

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

The **University of Puerto Rico, Medical Sciences Campus**, hereinafter known as the "Institution" (see Appendix A), 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. This Institution 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 this Institution, domestic or foreign, will be obligated by this Institution to conform to ethical principles which are at least equivalent to those of this Institution, as cited in the previous paragraph or as may be determined by the DHHS Secretary.

II. Institutional 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 Section 101(b)(1-6) or 101(l), all research covered by this Assurance will be reviewed and approved by the Institutional Review Board (IRB) which has been established under a Multiple Project Assurance (MPA) or as may be otherwise agree to by OPRR (see Part 1, II, G). The involvement of human subjects in

research covered by this Assurance will not be permitted until the IRB has reviewed and approved the research protocol and informed consent has been obtained from the subject or the subject's legal representative (see Sections 111, 116, and 117), unless properly waived by the IRB under Section 116(c), (d) or by any applicable waiver under Section 101(I).

C. This Institution assures that before human subjects are involved in nonexempt research covered by this Assurance, the IRB will give proper consideration to:

1. the risks to the subjects,
2. the anticipated benefits to the subjects and others,
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 Office of Research Administration (ORA) 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 provided for under section 118, applications and proposals lacking definite plans for involvement of human subjects will not require IRB review and approval prior to award. However, except for research exempted or waived under Section 101 (b) or (I), no human subjects may be involved in any project supported by such awards until IRB review and approval has been certified to the appropriate Federal department or agency.

As required under Section 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. This Institution 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 Part 2, I, D and II, K), as a prior condition for involvement in human subject research which is under the auspices of this Institution (see Part 1, III, A). Institutions that have entered into an Inter-Institutional Amendment (IIA) to this Assurance must submit a Single Project Assurance (SPA) to the Office for Protection from Research Risks (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. This Institution will ensure that any collaborating entities (i.e., those engaged in human subject research by virtue of subject accrual, transfer of identifiable information, and/or in exchange of something of value, such as material support [e.g., money, drugs, or identifiable specimens], coauthorship, intellectual property, or credits) materially engaged in the conduct of non-federally sponsored research involving human subjects will possess mechanisms to protect human research subjects that are at least equivalent to those procedures provided for in the ethical principles to which this Institution is committed (see Part 1, I).
- G. This Institution will comply with the requirements set forth in Section 114 of the regulations 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. This Institution will not accept, for the purpose of meeting the IRB review requirements, the review of any other IRB.
- H. This Institution will exercise appropriate administrative overview to ensure that the Institution's policies and procedures designed for protecting the rights and welfare of human subjects are being effectively applied in compliance with this Assurance.
- I. Description of this Institution's policy for the protection of human subjects is contained in its internal written procedures which are available to OPRR and other Federal departments or agencies, upon request. Appendix D to this Assurance abstracts pertinent organizational, personnel, and reporting procedures sufficient to describe the substance and relative prominence conferred upon the protection of subjects.

III. Applicability

- A. Except for research in which the only involvement of humans is in one or more of the categories exempted or waived under Section 101(b)(1-6) or 101(i), 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 this Institution, or

2. the research is conducted by or under the direction of any employee or agent of this Institution in connection with his or her Institutional responsibilities, or
 3. the research is conducted by or under the direction of any employee or agent of this Institution using any property or facility of this Institution, or
 4. the research involves the use of this Institution's non-public information to identify or contact human research subjects or prospective subjects.
- B. All human subject research which is exempt under Section 101(b)(1-6) or 101(i) will be conducted in accordance with: (1) the Belmont Report, (2) this Institution's administrative procedures to ensure valid claims of exemption, and (3) orderly accounting for such activities.
- C. Components of this Institution 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 Section 102(e) must be reviewed and approved, in compliance with Sections 101, 102, and 107 through 117.

