NIH Policy Manual

7410 - Review and Documentation of Protections for Human Subjects in Extramural Grant Applications and Research and Development Contract Proposals

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Transmittal Notice

1. **Explanation of Material Transmitted:** This chapter implements Part 46, Title 45, of the Code of Federal Regulations (CFR) (45 CFR 46) as amended. This chapter specifies policies of the NIH Extramural Program for the protection of human subjects involved in (a) grants and cooperative agreements including, but not limited to, National Research Service Award (NRSA) fellowships, training grants, career development awards, and (b) contracts that arise from solicitations for Research and Development (R&D) Contract proposals. While NIH has different levels of involvement and responsibilities in grants, cooperative agreements and contracts, NIH's responsibilities for the protections of human subjects in its funded research activities are the same and derive from policy and laws that apply to all types of NIH funding http://www.hhs.gov/ohrp/humansubjects/commonrule/index.html. The HHS Protection of Human Subjects regulations (45 CFR 46) applies to NIH grants, cooperative agreements (http://grants.nih.gov/grants/policy/hs/) and contracts (http://www.hhs.gov/policies/hhsar/subpart352-40s-70s.html#352.270-4Protectionofhumansubjects). This chapter replaces NIH Manual 54107, Review of Applications and Award of Grants Involving Human Subjects, dated 08/05/94. and NIH Manual 6380-1, Contracts Involving Human Subjects, dated 02/12/82.
2. **Filing Instructions:**

   Remove: NIH Manual 54107, Review of Applications and Award of Grants Involving Human Subjects, dated 08/05/94.
   Remove: NIH Manual 6380-1, Contracts Involving Human Subjects, dated 02/12/82.
   Insert: NIH Manual 7410, Review and Documentation of Protections for Human Subjects in Grant Applications and Contract Proposals, dated 05/08/12.

PLEASE NOTE: For information on:

- Content of this chapter, contact the issuing office listed above.

- NIH Manual System, contact the Division of Management Support, OMA on 301-496-2832, or enter this URL: http://oma.od.nih.gov/manualchapters/.
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A. Purpose

This chapter implements the application of Title 45 of the Code of Federal Regulations Part 46 (45 CFR 46), Protection of Human Subjects to requests for NIH funding. See http://ecfr.gpoaccess.gov/cgi/t/text/text-idx?c=ecfr&sid=903dfcf8d59fae7cdfc8829b4ba9e1c2&rgn=div8&view=text&node=45:1.0.1.1.25.1.1.18&idno=45. It is stated in § 46.120, Evaluation and disposition of applications and proposals for research to be conducted or supported by a Federal Department or Agency:

> (a) The department or agency head will evaluate all applications and proposals involving human subjects submitted to the department or agency through such officers and employees of the department or agency and such experts and consultants as the department or agency head determines to be appropriate. This evaluation will take into consideration the risks to the subjects, the adequacy of protection against these risks, the potential benefits of the research to the subjects and others, and the importance of the knowledge gained or to be gained.
>
> (b) On the basis of this evaluation, the department or agency head may approve or disapprove the application or proposal, or enter into negotiations to develop an approvable one.

NIH, through its Center for Scientific Review or a review branch maintained by an individual institute or center, evaluates all applications and proposals involving human subjects submitted to NIH. Risks to the subjects, the adequacy of protection against these risks, the potential benefits of the research to the subjects and others, and the importance of the knowledge gained or to be gained are all considered in evaluation. If the evaluation of protections for human subjects discloses concerns, NIH may bar funding and enter into negotiations to resolve such concerns.

The term, 'human subjects research', as it is used in this chapter, means 'non-exempt human subjects research' defined by http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#46.101. This chapter does not cover research conducted as part of NIH intramural activities, and does not directly address NIH policies inclusion of women, children and minorities, nor human embryonic stem cell research. Policy and guidance concerning inclusion policies can be found at: http://grants.nih.gov/grants/funding/women_min/women_min.htm. Policy and guidance concerning human embryonic stem cells can be found at: http://grants.nih.gov/grants/guide/notice-files/NOT-OD-10-020.html. This chapter provides guidance for peer review regarding assessment of the adequacy of human subjects protections in extramural grant applications and R&D contract proposals and describes

procedures by which NIH (in coordination with applicants and offerors) resolves concerns about human subject protections that may be identified during peer review.

NIH extramural awards may be in the form of grants, individual fellowships, training grants, career development awards, and cooperative agreements (hereinafter referred to as "grants"). Such awards also may be in the form of NIH contracts resulting from solicitations for Research and Development (R&D) Contract proposals. While the relevant laws and regulations pertaining to protections of human subjects apply similarly to NIH grants and contracts, certain NIH policy and administrative procedure, including oversight, differ depending on the nature of the funding. In these cases, grants and contracts are discussed separately.

Central to NIH oversight of research involving human subjects is a system of codes, originally developed by NIH in conjunction with what is now the Office of Human Research Protections (OHRP). The coding system has been updated and is maintained by NIH's Office of Extramural Programs (see Section D.5. of this document). This human subjects coding system categorizes and archives the use of humans subjects in each grant or contract as well as the determinations of peer review and NIH administration concerning the protections of human subjects.

B. Background

This document replaces NIH Manuals 54107 and 6380-1. Its preparation was required in order to consolidate the coding policies and practices concerning the use of human subjects in NIH grants and R&D contracts and to reflect NIH archiving requirements and database capabilities. Another key element of this manual chapter's background is the establishment of the Human Subjects Program in the Office of Extramural Programs. In June 2000, the Office for Human Research Protections (OHRP) replaced the Office for Protection from Research Risks (OPRR). OPRR had been operated under the Office of Extramural Research (OER) and was responsible for the implementation of human subjects protections policies at NIH and HHS. OHRP (http://www.hhs.gov/ohrp/) is located in the Office of the Assistant Secretary for Health, Department of Health and Human Services (HHS). OHRP helps ensure the protection of the rights, welfare, and wellbeing of subjects involved in research conducted or supported by HHS by providing clarification and guidance, developing educational programs and materials, maintaining regulatory oversight, and providing advice on ethical and regulatory issues in biomedical and social-behavioral research. The functions of OHRP are described at http://www.hhs.gov/ohrp/. The OER within NIH was delegated the responsibility for developing NIH policies concerning human subjects research, including coding and award policies (http://nih-extramural-intranet.od.nih.gov/nih/policies/hs/). The extramural Human Subjects Program is administratively situated within OER and is responsible for, prior to award, reviewing and approving proposed resolutions of human subjects concerns that have been identified through peer review or programmatic review. This program ensures the consistent implementation of the HHS regulations for the "Protection of Human Subjects" (45 CFR 46) http://ecfr.gpoaccess.gov/cgi/t/text/text-

idx?c=ecfr&tpl=/ecfrbrowse/Title45/45cfr46_main_02.tpl and other applicable Federal and NIH laws, regulations, and policies on various aspects of human subjects research.

