The Centers for Disease Control and Prevention (CDC[1]) has issued the
"Human Research Protections" Policy

1. **Reason for Issue**: This policy is CDC's first policy on Human Research Protections and it affirms CDC's commitment to protecting the rights and welfare of all participants in research. This policy will strengthen CDC's position as a leader in ethical public health research.

2. **Summary of Policy:** All of CDC's human research activities will be guided by the ethical principles of respect for persons, beneficence, and justice. The policy specifically:

   - Defines and describes the human research protection program
   - Explains the supporting regulation requirements
   - Provides example of activities not covered by human research regulations
   - Delineates responsibilities of investigators, supervisors, and other stakeholders necessary to support the human research protection program

3. **Related Issues:** CDC Policy, Distinguishing Public Health Research and Public Health Nonresearch

4. **Responsible Officials:** Office of the Associate Director for Science

5. **Material Superseded**: None

6. **Recertification:** This document is scheduled for recertification on or before the last working day of July 2015.

7. **Point of Contact:** Tom Jones, Policy Analyst, Management Analysis and Services Office 404-498-516.

   To go directly to the policy, click on the link below or enter the following URL into the location line of your browser.

   http://aops-mas-iis.cdc.gov/Policy/Doc/policy556.pdf

S/Carlton Duncan
Deputy Chief Operating Officer

[1] References to CDC also apply to the Agency for Toxic Substances and Disease Registry (ATSDR)

Category: Science Administration
CDC-SA-2010-01
Date of Issue: 7/29/2010
Proponent: Office of the Associate Director for Science

HUMAN RESEARCH PROTECTIONS

SECTIONS:

1. PURPOSE

This policy affirms the Centers for Disease Control and Prevention's (CDC) commitment to protecting the rights and welfare of all participants in research with which CDC is associated by enumerating specific roles, responsibilities, and procedures for CDC staff. Human research is defined and governed by HHS and other regulations:

> The Basic Policy for Protection of Human Research Subjects (the Common Rule), codified for HHS at Title 45, Part 46, Subpart A of the Code of Federal Regulations
>
> Additional HHS protections for specified vulnerable populations at Title 45, Part 46, Subparts B, C, and D of the Code of Federal Regulations
>
> Clinical investigations regulated by the Food and Drug Administration, particularly Title 21, Parts 50 and 56 of the Code of Federal Regulations

All of CDC's human research activities, whether subject to the above federal regulations or not, will be guided by the ethical principles of respect for persons, beneficence, and justice. Thus, this policy extends CDC's commitment beyond CDC activities covered by these regulations, to cover additional activities sponsored or supported by CDC or in which CDC has substantial involvement.

2. SCOPE

This policy applies to the following persons, whether located in the United States or another country:

- Employees or agents of CDC who intervene or interact with human research participants or obtain or use identifiable private information or specimens for research purposes;
- CDC employees who conduct or oversee, or lead a team that conducts or oversees, a clinical investigation;
- CDC employees who create, distribute, or disseminate information products or other resources (such as public-use datasets) outside CDC using information or specimens obtained during research or a clinical investigation;

- CDC employees who have the authority to allocate, commit, or release resources (including financial support, identifiable private information or specimens, or other tangible goods) for human research activities or clinical investigations by CDC programs or non-CDC entities; and
- CDC employees who have scientific or administrative oversight of persons in items the previous 4 items.

For guidance on interpreting the regulatory definition of human research, please see CDC Policy CDC-SA-2010-02, Distinguishing Public Health Research and Public Health Nonresearch. See the references section for additional Departmental and agency policies that apply to human research and clinical investigations.

This policy is not intended to create any new requirements for external partners; its scope is limited to procedures within the agency and existing legal requirements for external partners. If there are any statements in this policy that are unintentionally inconsistent with other regulations or agreements, this policy is superseded by regulations promulgated by the Office for Human Research Protections (OHRP) and by the Food and Drug Administration (FDA), as well as the terms of the Federalwide Assurance of Compliance between CDC and OHRP.

3. BACKGROUND

CDC's human research protection program (HRPP) is comprised of every component throughout the agency that participates in planning, reviewing, executing, or administratively supporting research involving human participants. Ethical responsibilities for human research protections extend, for example, to CDC investigators who directly interact with research participants, project officers who provide technical assistance, associate directors for science who provide an early line of critique to assure high-quality science and ethics, management officials who direct the allocation of agency resources, institutional review board (IRB) members who carry out the charge for autonomous review, contract specialists who authorize the disbursement of funds for human research, and laboratorians who analyze specimens that can be traced to unique individuals. CDC's IRBs play a vital but limited role in this enterprise; all components of CDC's human research protection program must remain accountable to the public trust.

CDC participates in several activities that incur specific regulatory responsibilities related to human research protections: conducting nonexempt human research or clinical investigations, supporting nonexempt human research, sponsoring clinical investigations, and managing the functions of CDC IRBs. These roles can occur in any combination; the policy section expands on their regulatory implications.

