that the appropriate IHS IRBs include one person who is primarily concerned with the welfare of handicapped children or mentally disabled persons.
- G. The IHS will provide both meeting space and sufficient staff to support the IRB's review and recordkeeping duties.

- H. The IHS recognizes that involvement in research activities of any OPRR-recognized Cooperative Protocol Research Programs will involve additional reporting and recordkeeping requirements related to human subject protections.
- I. The IHS is responsible for ensuring that it and all its affiliates comply fully with all applicable Federal, state, and Tribal policies and guidelines, including those concerning notification of seropositivity, counseling, and safeguarding confidentiality where research activities directly or indirectly involve the study of human immunodeficiency virus (HIV) and all other high risk research.

II. Division of Medical Systems Research and Development (DMSRD), and Area Research and Publication Committees (ARPCs)

- A. The jurisdiction of the DMSRD partially overlaps or duplicates the jurisdiction of the ARPCs.
 - 1. The Chair of the ARPC is the Chair of the Area IRB. The Chair does those "office of research administration" functions for research proposals for which the Area IRB has jurisdiction. That jurisdiction includes being the IRB of record for research involving the Area IHS.
 - 2. The Director of DMSRD is the Chair for the Headquarters IRB. The DMSRD Director does those "office of research administration" functions for research proposals for which IHS has jurisdiction.
 - 3. With the concurrence of both the Director of DMSRD and the Area IRB, and documented as a change to this MPA with OPRR approval, the Area IRB may have jurisdiction to review research protocols without a second review by the Headquarters IHS IRB, for all protocols that:
 - a. are not possibly greater than minimal risk; and
 - b. do not involve special groups (see this MPA, Section 2.I.B); and
 - c. are not covered by the FDA regulations (21 CFR Parts 50 and 56).

(The Area IRBs with jurisdiction to review research protocols without a second review by the Headquarters IRB are noted in Appendix A.)
 - 4. The Headquarters IRB has jurisdiction to do a second IHS IRB review, both for all protocols reviewed by Area IRBs that do not have jurisdiction to review some protocols without that second review, and for all protocols that:
 - a. are possibly greater than minimal risk; or
 - b. involve special groups (see this MPA, Section 2.I.B), or
 - c. are covered by FDA regulations (21 CFR Parts 50 and 56).

- B. The DMSRD and ARPCs will receive from investigators all research protocols which involve human subjects, keep investigators informed of decisions and administrative processing, and return all disapproved protocols to them.
- C. The DMSRD is responsible for reviewing for the Headquarters IHS IRB, and the ARPCs are responsible for reviewing for the Area IHS IRBs, the preliminary determinations of exemption by supervisors and for making the final determination based on § 46.101(b)(1-6) or 46.101(i). Notice of concurrence for all exempt research will be promptly conveyed in writing to the investigator. All nonexempt research will be forwarded to the appropriate IHS IRB(s).
- D. The DMSRD and ARPCs will make the preliminary determination of eligibility for expedited review procedures (see § 46.110) for their respective IHS IRBs, following the list of eligible research activities in 46FR8392. Expedited review of research activities will not be permitted where full board review is required.
- E. The Headquarters IRB has final responsibility to determine if an activity, thought not to be research by an Area IRB or by an ARPC for its Area IRB, is research for purposes of the regulations 45 CFR 46. The Headquarters IRB also has final responsibility to determine if research:
 - 1. that had been considered exempt, is not exempt from IRB review based on § 46.101(b)(1-6) or 46.101(i); or
 - 2. that had been considered eligible for review by only Area IRB(s), is possibly greater than minimal risk or involves a special group (see this MPA, Section 2.I.B.) or is covered by FDA regulations (21 CFR Parts 50 and 56); or
 - 3. that had been considered eligible for expedited review, is not eligible (see § 46.110) following the list of eligible research activities in 46FR8392.

The Headquarters IRB will promptly send notice of its nonconcurrence with an Area IRB's or ARPC's determination, in writing to that entity.