NIH/HHS-funded research involving human subjects must comply with all applicable Federal Law and HHS and NIH regulations and policies. These include, but are not limited to: Protections of Human Subjects regulations (45 CFR 46) and NIH extramural policies (http://grants.nih.gov/grants/policy/nihgps_2011/) regarding the inclusion of women, minorities, and children; data and safety monitoring for clinical trials; adverse event reporting; and education in the protection of human research participants for all senior/key personnel and senior/key contributors who will be involved in the design or conduct of the study that involves human subjects research. Compliance with all relevant Food and Drug Administration (FDA) regulations is required, including documentation that an Investigational New Drug (IND) number or Investigational Device Exemption (IDE) number has been obtained. Compliance and implementation of regulations and NIH extramural policies related to human subjects research are applicable to all recipients of NIH grants, cooperative agreements, and extramural R&D contracts that involve human subjects research. In the case of grant applications with Multiple Project Directors or Principal Investigators (PD/PI) and contract proposals with multiple investigators, the HHS human subjects regulations (45 CFR 46) apply to the multiple PD/PIs themselves, all investigators, and their institutions, including those outside the United States, who are engaged in human subjects research (http://grants.nih.gov/grants/foreign/human_subjects.htm?print=yes&).

C. Policy

1. The elements of OEP policy with respect to grant applications and R&D contract proposals involving human subjects are itemized as follows:
    a. RECEIPT
        1. Grant applications and R&D contract proposals must be assigned a pre-review human subjects code upon receipt.
        2. Scientific Review Officers (SROs) typically ensure appropriate initial codes have been assigned as part of their administrative review of grant applications (see Section D.4. of this document). For contract proposals, Contracting Officers (COs), Project Officers (POs) or Contracting Officer's Representatives (CORs, previously termed, Contracting Officer's Technical Representatives (COTRs)), and SROs may be involved in the determination of initial codes.
    b. REVIEW
        1. Grant applications and contract proposals must be reviewed or evaluated according to 45 CFR 46.120 and 42 CFR 52h.
        2. Contract proposals need to be evaluated for human subjects protections in a manner that is appropriate for the contract, i.e., (a) If a Technical Evaluation Plan for a solicitation includes peer review of proposals, the members of the peer review panel will perform the evaluation of human subjects protections. (b) For all other R&D contracts, officers and

employees of the department or agency and such experts and consultants as the department/agency determines to be appropriate will evaluate human subjects protections within the proposals.

3. A human subjects code (from the list in Section D.4. of this document) is assigned to reflect the outcome of the peer review evaluation of the human subjects protections and is specified in the final report, sometimes referred to as the summary statement for grant applications and the technical evaluation report for contract proposals. http://edocket.access.gpo.gov/cfr_2007/octqtr/42cfr52h.8.htm.

c. AWARD

1. Awardees must provide NIH with appropriate documentation related to their Federalwide Assurances (FWAs), Institutional Review Board (IRB) and training of key personnel in order to receive an award funding human subjects research.
2. Grant applications and contract proposals that have acceptable human subjects protections are coded accordingly and are not brought to the attention of OEP.
3. For grant applications and contract proposals that have been identified as having human subjects concerns (Code 44), which is a bar to funding unless issues can be resolved and the code updated, these concerns must be brought to the attention of OEP and need to be resolved prior to making an award. Such concerns typically are raised by the Scientific Review Group, but also may be raised by NIH Staff or an Institute or Center (IC) Council.
4. Under specific circumstances, there is the option to make a restricted award (Code 48) with specific terms and conditions of award that withhold funds for the human subjects research aspects until unacceptable ratings are resolved.

2. REQUIRED DOCUMENTATION TO ISSUE AN AWARD:
Before an IC issues a grant or contract involving human subjects research, the applicant or offeror must have declared and documented, if needed, the following:

a. ASSURANCE: Current Federalwide Assurance (FWA) if the applicant or offeror and/or any performance site(s) engaged in NIH-supported human subjects research does not already have a FWA on file with OHRP. If the FWA is already on file with OHRP, a certification from the offeror or applicant is required.
b. IRB APPROVAL: The proposed human subjects research in an application or proposal has received approval from an IRB registered with OHRP. The IRB approval date must be within 12 months before the budget or contract start date. If the applicant or offeror believes an exemption to human subjects research applies and such exemption is determined by the applicant or offerror's institution per its institutional policy consistent with 45 CFR 46, that information will be submitted instead of an IRB approval.

c. EDUCATION REQUIREMENT: All senior/key personnel and senior/key contributors engaged in the NIH-funded human subjects research have completed an appropriate education program in the protections for human subjects. Senior key personnel include all individuals responsible for the design or conduct of the study, including senior/key personnel at consortium participants or alternate performance sites if they are engaged in research that involves human subjects.

If any of these items is missing, appropriate IC staff must ensure proper receipt of the document prior to the issuance of an award or they may, with OEP approval, issue a restricted award (Code 48) that bars or limits the participation of human subjects in the NIH-funded research.

3. RESOLVING CONCERNS:
Resolution of human subjects concerns arising during peer review of a grant application or technical merit review of a contract proposal generally occurs before the research protocol is reviewed by an Institutional Review Board (IRB). This resolution is independent and unrelated to the institution's IRB review of the research protocol(s) connected with the research. For grant applications and contract proposals that are being considered for funding and have been identified as having unacceptable protections (Code 44), the applicant or offeror provides additional information or proposes written resolution(s) to the concern(s) that gave rise to the Code 44. After approval by the IC Program Officer or CO, the proposed resolution(s) of all issues related to protections for human subjects are submitted to the OEP. The proposed resolutions must be evaluated by OEP and considered in the context of current human subjects regulations, policies, and guidelines. The OEP evaluation of proposed resolutions is an activity that is distinct from peer review and evaluation, program review processes, and scoring of grant applications and contract proposals. The evaluation of proposed resolutions may involve OEP interactions with Program Officials and Project Officers (POs), COs, CORs and SROs to clarify protocol-related matters or answer questions. Once OEP approves the proposed resolution of the human subjects concerns that resulted in the initial assignment of an unacceptable code (e.g., Code 44), the OEP archives its determinations and enters a revised and final human subjects code in the appropriate database (e.g., IMPAC II), which lifts the bar so that an award can be made.
    a. Specifically for grant applications that NIH intends to fund:
        1. If an acceptable resolution to a human subjects concern has not been submitted, reviewed, or approved in response to the assignment of a Code 44, the IC may request that OEP lift the bar to funding by assignment of a Code 48.
            a. Code 48 awards require specific terms and conditions of award that restrict funds for human subjects research.
            b. Chief Grants Management Officers (GMOs), and POs of the NIH ICs must ensure that awards issued with restrictive terms and

conditions are closely monitored and that appropriate follow-up action in concert with the grantee and OEP is taken to address and resolve human subjects protections issues.

c. The Grantee institution is responsible for ensuring that all institutions collaborating with the Grantee meet these restrictions and any additional requirements.

d. If concerns are fully resolved, a code 54 or the proper exemption code will be assigned and funding will be provided for human subjects research.

2. Regarding Code 44s at the end of the fiscal year. At points near the end of the fiscal year, an IC may determine that there is insufficient time before the end of the fiscal year for the Grantee institution to obtain the institutional certification of IRB approval, a FWA from OHRP, or any other required documentation as stated in C.2. In such cases, the IC can issue an award with appropriate restrictions on funds related to human subjects research. In such cases, the IC can request OEP lift the bar to funding by its assignment of a restricted award (Code 48) to the application (http://nih-extramural-intranet.od.nih.gov/nih/policies/hs/restricted_awards.htm).
3. Applications without a FWA that also were designated as Code 44 will be sent to OEP for approval pending receipt of the FWA.

b. Specifically for contract proposals:

1. If an acceptable human subject protection resolution has not been submitted, reviewed or approved by OEP, human subjects research may not be conducted under the contract.
2. If there is a Prime Contractor and subcontractors, the Prime Contractor is responsible for ensuring that all institutions subcontracting, or otherwise collaborating, with the Prime Contractor meet contract requirements and observe applicable restrictions.