CDC's ethical responsibilities extend beyond the ambit of these specific regulated activities, such as carrying out research activities that entail risks to privacy or confidentiality but that do not involve identifiable private information as defined at 45 CFR 46.102(f); carrying out human research that is exempt from 45 CFR part 46; assisting or collaborating on human research or clinical investigations when CDC has no institutional responsibilities under human research regulations; setting priorities and allocating resources for research; and applying or disseminating knowledge derived from human research, such as coauthoring a manuscript or writing public health guidelines.

These regulatory and ethical responsibilities might differ from collaborators' responsibilities.

4. POLICY

All of CDC's human research activities, regardless of whether the research is subject to federal regulations, will be guided by the ethical principles of respect for persons, beneficence, and justice as defined in The Belmont Report.

CDC preserves the definitional distinction between HHS-defined human research and FDA-defined clinical investigations, because CDC conducts a nonnegligible number of clinical investigations that do not constitute human research as defined by HHS. Activities that meet the regulatory definitions of human research or clinical investigation may be exempt from some or all regulatory requirements, or CDC's role may be such that CDC has no regulatory responsibilities (because, for example, CDC is neither conducting nor supporting the activity).

A. *Activities covered by human research regulations*

For each role that incurs specific regulatory responsibilities related to human research protections, CDC will identify and comply with all relevant regulations.

- As an institution that conducts nonexempt human research[1] or clinical investigations (that is, whose employees or agents obtain research data from individuals through intervention or interaction with them; obtain identifiable, private information for research purposes; or directly oversee the administration of an investigational drug or device):
    - CDC must maintain a valid Federalwide Assurance (FWA); certify approval by a CDC or non-CDC IRB for each research activity; and, comply with 45 CFR part 46 (all subparts) and 21 CFR parts 50 and 56, as applicable
    - CDC may extend its FWA to cover human research activities of nonsupported collaborators
- As a federal institution agency that supports nonexempt human research:

CDC must confirm that each supported institution engaged in nonexempt human research holds a valid FWA and certifies IRB approval.

- As an institution that sponsors clinical investigations:

CDC must manage or supervise investigations in compliance with FDA requirements and assure, through investigators, that IRBs operate in compliance with 21 CFR part 56 and that investigators comply with FDA requirements.

- As an IRB organization that manages IRB functions:
    - CDC IRBs (or other designated IRBs) must review nonexempt human research activities that are to be conducted by CDC under CDC's FWA. CDC IRBs (or other designated IRBs) must also review clinical investigations conducted by CDC investigators
    - CDC may, with an appropriately documented agreement, review non-CDC-conducted, nonexempt human research activities under the corresponding FWA. CDC may also, with an appropriately documented agreement, review clinical investigations conducted by non-CDC investigators

Acting under the authority of the CDC institutional official for human research protections, the CDC Human Research Protection Office (HRPO) is responsible for leading the agency

[1] For CDC, "to conduct human research" is the same as "to be engaged in human research".

in protecting the rights and welfare of those who participate in CDC-sponsored public health research, through the practices of investigators, program leaders, and the CDC IRBs, and through relationships with external partners. HRPO must be located within the managerial purview of the institutional official.

All CDC-conducted activities that are covered by human research regulations will be reviewed, prospectively approved, and subject to continuing review at least annually by designated IRBs. The IRBs are authorized to approve, require modifications in, or disapprove the covered human research. For activities approved by the designated IRBs, further appropriate review and approval by CDC officials or other institutions may be required. CDC officials may not permit CDC investigators to conduct research that is disapproved, suspended, or terminated by the IRB of record, or for which IRB approval has lapsed.

HRPO shall develop and maintain written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, the head of any department or agency conducting or supporting the research (or designee), and any applicable regulatory body of any:

- Unanticipated problems involving risks to participants or others
- Serious or continuing noncompliance with the federal regulations or the requirements or determinations of the IRB(s); and
- Suspension or termination of IRB approval

HRPO will ensure that the designated IRBs agree to comply with the terms of CDC's FWA and other relevant regulations; possess appropriate knowledge of the local research context for all research to which the FWA applies; and have established written procedures for the following activities:

- Conducting IRB initial and continuing review (not less than once per year) of research, and reporting IRB findings to the investigator and CDC;
- Determining which projects require review more often than annually and which projects need verification from sources other than the investigator that no material changes have occurred since the previous IRB review; and
- Ensuring prompt reporting to the IRB of proposed changes in a research activity and for ensuring that such changes in approved research, during the period for which IRB approval has already been given, may not be initiated without IRB review and approval, except when necessary to eliminate apparent immediate hazards to the participants.