- F. By delegation from the Director of the IHS, the Director of DMSRD will review all research (whether exempt or not) and decide whether the IHS will permit the research. If approved by the IRB, but not permitted by the IHS, the Director of DMSRD will promptly convey notice to the investigator and the IHS IRB(s). Neither the Director of DMSRD nor any other office of the IHS may approve a research activity that has been disapproved by the appropriate IRB.
- G. The administration for the IRB of record, i.e., DMSRD or ARPC, will forward certification of IRB approval of proposed research to the appropriate Federal, state, or Tribal department or agency only after all IRB-required modifications have been incorporated to the satisfaction of the IHS IRB(s). If the Area IRB has the jurisdiction to review the proposed research without duplicate review by the Headquarters IRB (see this MPA, Section 2.II.A.3.), that ARPC will also forward a copy of the certification of IRB approval to the DMSRD for its records.

- H. The DMSRD and ARPCs will designate procedures for the retention of signed consent documents for at least three years past completion of the research activity.
- I. The DMSRD and ARPCs will ensure both:
 - 1. that all human subject research which is exempt under § 46.101(b)(1-6) or 46.101(i) does not pose greater than minimal risk to human subjects; and
 - 2. that all such research will be conducted in accordance with (a) the Belmont Report, and (b) the IHS's administrative procedures to ensure valid claims of exemption, and (c) orderly accounting for such activities (see this MPA, Section 1.III.B.).
- J. The DMSRD and ARPCs will maintain and arrange access for inspection of IRB records as provided for in § 46.115.
- K. The DMSRD and ARPCs are responsible for ensuring constructive communication among the research administrators, division and program heads, research investigators, clinical care staff, human subjects, Area and Service Unit Directors, Tribal officials, and other relevant officials to maintain a high level of awareness regarding the safeguarding of the rights and welfare of the subjects.
- L. The DMSRD and ARPCs will arrange for and document in its records that each individual who conducts or reviews human subject research has first been provided with a copy of this Assurance, as well as with ready access to copies of 45 CFR 46, regulations of other Federal departments or agencies as may apply, the Belmont Report, and all other pertinent Federal, state, and Tribal policies and guidelines related to the involvement of human subjects in research.
- M. The DMSRD will report promptly to the appropriate IHS IRBs, appropriate IHS officials, OPRR, and any other sponsoring or reviewing Federal, state, or Tribal department or agency head:
 - 1. any injuries to human subjects or other unanticipated problems involving risks to subjects or others; and
 - 2. any serious or continuing noncompliance with 45 CFR 46, other applicable Federal, state, or Tribal regulations, or requirements of the IRB; and
 - 3. any suspension or termination of IRB approval for research.
- N. The DMSRD will ensure:
 - 1. solicitation, receipt, and management of all assurances of compliance (whatever the appropriate format), and certifications of IRB review (where appropriate) for all affiliates to the IHS (including those listed in Appendix B); and
 - 2. subsequent submission of these documents to the proper authorities as a condition for involvement in human subject research activities sponsored by DHHS, or sponsored or reviewed by any other Federal, state, or Tribal department or agency for which this Assurance applies.

- O. The DMSRD will ensure that all affiliated performance sites, that are not otherwise required to submit assurances of compliance with 45 CFR 46 and other applicable Federal, state, or Tribal regulations for the protection of research subjects, at least document mechanisms to implement the equivalent of ethical principles to which the IHS is committed (see this MPA, Section 1.I.).
- P. When an IHS IRB accepts responsibility for review of research which is subject to this Assurance and conducted by any independent investigator who is not otherwise subject to the provisions of this or other Assurance, the DMSRD will obtain and retain a Noninstitutional Investigator Agreement (NIA) to document the investigator's commitment to abide:
 - 1. by the same requirements for the protection of human research subjects as does the IHS; and
 - 2. by the determinations of the appropriate IHS and non-IHS IRBs.
- Q. The DMSRD assumes responsibility for ensuring conformance with special reporting requirements for any OPRR-recognized Cooperative Protocol Research Programs in which the IHS participates.
- R. The DMSRD will ensure compliance with the requirements set forth in this Assurance and § 46.114 regarding cooperative research projects. In particular, when an IHS IRB relies on another institution with a DHHS MPA, the DMSRD will ensure that documentation of this reliance will be (a) in writing, (b) approved and signed by the Director of DMSRD, (c) approved and signed by the correlative officials of each of the other cooperating institutions, and (d) retained by the DMSRD for at least three years past completion of the related research project. Where an agreement between MPA IRBs is planned, the DMSRD will forward a copy of the required signed understanding to OPRR for inclusion in this Assurance as an addendum.
- S. The DMSRD will be responsible for procedural and recordkeeping audits not less than once every year for the purpose of detecting, correcting, and reporting (as required) administrative and/or material breaches in uniformly protecting the rights and welfare of human subjects as required at least by 45 CFR 46 and as may otherwise be additionally required by the IHS. These audits will cover all IHS IRBs, reviews by other institutions with a DHHS MPA upon which the IHS IRBs relied, and Inter-Institutional Amendments and Cooperative Project Assurances.