D. Definitions and Acronyms

1. **Application/Applicant:** An application is a request for financial support of a project, program, or activity submitted on specified forms and in accordance with OPDIV instructions. An applicant is any individual or other legal entity that directly or indirectly (e.g., through an affiliate), submits a grant application to the NIH (http://grants.nih.gov/grants/policy/policy.htm; http://grants.nih.gov/grants/how_to_apply.htm).
2. **Authorized Organizational Representative (AOR):** The authorized organizational representative is the designated representative of the applicant/recipient organization with authority to act on the organization's behalf in matters related to the award and administration of grants. In signing a grant application, this individual agrees that the organization will assume the obligations imposed by applicable Federal statutes and regulations and other terms and conditions of the award, including any assurances, if a

grant is awarded. These responsibilities include accountability both for the appropriate use of funds awarded and the performance of the grant-supported project or activities as specified in the approved application (http://grants.nih.gov/grants/policy/policy.htm; http://grants.nih.gov/grants/how_to_apply.htm).

3. **Assent:** A child's affirmative agreement to participate in research. Failure to object, absent affirmative agreement, should not be construed as assent.
4. **Child:** It is recognized that, for the purposes of inclusion of children in research, NIH defines children as individuals under the age of 21 (http://grants.nih.gov/grants/policy/hs/children.htm). However, per the HHS regulations and for the content of this Manual Chapter, a child is a person who has not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted. 45 CFR 46.402(c). State laws define what constitutes a "child," and such definitions dictate whether or not a person can legally consent to participate in a research study. Federal Regulations (45 CFR 46, subpart D) address HHS protections for children who participate in research, and rely on State definitions of "child" for consent purposes.
5. **Codes:** A coding system for funded research involving human subjects was created by NIH in conjunction with the, now disbanded, Office for Protection from Research Risks has been updated and maintained by OEP. At the time of receipt of a grant application or submission of a contract proposal, an initial human subjects code from the following list is assigned at the time of receipt and referral. The SRO may adjust the initial code to correct errors while planning and conducting peer review to ensure that human subjects information is included in the review:

   Code 10 – No human subjects involved
   Code 20 – Human subjects involved – No exemption designated
   Code E1 – Human subjects involved – Exemption category 1
   Code E2 – Human subjects involved – Exemption category 2
   Code E3 – Human subjects involved – Exemption category 3
   Code E4 – Human subjects involved – Exemption category 4
   Code E5 – Human subjects involved – Exemption category 5
   Code E6 – Human subjects involved – Exemption category 6

   Following peer review of a grant application or technical merit review of a contract proposal, a code from the following list is assigned:

   Code 10 – No human subjects involved
   Code 30 – Human subjects involved – Certified, no Scientific Review Group (SRG) or Technical Evaluation Panel (TEP) concerns
   Code 44 – Human subjects involved – SRG concerns, which may be resolved and recoded through OEP action.
   Code E1 – Human subjects involved – Exemption category 1

Code E2 – Human subjects involved – Exemption category 2
Code E3 – Human subjects involved – Exemption category 3
Code E4 – Human subjects involved – Exemption category 4
Code E5 – Human subjects involved – Exemption category 5
Code E6 – Human subjects involved – Exemption category 6
Code E7 – Human subjects involved – Multiple exemptions

For grant applications and contract proposals that the IC intends to fund and for which review has assigned a Code 44, OEP is contacted by the program officer or contract officer to oversee resolution of concerns that gave rise to the Code 44 assignment. According to the resolution process and/or budgetary conditions, OEP may change the code to one of the following:

Code 48 – Restricted award with terms and conditions which may be resolved and recoded through OEP action. An award can be made with unresolved human subjects protection concerns; terms restricting all human subjects research must be included on the Notice of Award (NoA) or the Terms of the Contract.
Code 54 – Previously coded 44 or 48 – Concerns resolved. If applications coded 44 or 48 are resolved to meet the criteria for one or more exemptions, OEP will assign the appropriate exemption code as certified by the institution.
Code E8 – Human subjects involved – Some or all human subjects regulations waived and so designated by OEP. Applicability of human subjects regulations waived in full or in part by the Secretary, HHS, under 45 CFR 46.101(i).

The above-listed codes comprise the various classifications available for coding NIH funded research involving human subjects.

6. **Common Rule:** The Federal Policy for the Protection of Human Subjects or the "Common Rule" was published in 1991 and codified in separate regulations by 15 Federal departments and agencies. The HHS regulations, 45 CFR part 46, include four subparts: subpart A, also known as the Federal Policy or the "Common Rule"; subpart B, additional protections for pregnant women, human fetuses, and neonates; subpart C, additional protections for prisoners; and subpart D, additional protections for children. (see http://www.hhs.gov/ohrp/humansubjects/commonrule/index.html).
7. **Contractor:** Any individual or other legal entity that (1) directly or indirectly (e.g., through an affiliate), submits offers for or is awarded, or reasonably may be expected to submit offers for or be awarded, a Government contract, including a contract for carriage under Government or commercial bills of lading, or a subcontract under a Government contract; or (2) conducts business, or reasonably may be expected to conduct business, with the Government as an agent or representative of another contractor (see Federal Acquisition Regulations Section 9.403 at https://www.acquisition.gov/far/current/html/Subpart%209_4.html#wp1083280). Complex contracts may specify a Prime Contractor and one or more Subcontractors (individuals or legal entities) that perform under the direction of the Prime Contractor.

8. **Contract Modification:** A modification in one or more aspects of an existing contract that has been negotiated and mutually agreed upon by the Contractor and the NIH Contracting Officer.
9. **Data and Safety Monitoring Policy:** NIH requires that all clinical trials have data and safety monitoring plans. (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-038.html and http://grants.nih.gov/grants/guide/notice-files/not98-084.html).
10. **"Engaged" Institution:** An institution becomes "engaged" in non-exempt human subjects research when its "employees or agents for the purposes of the research project obtain: (1) data about the living subjects of the research through intervention or interaction with them; (2) identifiable private information about the subjects of the research; or (3) the informed consent of human subjects for the research." (http://www.hhs.gov/ohrp/policy/engage08.html). One example of when an institution generally is considered *engaged* in a HHS-conducted or -supported non-exempt human subjects research project (and, therefore, needs to hold or obtain an FWA and certify IRB review and approval to HHS) when it receives an award through a grant or contract directly from HHS for the non-exempt human subjects research even where all activities involving human subjects are carried out by employees or agents of another institution. (http://www.hhs.gov/ohrp/policy/engage08.html). In such cases, the awardee institution bears ultimate responsibility for protecting human subjects under the award.
11. **Exempt:** A research activity in which the only involvement of human subjects will be in one or more of six categories defined in 45 CFR 46.101(b).
12. **Federalwide Assurance (FWA):** Through the FWA, an institution commits to HHS that it will comply with the requirements in the HHS Protection of Human Subjects regulations at 45 CFR part 46. (See http://www.hhs.gov/ohrp/assurances/index.html).
13. **Grantee:** The organization awarded a grant by the NIH Extramural Program that is responsible and accountable for the use of the funds provided and for the performance of the grant-supported project or activities. The grantee is the entire legal entity even if a particular component is designated in the award document. The grantee is legally responsible and accountable to NIH for the performance and financial aspects of the grant-supported project or activity.
14. **Human Subject (HS):** A living individual about whom an investigator (whether professional or student) conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information. Intervention includes both physical procedures by which data are gathered (e.g., venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes. Interaction includes communication or interpersonal contact between investigator and subject. Private information includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator) in order for obtaining the information to constitute

research involving human subjects (See 45 CFR 46.102(f) at: http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#46.101).