B. Activities not covered by human research regulations

CDC's ethical responsibilities extend beyond the ambit of specific regulated activities. The following related activities also require ethical judgment and action:

- Carrying out research activities that entail risks to privacy or confidentiality but that do not involve identifiable private information as defined at 45 CFR 46.102(f):
    - CDC is required to apply other legal protections of privacy and confidentiality, as applicable, including the Privacy Act, the HIPAA Privacy Rule, provisions of certificates and assurances of confidentiality under sections 301(d) and 308(d) of the Public Health Service Act, and other legal or policy requirements.

- CDC may, in the interests of research participants, apply stricter standards than legally required.

- Carrying out human research that is exempted or waived in accordance with 45 CFR 46.101(b) or (i):

CDC must apply principles of ethical research, including provisions for ensuring scientific quality and integrity, appropriate benefit-harm balance, just research, and, where practicable, for obtaining free and informed consent.

- Assisting or collaborating on human research or clinical investigations when CDC has no institutional responsibilities under human research regulations (such as providing nonfinancial technical assistance to a co-investigator or a ministry of health):
  - CDC must ensure that assisted or collaborative partners apply principles of ethical research and comply with local regulatory requirements.
  - CDC may extend coverage of CDC's FWA or CDC IRBs to nonsupported partners who are conducting human research or clinical investigations to facilitate application of ethical principles and regulatory norms.

- Setting priorities and allocating resources for research:

CDC must set priorities according to the principles of beneficence and justice, to the extent permitted by appropriations and allocation processes.

- Applying or disseminating knowledge derived from human research (such as coauthoring a manuscript or writing public health guidelines):
  - CDC must ensure that manuscripts, guidelines, released data, and other information products are based on information that was obtained in accordance with appropriate ethical principles and regulatory requirements.

o CDC must ensure that approved research yields information products that disseminate the knowledge gained. Failing to do so undermines the original justification and approval of such research.

5. RESPONSIBILITIES

All persons covered by this policy are responsible for being familiar with human research regulations, this policy, and related policies and practices as they relate to their official duties. In addition to role-based responsibilities listed below, individuals might have additional responsibilities that are not listed. This process begins with investigators and proceeds through National Centers and, where applicable, HRPO or a CDC IRB as described in the appendix.

A. Investigators

As defined below in the definition section, this includes all CDC employees and agents, as well as others acting under CDC's FWA through an individual investigator agreement.

1. Prior to serving as investigators, certify HRPO-approved education in research ethics and human research regulations and obtain certification of competency.
2. Maintain competency in research ethics and human research regulations and certify at least once every 3 years.
3. Submit proposed activities for human research review under National Center (NC) procedures, including research/nonresearch determinations and exempt/nonexempt

human research. Ensure that the design of proposed activities conforms to acceptable scientific, ethical, and legal requirements. Determine that the resources necessary to protect participants are present before conducting the research study. Declare competing interests.

4. For nonexempt human research or clinical investigations conducted by CDC, obtain IRB approval prior to CDC's conducting the activity. This approval must generally be obtained before involving human participants, unless CDC undertakes collaboration on a project that has previously been approved by one or more other IRBs.
    a. Adhere to all terms of IRB approval and implement the protocol as approved. Do not deviate from approved protocol except (a) when prior approval is obtained from the IRB of record or (b) when necessary to eliminate apparent immediate hazards to participants. Follow the protocol's monitoring plan, if any.
    b. Promptly inform the IRB of unanticipated problems involving risks to participants or others, deviations to eliminate apparent immediate hazards to participants, serious or continuing noncompliance, and substantive complaints from participants.
    c. Ensure that free and informed consent is obtained and documented from each participant or his/her legally authorized representative, unless the IRB of record has approved an alternative approach.
    d. Obtain continuing IRB approval before it lapses.
    e. Cease conducting a research activity when IRB approval lapses.
    f. Close research study with HRPO when CDC is no longer conducting the research activity.
5. Maintain study-related records according to legal and policy requirements.
6. Serve as primary contact for HRPO, or designate alternative contact.
7. Serve as primary contact for communication about human research protections with research partners.
8. Serve as primary contact with participants, when applicable.
9. Ensure appropriate protections, such as for privacy and confidentiality, when research is not covered by human research regulations (e.g., because it is exempt or because CDC is not engaged).
10. Ensure that collaborative partners and recipients of technical assistance apply appropriate ethical and regulatory norms.
11. Demonstrate that research-related information products that are submitted for clearance have been derived from research that complies with human research ethics and regulations.
12. Comply with required remediation and other sanctions.

B. Supervisors

This includes employees with responsibility for administrative supervision, such as team leaders, branch chiefs, division directors, and National Center directors.

1. Certify HRPO-approved education in research ethics and human research regulations and obtain certification of competency.