III. IHS Institutional Review Boards (IRBs)

- A. All IHS IRBs will review, and have the authority to approve, require modification in, or disapprove all research activities within their jurisdiction (see this MPA, Section 2.II.A.), including proposed changes in previously approved human subject research. For approved research, all IRBs will determine which activities require continuing review more frequently than every twelve months or need verification that no changes have occurred if there was a previous IRB review and approval.

- B. IRB decisions and requirements for modifications will be promptly conveyed to investigators and the DMSRD, in writing. Written notification of decisions to disapprove will be accompanied by reasons for the decision with provision of an opportunity for reply by the investigator, in person or in writing. The investigator may formally appeal an IRB decision only to the IRB(s) with jurisdiction.
- C. In compliance with 45 CFR 46 and provisions of this Assurance, all IHS IRBs will do initial and continuing convened IRB reviews and approvals for each project, unless the DMSRD or ARPCs properly find the project either (a) to be exempt under §§ 46.101(b) and 46.101(i), or (b) to be eligible for expedited review (see § 46.110), following the list of eligible research activities in 46FR8392. Continuing reviews will be done by the IHS IRB(s) of record, and will be preceded by IRB receipt of appropriate progress reports from the investigator, including available study-wide findings. Continuing reviews of projects that were properly approved by expedited review may be done by expedited review; continuing reviews of projects that were approved by a full IRB review must be by a full convened IRB.
- D. All IHS IRBs will observe the quorum requirements of § 46.108(b). In no case will the quorum for an IHS IRB be less than five. At least one American Indian or Alaska Native IRB member whose concerns are primarily in nonscientific areas, and at least one IRB member whose concerns are primarily in scientific areas, must be present both to start every convened IRB meeting, and during the discussion and decision for each protocol.
 - 1. No IRB may have a member participating in the IRB's initial or continuing review of any project in which the member has a conflicting interest, except to provide information requested by the IRB.
 - 2. All IHS IRBs must have effective knowledge of subject populations, institutional constraints, differing legal requirements, and other factors which can foreseeably contribute to a determination of risks and benefits to subjects and subjects' informed consent and can properly judge the adequacy of information to be presented to subjects in accordance with requirements of §§ 46.103(d), 46.107(a), 46.111, and 46.116.
- E. All IHS IRBs will determine, in accordance with the criteria found at § 46.111 and Federal, state, or Tribal policies and guidelines for involvement of human subjects in HIV and all other high-risk research, that protections for human research subjects are adequate.
- F. All IHS IRBs will ensure that legally effective informed consent will be obtained and documented in a manner that meets the requirements of § 46.116 and 46.117. The IRB will have the authority to observe or have a third party observe the consent process.
- G. All IHS IRBs will be sufficiently qualified through the experience and expertise of its members, and the diversity of the members' backgrounds including consideration of

the ethnic and cultural backgrounds of members and sensitivity to issues such as community attitudes and Tribal sovereignty, to promote respect for their advice and counsel in safeguarding the rights and welfare of human subjects, especially among American Indian and Alaska Native peoples and communities.