15. **Human Subject Concern:** Actual or potential risks or inadequate protections for human subjects who participate in the research described in any portion of the grant application or contract proposal, that a peer review panel or an NIH official (such as through a technical evaluation or OEP) deems to be of sufficient significance to warrant a bar to funding (Code 44). The concerns giving rise to the unacceptable designation must be resolved by the applicant or offeror before research involving human subjects can be conducted using NIH funds. Reviewer guidelines are described in: http://grants.nih.gov/grants/peer/guidelines_general/Human_Subjects_Protection_and_Inclusion.pdf.
16. **Human Protections Administrator (HPA) (e.g., Human Subjects Administrator or Human Subjects Contact Person):** The HPA should have comprehensive knowledge of all aspects of your institution's system of protections for human subjects, as well as be familiar with the institution's commitments under the FWA, and play a key role in ensuring that the institution fulfills its responsibilities under the FWA (http://www.hhs.gov/ohrp/assurances/forms/fwainstructions.html).
17. **Human Subjects Research Coordinator:** One or more NIH IC staff members designated by the IC Director to: (a) maintain liaison with OEP; (b) provide information about the HHS human subjects regulations and NIH guidelines and policies to IC staff; (c) assist and advise program staff on human subjects concerns presented to the National Advisory Council/Board; (d) serve as IC consultant to determine an appropriate course of action to manage research procedures that give rise to ethical concerns to avert possible hazardous consequences.
18. **Informed Consent:** Person's voluntary agreement, based upon adequate knowledge and understanding, to participate in human subjects research or undergo a medical procedure. In giving informed consent, people may not waive legal rights or release or appear to release an investigator or sponsor from liability for negligence. Go to 21 CFR 50.20 and 50.25.
19. **Institution:** Any public or private entity or agency (including Federal, State and other agencies) (45 CFR 46.102(b)).
20. **Institutional Review Board (IRB):** An administrative body established to protect the rights and welfare of human research subjects recruited to participate in research activities conducted under the auspices of the organization with which it is affiliated. The Institutional Review Board has the authority to approve, require modifications in, or disapprove all research activities that fall within its jurisdiction. (45 CFR 46 specifies the composition of the IRB and details its procedures and responsibilities). (http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#subparta)
21. **Legally Authorized Representative (LAR):** An individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research (45 CFR 46.102(c)).
22. **Minimal Risk:** Means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or

psychological examinations or tests (45 CFR 46.102(i)).

23. **Offeror:** Any individual or other legal entity that directly or indirectly (e.g., through an affiliate) submits an offer to enter into a contract with NIH.
24. **Peer Review:** Review of grant applications or R&D contract proposals performed in accordance with http://www.gpo.gov/fdsys/pkg/CFR-2010-title42-vol1/pdf/CFR-2010-title42-vol1-sec52h-2.pdf.
25. **Research and Development (R&D) Contract:** an identified, circumscribed activity, involving a single contract or two or more similar, related, or interdependent contracts, intended and designed to acquire new or fuller knowledge and understanding in the areas of biomedical or behavioral research and/or to use such knowledge and understanding to develop useful materials, devices, systems, or methods. http://ecfr.gpoaccess.gov/cgi/t/text/text-idx?c=ecfr&rgn=div5&view=text&node=42:1.0.1.4.35&idno=42.
26. **Technical Evaluation:** If the acquisition warrants formulation of a Technical Evaluation Plan, a technical evaluation for technical merit and, if applicable, human subjects protections is performed on each proposal. The technical evaluation is performed in accordance with http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#46.120. For contract proposals submitted to an NIH IC, the technical evaluation is generally managed by the IC's review branch. The review branch assigns a SRO who organizes a Technical Evaluation Panel (TEP) with the appropriate member composition to perform peer review of the submitted proposals.
27. **Technical Evaluation Plan:** A Contracting Officer shall require a Technical Evaluation Plan if HHS acquisition regulations require it for the proposed acquisition, or if the acquisition is considered sufficiently complex (http://www.hhs.gov/policies/hhsar/subpart307-71.html). For NIH contract proposals, the plan must include a list of potential evaluation panel members, a supporting rationale if non-federal evaluators will be included, a statement for the absence of apparent or actual conflict of interest, a description of the evaluation approach and a description of the methodology for evaluating key elements (see HHSAR 315.305(a)(3)).
28. **Technical Evaluation Report (TER):** A document that is prepared by an SRO or the chair of the Technical Evaluation Panel. The report contains technical evaluation summaries for all proposals received in response to a particular solicitation, documenting strengths and weaknesses, on a criterion-by-criterion and overall basis. The documented strengths, weaknesses and recommendations serve as the basis for later discussions with those offerors in the competitive range. The report reflects rankings and scores of each proposal and identifies each as acceptable or unacceptable. Policy for the initiation, review, evaluation, negotiation, and award of NIH biomedical and behavioral Research and Development (R&D) contract projects can be found at NIH Manual 6315-1. For the purposes of this chapter, the policies and procedures related to protections of human subjects described in this chapter and those described in Manual Chapter 6315-1 extend to all NIH extramural R&D contracts that involve human subjects in research.

29. **Acronyms:**

AOR: Authorized Organizational Representative
CFR: Code of Federal Regulations
CO: Contracting Officer (KO is an alternative acronym used in military settings.)
COR: Contracting Officer's Representative
COTR: Contracting Officer's Technical Representative (term discontinued as of January 1,
2012, http://www.whitehouse.gov/sites/default/files/omb/procurement/revisions-to-the-federal-acquisition-certification-for-contracting-officers-representatives.pdf)
FAR: Federal Acquisition Regulations
FDA: Food and Drug Administration
FWA: Federalwide Assurance
HPA: Human Protections Administrator
HSSAR: Health and Human Services Acquisition Regulations
IC: NIH Institute or Center
IRB: Institutional Review Board
LAR: Legally Authorized Representative
NoA: Notice of Award
OEP: NIH Office of Extramural Programs
OER: NIH Office of Extramural Research
OHRP: Office of Human Research Protections
PD: Project Director
PI: Principal Investigator
PO: NIH Program Officer
R&D: Research and Development
SRO: Scientific Review Officer
TEP: Technical Evaluation Panel
TER: Technical Evaluation Report

E. Responsibilities

This section of the chapter is informational and intended to provide a review of the responsibilities of the various parties in connection with conducting research on human subjects. It is descriptive regarding non-NIH employees and in that regard, it is not intended to assign responsibilities or set forth binding NIH policy for non-employees.

1. **Grantee:** The organization or individual awarded a grant or cooperative agreement by NIH that is responsible and accountable for the use of the funds provided and for the performance of the grant-supported project or activity. The grantee is the entire legal entity even if a particular component is designated in NoA. The grantee is legally responsible and accountable to NIH for the performance and financial aspects of the grant-supported project or activity. Also known as awardee or recipient (http://grants.nih.gov/grants/policy/nihgps_2011/).