PART 2 - RESPONSIBILITIES

I. Institution

- A. This Institution acknowledges that it bears full responsibility for the performance of all research involving human subjects, covered by this Assurance, including complying with Federal, state, or local laws as they may relate to such research.
1. This Institution will ensure that, unless specifically exempted by 45 CFR 46, all research covered by this assurance will be reviewed and approved by the IRB which has been established under an assurance of compliance negotiated with DHHS. The involvement of human subjects in research covered by this policy will not be permitted until the IRB has reviewed and approved the research protocol ensuring that an informed consent is required and obtained in accord with and to the extent required by 45 CFR 46.116. Certification of the IRB's review and approval for all DHHS funded research involving human subjects will be

submitted to DHHS with the application of proposal for funding or as soon as approved by the IRB. Furthermore, the IRB's review of research on a continuing basis will be conducted at appropriate intervals but not less than once per year. Non DHHS funded research involving human subjects will be handled in the same manner, whereas certification of the IRB's review and approval for research involving human subjects will be submitted to the sponsoring Institution as approved by the IRB.

2. It is the policy of this Institution, that unless informed consent has been specifically waived by the IRB in accordance with 45 CFR 46.116, no research investigator shall involve any human being as a subject in research unless the research investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative.
- B. This Institution 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), (2) prisoners (see 45 CFR 46 Subpart C), (3) children (see 45 CFR 46 Subpart D), (4) the cognitively impaired, or (5) other potentially vulnerable groups.
 - C. This Institution, including all its named components (see Appendix A), acknowledges and accepts its responsibilities for protecting the rights and welfare of human subjects of research covered by this Assurance.
 - D. This Institution 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 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. This Institution is responsible for ensuring that no performance site cooperating in the conduct of federally sponsored research for which this Assurance applies do so without Federal department or agency approval of an appropriate assurance of compliance and satisfaction of IRB certification requirements.
 - F. In accordance with the compositional requirements of Section 107, this Institution has established the IRB listed in the attached roster (see 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 IRB include one person who is primarily concerned with the welfare of handicapped children or mentally disabled persons.

- G. This Institution will provide both meeting space and sufficient staff to support the IRB's review and recordkeeping duties.
- H. This Institution recognizes that involvement in research activities of any OPRR-recognized Cooperative Protocol Research Programs (CPRPs) will involve additional reporting and recordkeeping requirements related to human subject protection.
- I. This Institution is responsible for ensuring that it and all its affiliates comply fully with all applicable Federal 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).
- J. This Institution will maintain one IRB in accordance with 45 CFR 46. The IRB will have the responsibility and authority in the Institution, its components and affiliates to review, approve, disapprove or require changes in appropriate research activities for the protection of human subjects.
- K. This Institution encourages and promotes constructive communication among the IRB, research investigators, research administrators, department heads, clinical care staff, other Institutional officials, and human subjects as a means of maintaining a high level of awareness regarding the safeguarding of the rights and welfare of the subjects.
- L. This Institution will exercise appropriate administrative overview carried out at least annually to ensure that its practices and procedures designed for the protection of the rights and welfare of human subjects are being effectively applied and are in compliance with the requirements of 45 CFR 46 (revised June 18, 1991) and this assurance.
- M. This Institution will ensure that all research projects involving human tissues and biological substances which may present a hazard or biohazard to laboratory personnel be forwarded to the Institutional Biosafety Committee.
- N. This Institution will comply with the requirements set forth in 45 CFR 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.
- O. This Institution shall provide each individual at the Institution conducting or reviewing human subject research with a copy of this Institutional assurance of

compliance and copies of any further modifications, which may be made to this assurance, with the exception of changes in IRB membership.

II. Office of Sponsored Programs (OSP)

- A. The OSP will review all research grants, contracts and solicitations to ensure that proposed research projects can be performed in the Institution or affiliates. The OSP will ensure that Institutional commitments are obtained, and proposed research projects meet all federal and local regulations.