1. All IHS IRBs will include:
 - a. both male and female members; and
 - b. members representing a variety of professions; and
 - c. at least two members whose primary expertise is in a nonscientific area; and
 - d. at least one member who is not otherwise affiliated with the IHS.
 2. Because IHS policy is to promote the self-determination by and cultural integrity of American Indian and Alaska Native communities (P.L. 94-437), all IHS IRBs will include two American Indian or Alaska Native members whose concerns are primarily in nonscientific areas.
 3. Where appropriate, all IHS IRBs will determine that adequate additional protections are ensured for fetuses and pregnant women, prisoners, and children, as required by Subparts B, C, and D of 45 CFR 46. The DMSRD will notify OPRR promptly when membership of any IHS IRB is modified to satisfy requirements of § 46.304 and when any IHS IRB fulfills its duties under § 46.305(c).
- H. Scheduled meetings of all IHS IRBs for review of each research activity will occur not less than every 12 months and may be more frequent, if required by the IRB on the basis of degree of risk to subjects. All IRBs may be called into an interim review session by the Chair at the request of any IRB member, Tribal official, or IHS official to consider any matter concerned with the rights and welfare of any subject.
- I. All IHS IRBs will prepare and maintain adequate documentation of its activities in accordance with § 46.115 and in conformance with requirements of the DMSRD.
- J. All IHS IRBs will forward to the DMSRD any significant or material finding or action, at least to include the following:
1. any injuries to human subjects, or any other unanticipated problems involving risks to human subjects or to other people; and
 2. any serious or continuing noncompliance with 45 CFR 46, other applicable Federal, state, or Tribal regulations, or requirements of the IRB; and
 3. any suspension or termination of IRB approval.
- K. In accordance with § 46.113, all IHS IRBs will have the authority to suspend or terminate previously approved research that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to subjects.

- L. All IHS IRBs will ensure effective input (consultants or voting or nonvoting members) for all initial and continuing reviews conducted on behalf of performance sites where there will be human research subjects. IRB minutes will document attendance of those other than regular voting members. The IRB membership rosters in Appendix C include people who are identified as knowledgeable about any affiliate institution that has entered into an Inter-Institutional Amendment or other Assurance in which a non-IHS IRB relies on one or more IHS IRBs.
- M. When two or more IHS IRBs review the same proposal, the conditions required by one sometimes may differ from those by the other.
 - 1. When two or more Area IRBs each are the IRB of record for a proposed research because it will be done in those Areas, if the IRBs require different conditions, each set of conditions applies to the research done in its Area.
 - 2. When duplicate reviews are done by both the Headquarters and Area IRBs, if the two reviews require different conditions, the conditions are additive (i.e., the total conditions are those by one IRB plus those by the other.)
 - 3. When duplicate reviews are done by both the Headquarters and Area IRBs, if the two reviews each require a condition addressing a similar topic, the condition that is more stringent in protecting the interests of the subject supersedes the similar but less stringent condition.
 - 4. When different IHS IRBs require mutually contradictory conditions, the IRBs will resolve the contradiction between them by negotiation.
- N. All IHS IRBs will act with reasonable dispatch, upon request, to provide full board review of protocols of OPRR-recognized Cooperative Protocol Research Programs (CPRP). The IRB will not employ expedited review procedures for CPRP protocols when they are to be entered into for the purpose of research. Although emergency medical care based on such protocols is permitted without prior IRB approval, patients receiving emergency care under these conditions will not be counted as research subjects and resultant data will not be used for research purposes.
- O. Certifications of IRB review and approval will be forwarded:
 - 1. to the appropriate Federal, state, or IRB department or agency for research sponsored or reviewed by such departments or agencies; and
 - 2. to the Director of DMSRD.

IV. IHS Area Directors, and Associate Director of Headquarters West

- A. Area Directors, through appropriate procedures established within their respective Areas, are responsible to ensure review of research protocols involving IHS Area personnel or resources for ethical considerations, scientific merit, and concordance with the commitment by the U.S. Government and IHS to the self-determination by

and cultural integrity of American Indian and Alaska Native communities (P.L. 94-437).

- B. Each IHS Area will have at least one IRB to review all human subject research. There are 12 Area IRBs. The membership of each Area IRB is appointed by the respective Area Director. The membership of the Headquarters IHS IRB is appointed by the Deputy Director of Headquarters Operations-West.

V. IHS Program Directors

- A. With the concurrence of the Director of DMSRD, Directors of IHS Programs (e.g., Cancer, Diabetes, Mental Health) who have received sufficient IHS training about IRBs and protection of human subjects and communities may be authorized to review protocols and activities to make the preliminary determination if the activity is research, and if so, is the research exempt from IRB review based on § 46.101(b)(1-6) or 46.101(i).
- B. Each authorized IHS Program Director will receive all protocols of research or of activity that may be research involving that program that have not been sent to the Area or Headquarters IHS IRB(s). The Program Director is responsible for the preliminary determination of non-research or exemption based on § 46.101(b)(1-6) or 46.101(i). Notice of concurrence for all non-research activity or exempt research will be promptly sent in writing to the initiator, with a copy to DMSRD and to the appropriate ARPC(s). All nonexempt research will be sent to the appropriate IHS (Area or Headquarters) IRB(s) for review.