2. **Contractor:** The Contractor is responsible for ensuring compliance with the financial and administrative aspects of the contract. The Contractor has primary responsibility for safeguarding the rights and welfare of the human subjects as described in the contract and by http://grants2.nih.gov/grants/policy/nihgps_2003/NIHGPS_Part5.htm - _Toc54600083(http://grants.nih.gov/grants/policy/hs/hs_policies.htm). For contracts in which there is a Prime Contractor and one or more Subcontractors, the Prime Contractor is responsible for ensuring that all subcontractors meet contract requirements and observe applicable restrictions.
3. **Authorized Organization Representative (AOR):** The AOR, sometimes referred to as the Signing Official (SO) is affiliated with the outside institution applying for a grant, has institutional authority to legally bind the outside institution in grants administration matters. The individual fulfilling this role may have any number of titles in the grantee organization. The label, "Signing Official," is used in conjunction with the NIH eRA Commons. The SO can register the grantee institution, and create and modify the institutional profile and user accounts. The SO also can view all its institution's grants, including status and award information. An SO can create additional SO accounts as well as accounts with any other role or combination of roles. For most grantee institutions, the Signing Official (SO) is located in its Office of Sponsored Research or equivalent. The AOR is the individual, named by the applicant organization, who is authorized to act for the applicant and to assume the obligations imposed by the Federal laws, regulations, requirements, and conditions that apply to grant applications or grant awards. This official is equivalent to the Signing Official in the eRA Commons, i.e., holds the SO Role. Responsibilities include:
    - Submitting the grant on behalf of the company, organization, institution, or Government.
    - Signing grant applications and the required certifications and/or assurances necessary to fulfill the requirements of the application process. (See AOR and SO athttp://grants.nih.gov/grants/glossary.htm.)
4. **Project Director or Principal Investigator (PD/PI):** The PD/PI is; or, in the case of Multi-PD/PI projects, are; responsible and accountable to the applicant organization, or as appropriate to a collaborating organization, for the proper conduct of the project or program, including the submission of all required reports. The presence of more than one PD/PI on an application or award diminishes neither the responsibility nor the accountability of any individual PD/PI. The applicant/grantee organization is responsible for securing and retaining the required written assurance signatures from each identified PD/PI on all applications, post-submission information, progress reports, and post-award prior approval requests. The PD/PI is responsible for ensuring compliance with the financial and administrative aspects of a grant. For those grants with multiple PD/PIs, OEP works with the individual designated in the grant application as the Contact. However all named PD/PIs are considered to be responsible for the financial and administrative aspects of the awardhttp://grants.nih.gov/grants/policy/nihgps_2011/nihgps_ch9.htm. The PD/PIs must:

a. Personally fulfill the NIH Human Subjects education requirement and identify other senior/key personnel and senior/key contributors who must fulfill this education requirement (http://grants1.nih.gov/grants/guide/notice-files/NOT-OD-00-039.html).
b. Address all points concerning protection of human subjects in applications and proposals.
c. Provide an adequate explanation in the grant application or contract proposal under the heading of Human Subjects, when an institutional determination of exemption is designated on the face page of the application, to permit a determination of the appropriateness of the designated exemption (http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#46.101).
d. The PD/PI must obtain the signature of the AOR (see above) for changes to the protections for human subjects made in response to peer review or NIH staff concerns.
e. Ensure annual IRB review of non-exempt research (including participating sites and subprojects).
f. Notify the IRB, NIH Institute or Center funding the project, and any other relevant agencies or organizations such as the FDA if adverse events occur (http://grants.nih.gov/grants/guide/notice-files/not99-107.html; http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-038.html; http://www.hhs.gov/ohrp/policy/advevntguid.html).

5. **Contractor's Project Director or Principal Investigator (PD/PI):** In cases in which the Contractor is a business or legal entity, the Contractor may identify an individual PD/PI who is a member of the team responsible for ensuring compliance with the scientific and technical aspects of a contract. The PD/PI must:
   a. Personally fulfill the NIH Human Subjects education requirement and identify other senior/key personnel and senior/key contributors who must fulfill this education requirement (http://grants1.nih.gov/grants/guide/notice-files/NOT-OD-00-039.html).
   b. Address all points concerning protections of human subjects in the proposal.
   c. When an institutional determination of exemption is designated on the face page of the application, provide an adequate explanation in the contract proposal to permit a determination of the appropriateness of the designated exemption; this information should be placed under the heading of Human Subjects (see 45 CFR 46.101(b)(1) through (6)) (http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#46.101).
   d. Work with the Contractor to ensure annual IRB review of non-exempt research (including participating sites and subprojects).
   e. Notify the IRB, NIH Institute or Center funding the contract, and any other relevant agencies or organizations such as the FDA if adverse events occur (http://grants.nih.gov/grants/guide/notice-files/not99-107.html; http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-038.html; http://www.hhs.gov/ohrp/policy/advevntguid.html).
6. **Scientific Review Officer (SRO) Responsibilities for:**

a. **Grant Applications:** SROs who administer the scientific and technical merit peer review of grant applications to conduct federally-supported human subjects research have the following responsibilities concerning human subjects protections:
    1. Administratively review applications to ensure pre-review codes are appropriately assigned to indicate involvement of human subjects.
    2. Manage peer review of the applications' scientific merits and ensure review of protections for human subjects involved in research.
        a. Review is conducted consistent with Federal regulations, 45 CFR 46.120 http://www.gpo.gov/fdsys/pkg/CFR-2002-title45-vol1/pdf/CFR-2002-title45-vol1-sec46-120.pdf and 42 CFR 52h (http://www.access.gpo.gov/nara/cfr/waisidx_03/42cfr52h_03.html) including:
            - Risk to Human Subjects
            - Adequacy of Protections Against Risks.
            - Potential Benefits of the Proposed Research
            - Importance of Knowledge to be Gained
        b. If there is an institutional determination of exemption claimed, this claim should be evaluated to determine if it is justified; if not, the application needs to be reviewed for HS protections according to the four points. (See http://grants.nih.gov/grants/guide/notice-files/NOT-OD-09-025.html).
    3. Preparing a Summary Statement
        a. For all discussed grant applications, the SRO will prepare summary statements that contain the written critiques based on the scientific and technical merit additional review criteria, review considerations, including documentation of the SRG's committee recommendations related to human subjects protections.
        b. In addition, including applications that are not discussed, the SRO will include written comments from reviewers concerning protections in the summary statement.
        c. The summary statement also will indicate a code for human subjects protections (e.g., Code 10, 30, 44, or appropriate Exemption number) and this code will be entered into the appropriate NIH database (e.g., IMPAC II). For multi-project applications, if a Code 44 is assigned to one or more of the projects, a Code 44 is assigned to the entire application.

b. **Contract Proposals: (See Appendices B and C for guidance.)** SROs who administer the technical evaluation of research and development contract proposals to conduct federally-supported human subjects research have the following responsibilities concerning human subjects protections:
    1. Administratively review applications to ensure pre-review codes are appropriately assigned to indicate involvement of human subjects.