III. Office of Compliance (OC)

- A. The OC 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.
- B. The OC is responsible for reviewing the preliminary determinations of exemption by investigators and for making the final determination based on Section
- C. The OC will make the preliminary determination of eligibility for expedited review procedures (see Section 110). Expedited review of research activities will not be permitted where full board review is required.
- D. The OC will review all research (whether exempt or not) and decide whether the Institution will permit the research. If approved by the IRB, but not permitted by the OC the OC will promptly convey notice to the investigator and the IRB Chair. Neither the OC nor any other office of the Institution may approve a research activity that has been disapproved by the appropriate IRB.
- E. The OC will forward certification of IRB approval of proposed research to the appropriate Federal department or agency only after all IRB-required modifications have been incorporated to the satisfaction of the IRB.
- F. The OC will designate procedures for the retention of signed consent documents for at least three years past completion of the research activity.
- G. The OC will maintain and arrange access for inspection of IRB records as provided for in Section 115.
- H. The OC is responsible for ensuring constructive communication among the research administrators, department heads, research investigators, clinical care staff, human subjects, and Institutional officials as a means of maintaining a high

level of awareness regarding the safeguarding of the rights and welfare of the subjects.

- I. The OC 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 policies and guidelines related to the involvement of human subjects in research.
- J. The OC will report promptly to the IRB, appropriate Institutional officials, the Office for Protection from Research Risks (OPRR), and any other sponsoring Federal department or agency head:
 - 1. any injuries to human subjects or other unanticipated problems involving risks to subjects or others,
 - 2. any serious or continuing noncompliance with the regulations or requirements of the IRB, and
 - 3. any suspension or termination of IRB approval for research.
- K. The OC will ensure (a) solicitation (or confirmation where applicable assurance to comply already exist), receipt, and management of all assurances of compliance (whatever the appropriate format), and certifications of IRB review (where appropriate) for all performance sites to this Institution (including those listed in Appendix B), and (b) subsequent submission of new documents to the proper Federal department or agency authorities (e.g., OPRR for DHHS) as a condition for involvement of each site in human subject research activities sponsored by DHHS or any other Federal department or agency for which this Assurance applies.
- L. The OC will ensure that all affiliated performance sites that are not otherwise required to submit assurances of compliance with Federal regulations for the protection of research subjects at least document mechanisms to implement the equivalent of ethical principles to which this Institution is committed (see Part 1, I).
- M. When an IRB of this Institution 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 Assurance, the OC will either: (a) obtain and retain an NonInstitutional Investigator Agreement (NIA) for CPRP activities (with copies to the investigator and the authorizing CPRP) or (b) obtain an Agreement for an Independent Investigator (All) for review and approval by the appropriate Federal department or agency for non-CPRP activities to document the investigator's commitment to abide: (1) by the

same requirements for the protection of human research subjects as does this Institution(s) and (2) the determinations of the IRB.

- N. The OC assumes responsibility for ensuring conformance with special reporting requirements for any OPRR-recognized CPRPs in which the signatory Institution(s) participate(s).
- O. The OC 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 the regulations and as may otherwise be additionally required by this Institution.
- P. The OC will ensure compliance with the requirements set forth in this Assurance and Section 114 regarding cooperative research projects. For all Cooperative Amendments (CAs) the OC will forward the original of the required signed understanding to OPRR for approval and inclusion in this Assurance as an addendum.
- Q. When the OC determines that a research project will not be performed by the Institution, it will notify the IRB of the determination. The OC understand and agrees that a research project that has not been approved by the IRB cannot and will not be approved nor accepted by the OC, any other Institutional official nor by the Institutional authorized official.

IV. Institutional Review Board (IRB)

- A. The IRB(s) will review, and have the authority to approve, require modification in, or disapprove all research activities, including proposed changes in previously approved human subject research. For approved research, the IRB 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 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 writing.
- C. Initial and continuing convened IRB reviews and approvals will occur in compliance with 45 CFR 46 and provisions of this Assurance for each project unless properly found to be exempt (Section 101[b] or [i]) by the OC. Continuing

reviews will be preceded by IRB receipt of appropriate progress reports from the investigator, including available study-wide findings.