2. Maintain competency in research ethics and human research regulations and certify at least once every 3 years.
3. Ensure that each human research activity has adequate resources, such as enrollment capacity, time for completion, and qualified staff.
4. Authorize commitment of financial and nonfinancial support for human research.
5. Ensure that research staff have adequate provisions for conducting human research, including education, experience, and supervision in appropriate scientific, ethical, legal, and policy-related practices. Facilitate preparation, review, and maintenance of human research activities.
6. Promote and permit service on CDC IRBs on balance with other needs in supervised program.
7. Enforce remediation and other sanctions of CDC research staff when applicable, such as revoking authorship or other credit, disallowing service as an investigator, and initiating personnel actions.
8. Authorize release of nonfinancial support for human research, including identifiable private information, supplies, products, drug, other tangible support.
9. Ensure appropriate protections, such as for privacy and confidentiality, when research is not covered by human research regulations (e.g., because it is exempt or because CDC is not engaged).
10. Ensure that collaborative partners and recipients of technical assistance apply appropriate ethical and regulatory norms.
11. Demonstrate that research-related information products that are submitted for clearance have been derived from research that complies with human research ethics and regulations.

C. Associate Directors for Science

This includes Associate Directors for Science or equivalent scientific oversight roles at branch, division, and National Center levels.

1. Certify HRPO-approved education in research ethics and human research regulations and obtain certification of competency.
2. Maintain competency in research ethics and human research regulations and certify at least once every 3 years.
3. Provide guidance to and mentor investigators and supervisors on scientific, ethical, legal, and policy-related practices for human research.
4. Perform timely regulatory, ethical, and scientific reviews when routing proposals, including research categorization, human participant involvement, agency engagement, regulatory exemptions, routing to CDC or non-CDC IRB, and other related reviews. Ensure that the research uses procedures consistent with sound research design sufficient to yield the expected knowledge and that each protocol has sufficient resources. Determine that the resources necessary to protect participants are present before permitting the research study. Assess investigators' competing interests.
5. As a condition for clearing information products, ensure appropriate compliance with scientific, ethical, legal, and policy-related requirements. Require that research-related

information products that are submitted for clearance have been derived from research that complies with human research ethics and regulations.

6. Facilitate enforcement of remediation and other sanctions of CDC research staff, when applicable.
7. Authorize release of nonfinancial support for human research, including identifiable private information, supplies, products, drug, other tangible support.
8. Ensure appropriate protections, such as for privacy and confidentiality, when research is not covered by human research regulations (e.g., because it is exempt or because CDC is not engaged).
9. Ensure that collaborative partners and recipients of technical assistance apply appropriate ethical and regulatory norms.

D. Human Research Protection Coordinators

This includes Human Research Protection Coordinators or equivalent human research analyst roles at branch, division, and National Center levels.

1. Certify HRPO-approved education in research ethics and human research regulations and obtain certification of competency.
2. Maintain competency in research ethics and human research regulations and certify at least once every 3 years.
3. Provide guidance to investigators and supervisors on scientific, ethical, legal, and policy-related practices for human research.
4. Perform timely regulatory and ethical reviews when routing proposals, including research categorization, human participant involvement, agency engagement, regulatory exemptions, routing to CDC or non-CDC IRB, and other related reviews.
5. Coordinate and facilitate formal communication with HRPO and IRBs of record.
6. Ensure appropriate protections, such as for privacy and confidentiality, when research is not covered by human research regulations (e.g., because it is exempt or because CDC is not engaged).
7. Ensure that collaborative partners and recipients of technical assistance apply appropriate ethical and regulatory norms.
8. Demonstrate that research-related information products that are submitted for clearance have been derived from research that complies with human research ethics and regulations.

E. Other program staff

This includes other staff at the team, branch, division, or National Center level with responsibilities in CDC's human research protection program, such as contracting officers.

1. Ensure that funding proposals comply with human research regulations. When necessary, ensure that awardees hold a valid FWA and certify IRB approval.
2. Authorize disbursement of funds for human research activities (whether through assistance or acquisition mechanisms) only after human research protection requirements are met and documented.

F. Institutional official

The designated Signatory Official on CDC's FWA is authorized to do the following:

1. Exercise the responsibility of the CDC Director, under 45 CFR 46.103(c), to provide formal, legally binding assurance regarding policy.
2. Exercise the authority and responsibility for assuring CDC-wide compliance with all applicable laws, regulations, policies, and standards regarding the protecting the rights and welfare of human participants of research conducted or supported by CDC.
3. Serve as the institutional official for purposes of compliance with 45 CFR part 46 and 21 CFR parts 50 and 56.
4. Set the tone for the agency by promoting an institutional culture of respect and conscience, so that the ethical conduct of human research is supported at the highest levels of the organization.
5. Ensure that the human research protection program functions effectively and that CDC provides the resources and support necessary to comply with all requirements applicable to human research. Monitor and measure the effectiveness of CDC's human research protection program, plan improvements based on those measures, implement planned improvements, and monitor and measure the effectiveness of those improvements.
6. Designate IRBs that will review research covered by CDC's FWA as well as clinical investigations covered by FDA regulations.
7. Provide sufficient resources, space, and staff to support the IRBs' review and record-keeping duties.
8. Respect, support, and defend the autonomy of CDC IRBs and other IRBs of record to act within their purview.
9. Ensure effective institutionwide communication and guidance on human research protections.
10. Ensure that investigators fulfill their scientific, ethical, legal, and policy-related responsibilities.
11. Provide investigators with ways to obtain answers to questions, express concerns, and convey suggestions regarding the HRPP to someone outside of the IRB.
12. Encourage all staff involved in the conduct or oversight of human research to participate in ongoing education activities.
13. Ensure appropriate protections, such as for privacy and confidentiality, when research is not covered by human research regulations (e.g., because it is exempt or because CDC is not engaged).
14. Ensure that collaborative partners and recipients of technical assistance apply appropriate ethical and regulatory norms.
15. Require that research-related information products that are submitted for clearance have been derived from research that complies with human research ethics and regulations.