2. Manage scientific merit peer review in accordance with https://www.acquisition.gov/far/90-37/html/15.html andhttp://www.hhs.gov/policies/hhsar/subpart315.html#315.305Proposalevaluation and to ensure review of protections for human subjects involved in research.
    a. Review is conducted consistent with the Federal regulations, 45 CFR 46.120, (http://www.gpo.gov/fdsys/pkg/CFR-2002-title45-vol1/pdf/CFR-2002-title45-vol1-sec46-120.pdf) and 42 CFR 52h, (http://www.access.gpo.gov/nara/cfr/waisidx_03/42cfr52h_03.html) . The regulations 45 CFR 46.120 specifically require review of the following four points:
        - Risk to Human Subjects
        - Adequacy of Protections Against Risks
        - Potential Benefits of the Proposed Research
        - Importance of Knowledge to be Gained
3. If there is an institutional determination of exemption claimed, this claim should be evaluated to determine if it is justified; if not, the proposal needs to be reviewed for HS protections according to the four points.
4. Human subjects protections may be included as part of the technical merit review criteria. However, if human subjects protections are not specifically included in the criteria, the SRO instructs reviewers to evaluate human subjects protections as a special consideration and vote on the adequacy of the protections. In order to provide a complete evaluation of each proposal, the discussion and vote on the adequacy of protections should be done regardless of whether the technical merit review determines the overall proposal to be acceptable.
5. Preparing a Technical Evaluation Report (TER). The SRO will prepare a TER that includes for each proposal the reviewers' written critiques based on the technical merit criteria and all special considerations, documenting the SRG committee recommendations related to human subjects protections. The SRO will include written comments from reviewers concerning protections in the TER. The TER also will indicate a code for human subjects protections (e.g., Code 10, 30, 44, or appropriate Exemption number). The SRO will prepare a summary page that identifies all contract proposals with an acceptable technical merit score, but were determined to have unacceptable protections for human subjects.

7. **National Advisory Council or Board:** For grant applications, the NIH National Advisory Councils or Boards (Councils) perform the second level of peer review. For those applications that have received a Code 44, the Council may consider them for funding according to approved Council procedures (NIH Manual 54513) pending satisfactory resolution of all human subject concerns by OEP. Following Council review, the IC awarding unit records any specific Council comments and recommendations regarding these applications and ensures the appropriate

documentation is filed in the official grant file and appropriate NIH database.

8. **Program Official (PO) Responsibilities for:**
    a. **Grant Applications:** Working with the Grants Management specialist, the PO is the intermediary between OEP and the PD/PI in the process of resolving concerns related to human subjects for grants or cooperative agreements. Prior to Council meetings, the PO assesses each application that is going to be reviewed by the Council to determine which applications have SRG-identified human subjects concerns. In addition, the PO examines the human subjects codes, requested exemptions, and human subjects protection plans (including DSMBs/DSMPs) to identify additional concerns. If necessary, the PO requests supplementary information from the PD/PI. If POs have any questions or concerns regarding the protection of human subjects or the appropriateness of the codes in an application that is intended for funding, they may consult the IC's Human Subjects Research Coordinator, the IC staff member assigned responsibility for matters related to human subjects protections, or OEP. If either the Program Officer or the Grants Management Specialist disagrees with the assigned human subjects code, they may discuss their concerns with OEP. However, only OEP can change the code.
    b. **Contract Proposals:** One or more POs may be involved in the planning, solicitation, source selection, and administration of a contract. For each contract, a PO, with appropriate additional training, is designated as the COR. The COR works with the CO, who is the intermediary between OEP and the PD/PI in the process of resolving concerns related to human subjects. For those contract proposals that may go on to negotiation, the COR, or a PO working on the solicitation, determines which proposals have TEP-identified human subjects concerns. In addition, the human subjects codes, requested exemptions, and human subjects protection plans (including DSMBs/DSMPs) are examined. If necessary, supplementary information from the PD/PI may be requested by the CO. If there are questions or concerns regarding the protection of human subjects or the appropriateness of the codes for a proposal that is in negotiations, the CO may consult the IC's Human Subjects Research Coordinator or OEP. If there is disagreement with the assigned human subjects code, the matter may discussed with OEP. However, only OEP can change the code.
9. **The IC Contracting Officer (CO):**
    a. **Preparation of Solicitations and Announcements –** The CO, in collaboration with one or more POs and the COR, is responsible for preparing R&D contract solicitations. In these documents, the offeror should be instructed to address the four points of human subjects protections under a separate human subjects section. Section M. Evaluation Factors for Award, of each solicitation should specify that protections of human subjects are considered in the scientific merit review, either as a one of the review criteria or as a special consideration. The solicitation should indicate that this section will undergo technical evaluation and acceptability of human subjects protection will be considered in the evaluation of technical merit. A determination of unacceptable protections is a

bar to funding and must be resolved before an award is made.

b. **Evaluation of Contract Proposals –** The CO arranges for evaluation of contract proposals. For acquisitions in which the contracted activities meet the definition of Human Subjects Research, evaluation is accomplished using peer review, as is done with all other NIH R&D contracts. When the Technical Evaluation Plan for a solicitation includes peer review, the members of the peer review panel will perform the evaluation of human subjects protections. For all other contracted work, officers and employees of the department or agency and such experts and consultants as the department/agency determines to be appropriate will evaluate human subjects protections. The CO and COR receive the TER. The summary page of the TER is prepared listing the proposals in order of their technical merit, indicating those proposals that have been designated as having unacceptable ratings for protections for human subjects.

c. **Post-Review Evaluation of Contract Proposals -** In source selection for contract awards, the CO may take into account, in addition to all other eligibility requirements and evaluation factors, such issues as whether:

    1. The offeror has previously been subject to a termination or suspension under 45 CFR 46.123 or 45 CFR Part 74.13, and is listed at https://www.epls.gov/.
    2. The offeror or the persons who would direct the scientific and technical aspects of a project, are judged to have failed materially to discharge their responsibilities to protect the rights and welfare of subjects in their care, whether or not HHS funds were involved.
    3. Adequate steps have been taken to eliminate past deficiencies where they have existed.
    4. In negotiations, the CO acts as the intermediary between OEP and the PD/PI in the process of resolving concerns related to human subjects protections that led to an unacceptable rating (Code 44). Such resolution is done in conjunction with OEP. Once resolution has been accomplished, OEP documents the resolution by communication with the CO and changes the code for the proposal from 44 to 54 in OEP records. If changes in the proposed research result from resolution of human subjects concerns, these changes should be transmitted to the offeror and recorded in the appropriate contract files and NIH databases.