- D. The IRB will observe the quorum requirements of Section 108(b). This Institution's IRB has 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 Sections 103(d), 107(a), 111, and 116.
- E. The IRB will determine, in accordance with the criteria found at 45 CFR 46.111 and Federal policies and guidelines for involvement of human subjects in HIV research, that protection for human research subjects are adequate.
- F. The IRB will ensure that legally effective informed consent will be obtained and documented in a manner that meets the requirements of Sections 116 and 117. The IRB will have the authority to observe or have a third party observe the consent process.
- G. Where appropriate, the IRB will determine that adequate additional protection are ensured for fetuses, pregnant women, prisoners, and children, as required by Subparts B, C, and D of 45 CFR 46. The IRB will notify OPRR promptly when IRB membership is modified to satisfy requirements of 45 CFR 46.304 and when the IRB fulfills its duties under 45 CFR 46.305(c).
- H. Scheduled meetings of the IRB(s) 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. The IRB may be called into an interim review session by the Chairperson at the request of any IRB member or Institutional official to consider any matter concerned with the rights and welfare of any subject.
- I. The IRB will prepare and maintain adequate documentation of its activities in accordance with Section 46.115 and in conformance with Office of Research Administration requirements.
- J. The IRB will forward to the Office of Sponsored Programs and the Office of Legal Aides any significant or material finding or action, at least to include the following:
 - 1. injuries or any other unanticipated problems involving risks to subjects or others,

2. any serious or continuing noncompliance with the regulations or requirements of the IRB, and
 3. any suspension or termination of IRB approval.
- K. In accordance with Section 113, the IRB 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. The IRB for this Institution 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 list(s) in Appendix C includes those who are identified as knowledgeable about any affiliate Institution having entered into an Inter-Institutional Amendment or other Institutional performance site for which an Assurance is required when relying on the IRB of this Institution.
- M. The IRB 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.
- N. Certifications of IRB review and approval will be forwarded by the IRB to the appropriate Federal department or agency for research sponsored by such departments or agencies.
- O. The IRB assumes responsibility for ensuring conformance with special reporting requirements for any OPRR recognized Cooperative Protocol Research Programs in which the signatory Institution participate.
- IV. Research Investigator
- 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 will not make the final determination of exemption from applicable Federal regulations or provisions of this Assurance.
 - 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 OC.
 - 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 IRB, as often as and in the manner prescribed by the approving IRB 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 or 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 Section 116[f]). However, such activities will not be counted as research nor the data used in support of research.
 - H. Research investigators will advise the IRB, Office of Compliance and the appropriate officials of other Institutions of the intent to admit 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.
- V. Affiliated Institutions and Investigators
- A. Each performance site to this Institution that is involved in federally sponsored research activities must provide to the Office of Compliance an appropriate written assurance of compliance with the Belmont Report and the Federal

Policy, to include Subparts B, C, and D or 45 CFR 46 where appropriate (or equivalent protection if a foreign site), for review and approval, as specified by the sponsoring Federal department or agency (e.g., by OPRR for DHHS), prior to involvement of human subjects or expenditure of funds or other support to do so.

- B. Each Institutional performance site must respond to a request by the Office of Compliance of this Institution for an Inter-Institutional Amendment, SPA, or CPA (as appropriate), whichever is most suited to the circumstances.
- C. Each non-Institutional performance site (e.g., a private practice physician not otherwise an employee of this Institution or who otherwise would not ordinarily be bound by the provisions of this Assurance or any other applicable Institutional Assurance) who is involved in human subject research of this Institution must respond to a request by the Office of Compliance of this Institution for either an Agreement for an Independent Investigator or a NonInstitutional Investigator Agreement, as appropriate, depending on the nature of the research activity.
- D. Performance sites that are not legally inseparable components of this Institution (whether an Institutional or non-Institutional performance site) are not authorized to cite this Assurance.