Neither the institutional official nor any other CDC official may approve research that has been disapproved or not yet approved by the IRB of record or whose IRB approval has lapsed or been suspended or terminated.

G. Human Research Protection Office (and successor offices)

The chief of HRPO shall be designated on CDC's FWA as the Human Protections Administrator. The HRPO chief exercises operational responsibility for CDC's human research protection program and is responsible for maintaining comprehensive knowledge of all aspects of CDC's human research protection program, for being familiar with CDC's commitments under the FWA, and for playing a key role in ensuring that CDC fulfills its responsibilities under the FWA. Through this policy, the institutional official delegates the following responsibilities to the chief of HRPO, who may redelegate these responsibilities to HRPO staff through written operating procedures.

1. Serve as a knowledgeable point of contact for OHRP, FDA, and other federal agencies regarding research ethics and human research regulations.
2. Maintain CDC's FWA and IRB registrations, including timely revisions to CDC IRB rosters and the list of IRBs on whom CDC may rely.
3. Recruit and appoint members to CDC IRBs, in consultation with the respective board chairs. Appoint the IRB chair and vice-chairs. Manage support for unaffiliated IRB members. Suspend or terminate the membership of any individual who does not fulfill membership responsibilities.
4. Perform periodic evaluation of the performance of administrative staff and IRB members.
5. Ensure that administrative staff, IRB members, and investigators are knowledgeable to conduct research in accordance with ethical standards and all applicable regulations. Develop and implement an educational plan for administrative staff, IRB members, and investigators.
6. Work with the HRPO chief's supervisors to ensure that adequate personnel, space, and other resources are allocated to the HRPP.
7. Review and determine which activities involving CDC investigators are exempt under 45 CFR 46.101(b).
8. Review and sign IRB authorization agreements, individual investigator agreements, and similar documents between CDC's HRPP and other parties, as appropriate.
9. Serve as the contact for correspondence addressing human research with OHRP, FDA, and other agencies as applicable, including incident reports, certifications under 45 CFR part 46 subpart C, and the PHS Policy on Informing Those Tested About HIV Serostatus.
10. Develop, review, and approve standard operating procedures (SOPs) for the HRPP, including HRPO's administrative functions and IRB functions.
11. Oversee daily operations of the HRPP and IRBs in accordance with the SOPs.
12. Assess and manage institutional competing interests. Manage IRB members' competing interests.

H. NCHS and NIOSH

NCHS and NIOSH each support a CDC IRB. Each of these IRBs operates as part of CDC as an IRB organization under the terms of CDC's FWA.

1. To support management of these IRBs that is efficient and complies with CDC's legal and ethical obligations, the CDC institutional official and the chief of HRPO may

delegate specific authorities and responsibilities to the Directors or Associate Directors for Science of NCHS and NIOSH through standard operating procedures.

2. These authorities and responsibilities may be redelegated, for example, to a human research protection coordinator or an IRB administrator.

3. To the extent feasible, these authorities and responsibilities shall be coordinated with HRPO's standard operating procedures.

I. Procurement and Grants Office

The CDC Procurement and Grants Office shall ensure that no funds are disbursed to an awardee in support of nonexempt human research, whether through an assistance mechanism or an acquisition mechanism, unless each awardee that will become engaged in nonexempt human research holds a valid federalwide assurance with OHRP and certifies that the research has been reviewed and approved by an IRB provided for in the approved assurance and will be subject to continuing review by the IRB.

J. CDC IRBs

1. Members must fulfill membership responsibilities as stipulated in HRPO SOPs, including meeting attendance and declarations of competing interests.

2. Foremost, members must protect the rights and welfare of research participants in all research under their purview, whether conducted by CDC or by an outside institution relying on a CDC IRB. Board actions must comply with ethical norms and legal and policy-related requirements, including federal human research regulations, guidance, and Departmental[2] and CDC [3] policy. This policy expressly releases CDC IRB members from any perceived responsibility to protect CDC, its programs, or its investigators, except where such protections are in the interests of research participants or compliance with ethical norms and legal and policy-related requirements.