10. **Grants Management Specialists (GMS):** The GMS is responsible for:

    a. **Just-In-Time Requests (JIT) for a Grant Applicant:** In the application process, certain elements of a grant application may be submitted after the peer review meeting, at the time the grant application is under consideration for funding in accord with NIH JIT procedures. Standard JIT elements that relate to Human Subjects include certification of IRB approval of the proposed use of human subjects (or an institutional determination of exemption, if applicable) and evidence of compliance with the human subjects protections training requirement for the PD/PI and Key Personnel involved in human subjects research. Applicants will be notified (primarily by e-mail) when JIT information

is needed. In addition to these standard elements, the PO and GMS determine what additional information, if any, needs to be submitted in order to complete requirements to make an award. NIH requests for additional information are sent by the PO to the PD/PI and AOR. The correspondence also should remind the PD/PI that resolving concerns may result in substantive changes to the project, and these changes must be included in the information provided to the IRB for review and approval. The following information related to protections of human subjects is included in the JIT request, unless provided as part of the application:

1. Applicant responses to resolve SRG concerns in human subjects protections that resulted in an unacceptable code.
2. OHRP Institutional FWA number. The grantee organization must have its own FWA, even if relying on the IRB of another organization.
3. Certification of IRB review and approval of the most recent revision of the human subjects research – unless the research is exempt, in which the applicant must submit a certification of institutional determination of exemption to NIH. The IRB approval date must be within 12 months of the budget period start date. Certification of IRB review and approval may be conveyed using OHRP's form OMB No. 0990-0263 "Protection of Human Subjects Assurance Identification/IRB Certification/Declaration of Exemption" (http://www.hhs.gov/ohrp/assurances/forms/ and http://www.healtheffects.org/RFA/Forms/Form9.pdf) or a letter with comparable information. IRB documentation should include, if applicable, the following:
    a. A description of the information reviewed by the IRB.
    b. Identification of research involving pregnant women, human fetuses and neonates (Subpart B), prisoners (Subpart C) and/or children (Subpart D).
    c. Valid date of IRB approval. The date must be within the past 12 months, and must represent final (i.e. not conditional) IRB approval.
    d. Documentation of compliance with the education requirement for investigators engaged in NIH-supported research involving human subject participants (http://grants1.nih.gov/grants/guide/notice-files/NOT-OD-00-039.html).

b. **Applications that Lack Definite Plans for the Involvement of Human Subjects (i.e., Delayed Onset Human Subjects Research):** Restrictive terms must be included by the GMS in the NoA for studies that cannot be described prior to award. The restriction may not be lifted until the grantee submits to the NIH for prior approval the detailed information required to document protection for Human Subjects, certification of IRB approval, or, if all of the research meets the criteria for one or more exemptions, a certification of institutional determination of exemptions(s) and a justification sufficient to allow a determination that the claimed exemption is justified.

c. **Restricted Awards for Research with Unresolved Human Subjects Protection Concerns:** With a restricted award, only activities that do not directly involve human subjects (i.e., are clearly distinct and independent from those activities that do involve human subjects) may be conducted. The Grantee may not draw funds from the Payment Management System or make obligations against Federal funds for research involving human subjects at any site engaged in non-exempt research for any period. In addition, affiliated institutions may not recruit human subjects proposed for study or otherwise become involved with human subjects prior to resolution of all concerns. At any time during the award period, NIH staff may request that OEP change the human subjects code so that a restricted award can be issued (https://hs.od.nih.gov/default.aspx).
d. To lift the bar, the applicant must communicate their response to the PO who submits the information to OEP for evaluation and approval. Once approved, the restrictions on human subjects research may be lifted through the issuance of a revised NoA.

11. **Office of Extramural Programs (OEP):**

The OEP, through its Human Subjects Program is responsible for definition and use of codes that categorize the involvement of human subjects in NIH-supported research. OEP establishes and implements policy for: (1) the coding of grant applications and contract proposals involving human subjects; (2) the review and approval of proposed resolutions of unacceptable human subjects protections; and (3) the changing of unacceptable or incorrect human subjects codes prior to funding. For NIH grant applications and contract proposals, the process for resolving unacceptable human subjects protections is an OEP function. The OEP's Procedures for Changing Codes are outlined at: https://hs.od.nih.gov/default.aspx.

In addition, award documentation must include:

a. Correspondence with PD/PI and/or AOR resolving the concern(s) countersigned by the AOR
b. Program approval of the resolution for grant applications or CO approval of the resolution for contract proposals

For NIH grant applications and contract proposals that have been coded as having unacceptable protections for human subjects, OEP is responsible for assessing HS protections, for resolution of the concerns, and for human subject code changes prior to award or prior to lifting a human subjects restriction.

F. Procedures

Use the Codes provided in D.5 of this Chapter.

1. **Receipt of grant applications and contract proposals:** When a grant application or contract proposal is received by NIH, an initial determination is made as to whether

human subjects are involved. The Codes that may be assigned at the time of receipt of a grant application or contract proposal are as follows:

Code 10 – No human subjects involved
Code 20 – Human subjects involved – No exemption designated
Code E1 – Human subjects involved – Exemption category 1
Code E2 – Human subjects involved – Exemption category 2
Code E3 – Human subjects involved – Exemption category 3
Code E4 – Human subjects involved – Exemption category 4
Code E5 – Human subjects involved – Exemption category 5
Code E6 – Human subjects involved – Exemption category 6

The initial human subjects code is part of the administrative review of the application by the SRO in planning and conducting peer review to ensure that human subjects information is included in the review.

a. For grant applications, this determination is based on information provided on the application face page by the applicant and is recorded by the Division of Receipt and Referral, Center for Scientific Review and then verified by the SRO. If the applicant incorrectly filled-in whether or not human subjects are to be involved in the research, the SRO should enter the correct code into the appropriate database (e.g., IMPAC II).
b. For contract proposals, this determination is self-selected by the offeror according to directions specified in the solicitation to be included on the first page of the contract proposal. The initial code may also be assigned by the CO or designee based on the particulars of the work that the IC intends to accomplish and conveyed to the SRO on a cover sheet to the contract proposal. Based on what is proposed by the offeror, the SRO has responsibility to ensure the correct code is selected.

2. **Evaluation of protections for human subjects in grant applications and contract proposals:** The Federal regulations for protections of human subjects (45 CFR 46.120) require that the evaluation of applications and proposals to conduct federally-supported human subjects research consider:
   a. Risk to Human Subjects.
   b. Protections Against Risks.
   c. Potential Benefits of the Proposed Research to Human Subjects and Others.
   d. Importance of Knowledge to be Gained.

For Grant applications: The initial review is expected to reflect the collective standards of the professions represented within the SRG. If the SRG provides written critiques noting human subjects concerns, the SRO includes these concerns in the Human Subjects (Resume) section of the summary statement. To meet review expectations, sufficient information for members of the SRG to determine that the proposed research meets the requirements of 45 CFR 46, applicants for NIH grants are instructed in Part II: Supplemental Instructions for Preparing the Protection of Human

Subjects Section of the Research Plan (http://grants.nih.gov/grants/funding/phs398/phs398.html) to consider and discuss the following:

1. Risk to Human Subjects
2. Protections Against Risks
3. Potential Benefits
4. Importance of Knowledge to be Gained

In addition for research involving Clinical Trials applicants should provide:

5. Data and Safety Monitoring Plan, and
6. For Phase III clinical trials and multi-site trials with more than minimal risk, a Data Safety and Monitoring Board. (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-038.html and http://grants.nih.gov/grants/guide/notice-files/not98-084.html).

Offerors of contract proposals that involve human subjects in research are given instructions to include a human subjects section that conforms to format of the human subjects section for grant applications.

The SRG discusses the human subjects protection issues and resolves differences among reviewers when possible. Consideration of the informed consent/assent procedures as well as data and safety monitoring plans and boards for clinical trials are considered as part of the human subjects protection discussion. The SRG may make the following recommendations:

1. Acceptable Risks and/or Protections (Code 30)
2. Unacceptable Risks and/or Inadequate Protections (Code 44)
3. Not applicable (Code 10 if no Human Subjects or Exemption Code for exempt Human Subjects research)

For research that involves human subjects but does not involve one of the six categories of research that are exempt under 45 CFR Part 46.101(b), peer review will evaluate the justification for involvement of human subjects and the proposed protections from research risk relating to their participation according to the following five review criteria: 1) risk to subjects, 2) adequacy of protection against risks, 3) potential benefits to the subjects and others, 4) importance of the knowledge to be gained, and 5) data and safety monitoring for clinical trials. For research that involves human subjects and meets the criteria for one or more of the six categories of research that are exempt under 45 CFR Part 46, the committee will evaluate: 1) the justification for the exemption, 2) human subjects involvement and characteristics, and 3) sources of materials. (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-09-025.html).