VI. Research Investigators

- A. Research investigators acknowledge and accept their responsibility for protecting the rights and welfare of human research subjects and for complying with all applicable provisions of this Assurance.
- B. Research investigators who intend to involve human research subjects, and anyone who intends to do an activity that is possibly research, will not make the final determination that the activity is not research and, if it research, that it is exempt from 45 CFR 46, other applicable Federal, state, or Tribal regulations, or certain provisions of this Assurance. The IHS IRBs make that determination (see this MPA, Sections 2.II.A-D.); the Headquarters IRB has final authority to make those determinations (see this MPA, Section 2.II.E.).
- C. Research investigators are responsible for providing a copy of the IRB-approved and signed informed consent document to each subject at the time of consent, unless the IRB has specifically waived this requirement. All signed consent documents are to be retained in a manner approved by the DMSRD or ARPC(s).
- D. Research investigators will promptly report proposed changes in previously approved human subject research activities to the IRB. The proposed changes will not be

initiated without IRB review and approval, except where necessary to eliminate apparent immediate hazards to the subjects.

- E. Research investigators are responsible for reporting progress of approved research to the DMSRD or ARPC(s), as often as and in the manner prescribed by the approving IRB(s) on the basis of risks to subjects, but no less than once per year.
- F. Research investigators will promptly report to the IRB any injuries or other unanticipated problems involving risks to subjects and others.
- G. No research investigator who is obligated by the provisions of this Assurance, any associated Inter-Institutional Amendment, or Noninstitutional Investigator Agreement will seek to obtain research credit for, or use data from, patient interventions that constitute the provision of emergency medical care without prior IRB approval. A physician may provide emergency medical care to a patient without prior IRB review and approval, to the extent permitted by law [see § 46.116(f)]. However, such activities will not be counted as research nor the data used in support of research.
- H. Research investigators will advise all appropriate IHS and non-IHS IRB(s), DMSRD or ARPC(s), and the appropriate officials of other institutions (such as hospitals) of the intent to admit to those other institutions any human subjects who are involved in research protocols for which this Assurance or any related Inter-Institutional Amendment or Noninstitutional Investigator Agreement applies. When such admission is planned or a frequent occurrence, those institutions must possess an applicable OPRR-approved Assurance prior to involvement of such persons as human subjects in those research protocols.

VII. Affiliated Institutions and Investigators

- A. Each affiliate to the IHS that is involved in DHHS-sponsored research activities must provide to the DMSRD an appropriate written assurance of compliance with the Belmont Report and 45 CFR 46 (or equivalent protections if a foreign site).
- B. Each affiliate institution must respond to a request by the DMSRD for an Inter-Institutional Amendment or for a Single Project Assurance (standard or modified), when and as appropriate, whichever is most suited to the circumstances.
- C. Each non-institutional affiliate (e.g., a private practice physician not otherwise an employee of the IHS or who otherwise would not ordinarily be bound by the provisions of this Assurance) who is involved in human subject research of the IHS must respond to a request by the DMSRD for a Noninstitutional Investigator Agreement when required.
- D. Performance sites that are not legally inseparable components of the IHS (whether an institutional or non-institutional affiliate) are not authorized to cite this Assurance.

PART 3 - SIGNATURES

I. IHS Endorsements

The officials signing below assure that any research activity conducted, supported, or otherwise subject to DHHS or other Federal departments or agencies that are authorized to rely on this Assurance (Parts 1, 2, 3 and Appendices) or any other sources provided for in this Assurance, will be reviewed and approved by the appropriate IHS IRBs in accordance with the requirements of all applicable Subparts of Part 46, Title 45 of the Code of Federal Regulations, with this Assurance, and the stipulations of the IHS IRBs.