3. Chairs and vice-chairs, with assistance from HRPO staff, are responsible for leading and setting the tone for each IRB, running convened meetings, striving for an appropriate degree of consistency across actions within and between CDC IRBs, overseeing the development and actions of members, and serving on the CDC IRB executive committee.

4. Chairs have full discretion over the appointment and retention of members on their boards, in compliance with legal and policy-related requirements for board composition.

5. As an IRB organization, CDC promotes open communication between CDC IRB members and CDC investigators. Nonetheless, chairs have full discretion over the management of board meetings, in compliance with legal and policy-related requirements for board meetings.

6. The CDC IRB executive committee, comprised of CDC IRB chairs and vice-chairs and the HRPO chief, is responsible for ratifying standard procedures related to the management of board functions. Furthermore, the executive committee is a resource for boards seeking guidance on complex or difficult actions, such as termination of

[2] Departmental policies include the PHS Policy on Informing Those Tested About HIV Serostatus.
[3] CDC policies include Inclusion of Women and Racial and Ethnic Minorities in Research and Inclusion of Persons under the Age of 21 in Research.

approval. Because each board is autonomous, this resource is used at the discretion of the board itself.

6. ACRONYMS AND ABBREVIATIONS

ADS – Associate Director for Science

FDA – Food and Drug Administration

FWA – federalwide assurance

HHS – Department of Health and Human Services

HRPC – human research protection coordinator

HRPO – Human Research Protection Office

HRPP – Human Research Protection Program

IRB – institutional review board

NC – national center

NCHS – National Center for Health Statistics

NIOSH – National Institute for Occupational Safety and Health

OHRP – Office for Human Research Protections

SOP – standard operating procedure

7. DEFINITIONS

Agent – A nonemployee of CDC who conducts research under CDC's FWA. This generally includes all persons cleared for access to CDC networks and who use CDC networks or physical facilities for human research activities.

Clinical investigation – any experiment that involves a test article and one or more human participants and that either is subject to requirements for prior submission to the FDA or the results of which are intended to be submitted later to, or held for inspection by, the FDA as part of an application for a research or marketing permit. The term does not include certain nonclinical laboratory studies.

Conduct a clinical investigation – direct the administration to, dispensing of, or use involving a test article with a participant.

Conduct research – To be engaged in human research by obtaining, using, studying, or analyzing data about living individuals through intervention or interaction with them for research purposes or by obtaining using, studying, or analyzing individually identifiable private information about living individuals for research purposes.

Engagement – An institution becomes engaged in human subjects research when its employees or agents (i) obtain data about living individuals through intervention or interaction with them for research purposes; or (ii) obtain individually identifiable private information about living individuals for research purposes. Furthermore, an institution is automatically considered to be engaged in human subjects research whenever it receives a direct HHS award to support such research, even where all activities involving human subjects are carried out by a subcontractor or collaborator.

Exempt human subjects research - Categories of research to which the Federal regulations for human research protections do not apply. Research involving prisoners and some research involving children are not exempt. See also 45 CFR 46.101(b), (i).

Federalwide assurance – A written document submitted by an institution that is engaged in nonexempt human research conducted or supported by HHS. Through the assurance, an institution commits to HHS that it will comply with the requirements set forth in the regulations for the protection of human participants at 45 CFR part 46.

Human research protection coordinator – Individual designated by each NC and some divisions to coordinate human research protections within the NC or division, by serving as a resource to investigators and other program staff and as a point of contact with other portions of CDC's human research protection program.

Human Research Protection Office – The organizational unit within CDC that is charged with facilitating the work of CDC IRBs and providing assistance and training for CDC staff engaged in research involving human participants, including clinical investigations.

Human subject or participant – A living person about whom an investigator conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information (e.g., medical records, employment records, or school records). In a clinical investigation, a human who participates in an investigation, as a recipient of a test article, as an individual on whom or on whose specimen an investigational device is used, or as a control.

Institutional official – The individual who is legally authorized to act for the institution and, on behalf of the institution, obligates the institution to the FWA and other ethical commitments regarding human research.

Institutional review board – A formally appointed ethics review committee established to ensure that research involving human participants conforms to ethical principles and federal regulations.

Investigator – Any individual who is involved in conducting human research activities.

IRB of record – The designated IRB that oversees a specific research activity or clinical investigation conducted by an investigator or institution.

Research – A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.

Sponsor – A person (e.g., an individual, corporation, or agency) who initiates a clinical investigation.

Support – Provision of funding, identifiable private information, or supplies, products, drug, other tangible support. Does not include mere provision of Federal staff time and assistance absent other forms of financial or material support.

Test article – Any drug, biological product, or medical device for human use.

8. REFERENCES

The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research*. April 18, 1979 [http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.htm]

CDC Delegations of Authority. Administrative Authorities/General. Protection of Human Research Subjects (Institutional Official – Human Research Subjects) [http://intraspn.cdc.gov/maso/DOA/docs/doa_329.htm]

CDC Policy CDC-GA-2005-06 Clearance of Information Products Disseminated Outside CDC for Public Use [http://aops-mas-iis.cdc.gov/Policy/Doc/policy66.htm]

CDC Policy CDC-GA-2005-14 CDC/ATSDR Policy on Releasing and Sharing Data [http://aops-mas-iis.cdc.gov/Policy/Doc/policy385.htm]

CDC Policy CDC-GA-1996-01 Inclusion of Women and Racial and Ethnic Minorities in Research [http://aops-mas-iis.cdc.gov/Policy/Doc/policy17.htm]

CDC Policy CDC-GA-2006-01 Inclusion of Persons under the Age of 21 in Research [http://aops-mas-iis.cdc.gov/Policy/Doc/policy496.htm]

CDC Policy CDC-SA-2010-02 Distinguishing Public Health Research and Public Health Nonresearch [http://aops-mas-iis.cdc.gov/Policy/Doc/policy557.pdf]

CDC Policy CDC-GA-1999-02 CDC and ATSDR Specimen and Data Bank Policy [http://aops-mas-iis.cdc.gov/Policy/Doc/policy97.htm]

Code of Federal Regulations, Title 45, Part 46. [http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm]

Code of Federal Regulations, Title 21, Parts 50, 56, 312, and 812. [http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm]

PHS Policy on Informing Those Tested About HIV Serostatus [http://www.hhs.gov/ohrp/humansubjects/guidance/hsdc88jun.htm]

OHRP Guidance on Research Involving Coded Private Information or Biological Specimens [http://hhs.gov/ohrp/humansubjects/guidance/cdebiol.htm]

OHRP Guidance on Engagement of Institutions in Human Subjects Research [http://hhs.gov/ohrp/humansubjects/guidance/engage08.html]

APPENDIX

Procedures

Activities that meet the regulatory definitions of human research or clinical investigation may be exempt from some or all regulatory requirements, or CDC's role may be such that CDC has no regulatory responsibilities (because, for example, CDC is neither conducting nor supporting the activity). Therefore, CDC's human research protection program implements a multi-tiered process for carefully categorizing activities according to these definitions and their respective regulatory and ethical requirements. This process begins with investigators and proceeds through National Centers and, where applicable, HRPO or a CDC IRB.

(1) Investigators

HHS-defined research involving human participants

For each activity that involves obtaining, using, studying, or analyzing information from or about individual humans, a CDC investigator provisionally determines the following in consultation with the human research protection coordinator:

a. Whether the activity constitutes research, as defined at 45 CFR 46.102(d) and interpreted in CDC Policy CDC-SA-2010-02, Distinguishing Public Health Research and Public Health Nonresearch;

b. If the activity constitutes research, whether it involves human participants (§102(f));

c. If the activity is research involving human participants, whether CDC is conducting (i.e., is engaged in) or supporting the human research activity;

d. If CDC is conducting the human research activity, whether it is exempt per 45 CFR 46.101(b);

e. If CDC is conducting a nonexempt human research activity;

f. Whether to seek approval by a CDC IRB or an IRB on which CDC relies, and

g. Whether nonsupported research partners are also engaged in nonexempt human research;

h. If CDC is supporting the human research activity, whether supported research partners are engaged in human research, and if so whether the human research is exempt or nonexempt.

i. If an activity constitutes human research but CDC is neither conducting nor supporting the activity, the investigator determines that CDC's association with and participation in the research activity is consistent with ethical norms.

j. If a research activity is undertaken without the intention of involving human participants, but it is later proposed to involve human participants in the research, the investigator reiterates this decision process and pursues appropriate approval prior to the involvement of human participants.

k. If an activity description lacks definite plans for involvement of human participants, no human participants may be involved in the activity until the investigator reiterates this decision process and pursues appropriate approval.

l. The investigator initiates review sufficient to document decisions about whether an activity constitutes research or not, involves human participants or not, is conducted or not conducted by CDC, is exempt or not, is supported or not supported by CDC, and involves research partners for which additional documentation may be required.

m. The investigator must receive appropriate permission or approval before undertaking any research activity that involves obtaining or using information from or about individual humans.

FDA-defined clinical investigations

For each activity that involves a drug, biologic, or device (including *in vitro* diagnostics), a CDC investigator determines the following:

a. Whether the activity constitutes a clinical investigation involving one or more human participants, including

b. Whether the investigation is an experiment in which a drug or biologic is administered or dispensed to a human participant, except for the use of a marketed drug in the course of medical practice, and

c. Whether the investigation is intended to determine the safety or effectiveness of a device;

d. If the activity constitutes a clinical investigation,

- Whether CDC initiates the investigation, and
- Whether the CDC investigator directs or dispenses the test article or uses it with a human participant (including a human specimen).

e. If an activity constitutes a clinical investigation but CDC is neither conducting nor sponsoring the investigation, the investigator determines that CDC's association with and participation in the investigation is consistent with ethical norms.