A. Primary Signatory Institution

1. AUTHORIZED INSTITUTIONAL OFFICIAL

Signature: _____ Date: _____
Name: Michael H. Trujillo, MD, MPH
Title: Director
Institution: Indian Health Service
Address: 5600 Fishers Lane
Parklawn Building, Room 6-05
Rockville, MD 20857
Phone: (301) 443-1083

2. PRIMARY CONTACT

Signature: _____ Date: _____
Name: William L. Freeman, MD, MPH
Title: Director
Institution: DMSRD, Indian Health Service
Address: 5300 Homestead Road NE
Albuquerque, NM 87110-1293
Phone: (505) 837-4141

B. Other Signatory Institutions

[none]

FOR DHHS USE ONLY

II. Office for Protection from Research Risks (DHHS) Approval

A. DHHS RECOMMENDING OFFICIAL

Signature: _____ Date: _____

Name: Katherine Duncan, M.D.

Title: Adjunct Medical Officer

Address: Division of Human Subject Protections

Office for Protection from Research Risks (OPRR)

6100 Executive Boulevard

Suite 3B10, MSC 7507

Rockville, MD 20892-7507

Phone: (301) 496-7005

EFFECTIVE DATE OF ASSURANCE: _____

EXPIRATION DATE OF ASSURANCE: _____

B. DHHS APPROVING OFFICIAL

Signature: _____ Date: _____

Name: Clifford C. Scharke, D.M.D., M.P.H.

Title: Chief, Assurance Branch

Address: Division of Human Subject Protections

Office for Protection from Research Risks (OPRR)

6100 Executive Boulevard

Suite 3B10, MSC 7507

Rockville, MD 20892-7507

Phone: (301) 496-7005

PART 4 - APPENDICES

Appendix A

DHHS MPA# 1493

Date: \

COMPONENTS WHICH ARE LEGALLY INSEPARABLE FROM EACH DESIGNATED SIGNATORY INSTITUTION AND ARE AUTHORIZED TO CITE THIS MPA OR PARTICIPATE IN RESEARCH OF THE SIGNATORY

Names, Cities, and States

Signatory Institution #1 (i.e., Primary): Indian Health Service, Rockville, MD

Components Authorized to Cite or Participate

<u>Aberdeen Area</u>	<u>Rapid City</u>	<u>SD</u>
<u>Alaska Area</u>	<u>Anchorage</u>	<u>AK</u>
<u>Albuquerque Area</u>	<u>Albuquerque</u>	<u>NM</u>
<u>Bemidji Area</u>	<u>Bemidji</u>	<u>MN</u>
<u>Billings Area</u>	<u>Billings</u>	<u>MT</u>
<u>California Area</u>	<u>Sacramento</u>	<u>CA</u>
<u>Nashville Area</u>	<u>Nashville</u>	<u>TN</u>
<u>Navajo Area</u>	<u>Window Rock</u>	<u>AZ</u>
<u>Oklahoma Area</u>	<u>Oklahoma City</u>	<u>OK</u>
<u>Phoenix Area</u>	<u>Phoenix</u>	<u>AZ</u>
<u>Phoenix Indian Medical Center</u>	<u>Phoenix</u>	<u>AZ</u>
<u>Portland Area</u>	<u>Portland</u>	<u>OR</u>
<u>Headquarters</u>	<u>Albuquerque</u>	<u>NM</u>

* Area IRBs with jurisdiction to review certain protocols without a second review (see this MPA, Section 2.II.A.3.).

Signatory Institution #2: none

Appendix B

DHHS MPA #: 1493

Date: \

STANDING AFFILIATES WHICH ARE LEGALLY SEPARATE FROM EACH
DESIGNATED SIGNATORY INSTITUTION WHERE OPRR-APPROVED INTER-
INSTITUTIONAL AMENDMENTS ARE REQUIRED

Names, Cities, and States

Signatory Institution #1 (i.e., Primary): Indian Health Service

Affiliate Institutions: none

Signatory Institution #2: none

Appendix C

DHHS MPA #: 1493

Date: \

INSTITUTIONAL REVIEW BOARD (IRB) MEMBERSHIP ROSTERS:

PART 5 - ATTACHMENTS

A. OPRR Reports - 45 CFR 46

B. The Belmont Report

C. Inter-Institutional Amendment

[none]

D. Noninstitutional Investigator Agreement

[none]

E. OPRR-Recognized Cooperative Protocol Research Programs

[none]