- The investigator initiates review sufficient to document decisions about whether an activity constitutes a clinical investigation or not, involves CDC as a sponsor or investigator, and involves research partners for which additional documentation may be required.
- The investigator must receive appropriate approval before undertaking any clinical investigation.

Activities that meet both the HHS definition and the FDA definition

If an activity meets both definitions, the investigator is responsible for obtaining appropriate approval under both HHS and FDA regulations before undertaking the activity. This generally occurs in a single review process which entails additional regulatory burden only where the regulations entail different requirements, in which case the stricter requirements prevail.

Activities that meet neither the HHS definition nor the FDA definition

a. The investigator initiates review sufficient to document decisions that an activity meets neither definition if the activity involves obtaining or using information on or about individuals or involves use of drugs or devices.

b. The investigator must obtain documented decisions from the National Center before undertaking such activities.

(2) Division-level oversight officials

a. For each proposed activity, the division ADS or designee documents the following:

- whether the activity constitutes research, as defined at 45 CFR 46.102(d) and interpreted in CDC Policy CDC-SA-2010-02, Distinguishing Public Health Research and Public Health Nonresearch;
- if the activity constitutes research, whether it involves human participants (§102(f));
- for nonexempt human research, whether CDC is conducting (i.e., is engaged in) the human research activity; and,
- whether the activity constitutes a clinical investigation involving one or more human participants and one or more CDC investigators.

b. The division ADS or designee determines whether the proposed research or clinical investigation satisfies appropriate legal, ethical, and scientific norms. The division ADS or designee ensures that the research uses procedures consistent with sound research design sufficient to yield the expected knowledge and that each protocol has sufficient resources and determines that the resources necessary to protect participants are present before permitting the research study.

c. The division ADS or designee routes to the NC ADS or designee requests for exemption or for IRB review of nonexempt, CDC-conducted human research or clinical investigations.

(3) NC-level oversight officials

a. For each proposed activity, the NC ADS, NC HRPC, or designee documents the following:

- whether the activity constitutes research, as defined at 45 CFR 46.102(d) and interpreted in CDC Policy CDC-SA-2010-02, Distinguishing Public Health Research and Public Health Nonresearch;
- if the activity constitutes research, whether it involves human participants (§102(f));
- whether CDC is conducting (i.e., is engaged in) the human research activity; and,
- if CDC is conducting the human research activity, whether it is exempt per 45 CFR 46.101(b);
- whether the activity constitutes a clinical investigation involving one or more human participants and one or more CDC investigators.

b. The NC ADS or designee determines whether the proposed research or clinical investigation satisfies appropriate legal, ethical, and scientific norms. The NC ADS or designee ensures that the research uses procedures consistent with sound research design sufficient to yield the expected knowledge and that each protocol has sufficient resources and determines that the resources necessary to protect participants are present before permitting the research study.

c. The NC ADS or designee routes to HRPO requests for exemption or for IRB review of nonexempt, CDC-conducted human research or clinical investigations.

(4) HRPO

The HRPO-specific procedures described in this section may also be carried out under authorities that has be delegated to the ADSs of National Center for Health Statistics (NCHS) and National Institute for Occupational Safety and Health (NIOSH), as applicable.

a. HRPO reviews nonresearch activities only in the following circumstances:

- The activity is a clinical investigation that requires IRB approval
- The activity entails a request to test HIV serostatus that is linked to participants by an identifier and for which a participant might not receive the test result; or
- A scientific program consults with HRPO about interpreting the definition of research

b. When HRPO receives a request to review a human research activity for which no specific human research regulations apply to CDC, HRPO may decline to manage further review of the activity; HRPO must notify the requesting program accordingly.

c. When an investigator requests a finding that a human research activity is exempt per 45 CFR 46.101(b), the chief of HRPO, or designee, renders and documents that finding on behalf of CDC. If the activity is deemed nonexempt, it is referred back to the program for rerouting.

d. When an investigator requests review by a CDC IRB for a nonexempt human research activity conducted by CDC (i.e., in which CDC is engaged), or for a clinical investigation conducted by CDC, HRPO manages the review. When an activity falls under more than one set of requirements, HRPO ensures that the reviewing IRB applies the stricter requirements.

e. When an investigator requests review by a non-CDC IRB for a nonexempt human research activity conducted by CDC (i.e., in which CDC is engaged), or for a clinical investigation conducted by CDC, HRPO manages the process of arranging an IRB authorization agreement and listing the reviewing IRB on CDC's FWA.

f. When an outside institution requests review by a CDC IRB for a nonexempt human research activity or clinical investigation conducted by that institution, HRPO manages the IRB authorization agreement and IRB review. When an activity falls under more than one set of requirements, HRPO ensures that the reviewing IRB applies the stricter requirements.