An application may be designated Not Recommended for Further Consideration (NRFC) by the Scientific Review Group if it lacks significant and substantial merit;

presents serious ethical problems in the protection of human subjects from research risks; or presents serious ethical problems in the use of vertebrate animals, biohazards, and/or select agents. Applications designated as NRFC do not proceed to the second level of peer review (National Advisory Council/Board) because they cannot be funded. (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-09-024.html).

The SRO has responsibility to document the written critiques and committee recommendations regarding Human Subjects protections in the summary statement. Review results concerning humans subjects shall be coded as detailed below:

Code 10 – No human subjects involved as indicated by the SRG
Code 30 – Human subjects involved – Certified, no SRG concerns
Code 44 – Human subjects involved – SRG concerns
Code E1 – Human subjects involved – Exemption category 1
Code E2 – Human subjects involved – Exemption category 2
Code E3 – Human subjects involved – Exemption category 3
Code E4 – Human subjects involved – Exemption category 4
Code E5 – Human subjects involved – Exemption category 5
Code E6 – Human subjects involved – Exemption category 6
Code E7 – Human subjects involved – Multiple exemptions

The appropriate code is assigned to each grant application, including those that are not discussed (ND). If the grant application indicates that the Human Subjects research is exempt from the requirements of the HHS regulations, the SRG will evaluate whether the information provided conforms to one or more categories of exempt research and whether the application adequately justifies the claim for exemption(s). If an exemption from continuing IRB review is claimed and the SRG determines that the information provided does not justify the claim, then the SRG should indicate that human subjects protections are unacceptable. If the application is rated unacceptable, the summary statement Human Subjects Resume section must summarize the concerns of the reviewers.

When it is determined that human subjects will be involved at any time during the proposed project period, the project will be coded as involving human subjects for the entire project period. The designation given by the SRG will be used for all years of the award if activities involving human subjects are planned at any time during the proposed project period.

For contract proposals: For each proposal, the TER must include the recommendations and codes as described above (Acceptable or Unacceptable) of the Technical Evaluation Panel (TEP). If human subjects will be involved at any time during the proposed contract period, the project is coded as involving human subjects for the entire project period. Use the designation given by the TEP for all years of the award if activities involving human subjects are planned at any time during the contract period.

Working with the offeror, the CO must resolve unacceptable ratings of human subjects protections in consultation with OEP before contract award. OEP will request a copy of the proposal, if needed.

For each contract proposal, the SRO assigns to the TER a human subjects protections code(s) from the following list:

Code 10 – No human subjects involved as indicated by the TEP
Code 30 – Human subjects involved – Certified, no TEP concerns
Code 44 – Human subjects involved – TEP concerns
Code E1 – Human subjects involved – Exemption category 1
Code E2 – Human subjects involved – Exemption category 2
Code E3 – Human subjects involved – Exemption category 3
Code E4 – Human subjects involved – Exemption category 4
Code E5 – Human subjects involved – Exemption category 5
Code E6 – Human subjects involved – Exemption category 6
Code E7 – Human subjects involved – Multiple exemptions

The appropriate code is assigned to each contract proposal, including those that do not receive an acceptable technical merit score. If the contract proposal indicates that the Human Subjects research is exempt from the requirements of the HHS regulations, the TEP will evaluate whether the information provided conforms to one or more categories of exempt research and whether the application adequately justifies the claim for exemption(s). If an exemption from continuing IRB review is claimed and the TEP determines that the information provided does not justify the claim, then the TEP should indicate that human subjects protections are unacceptable and the TER must contain the written reviewer critiques to document the concerns.

3. **Consultation with OEP and change of code:**

   The OEP may be consulted at any time during the receipt and referral, review, or award processes. If protections of human subjects are rated unacceptable based on SRG recommendations and written reviewer critiques, the matter must be referred to OEP via its web sites for resolution: see the OEP Human Subjects Web Site at http://nih-extramural-intranet.od.nih.gov/d/nih/policies/hs/index.htm for specific links. Based on the information from the applicant or contractor as transmitted by the PO or CO, the OEP will review the matter and may, if the concerns have been addressed adequately, change the code to lift the bar to award.
4. **Grant Award:**

   Grant applications involving human subjects may proceed through the award process if there are no human subjects concerns (Code 30) or if the PO, working with the applicant, has resolved the concerns in consultation with OEP (Code 44 changed to Code 54). If the applicant proposes subcontracts that involve human subjects, the PO

must document that all engaged institutions have a FWA and have obtained appropriate IRB approval or institutional determination of exemption.

With respect to any research project or any class of research projects, the awarding IC may impose additional conditions prior to or at the time of award when deemed necessary for the protection of human subjects. It is the responsibility of the IC to monitor an institution's compliance with any restrictive term and condition of award.

Under circumstances in which all activities involving human subjects are carried out by agents or employees of other institutions (i.e., subrecipients), the applicant organization may request that OHRP determine that a specific grantee/awardee institution is not engaged. In these circumstances, OHRP notifies the NIH Office of Policy for Extramural Research Administration (OPERA). If an institution claims to have such a determination, the awarding IC staff should complete the following steps prior to issuing a grant:

a. Obtain from OPERA a copy of the OHRP letter or email stating that the institution is not considered by OHRP to be engaged. The documentation must include reference to the specific grant number or contract number and clearly be from an OHRP official.
b. Obtain a certification letter from the grantee, signed by the Authorized Organization Representative, providing the following:
    1. The FWA number, date of favorable IRB action (e.g., approval) or institutional determination of exemption, and name of the consortium institution that has reviewed and approved the application on behalf of the institution.
    2. A statement that, notwithstanding the OHRP determination of nonengagement, the institution accepts responsibility for protecting human subjects in research conducted under the NIH award and for compliance with Federal regulations for the protection of human subjects (at all consortium sites) and will ensure that all consortium sites have FWAs and that human subjects research will only be conducted under a valid IRB certification in accord with 45 CFR 46.
c. The official grant folder should be updated appropriately by including items a. and b. above, and an administrative note referencing the documentation.

At the discretion of the IC, a special term may be placed on the award as follows:

> This award acknowledges that the (insert name of secondary institution) has accepted the responsibility for the IRB review and approval of this application. However, the prime grantee institution continues to be responsible for all human subjects research conducted under the award, and will provide oversight and monitoring of all human subjects research activities commensurate with its legal role and responsibilities to assure appropriate protections for human subjects in research.

See the memo dated April 25, 2008 to GMAC Principals for additional information found at: http://nih-extramural-intranet.od.nih.gov/nih/topics/human_opera_engagement_guidance.pdf

Periodic Review:
The PO is responsible for documenting that the research protocol(s) undergo IRB review and approval at intervals appropriate to the degree of risk, but not less than once per year. The grantee must submit a copy of an acceptable IRB approval annually.

Early termination of research support:
NIH staff shall conduct early termination of research funding and evaluation of subsequent proposals in accordance with prevailing grants policy.

5. **Contract Award:**

Negotiations, Selection and Award:
If the contract does not include the conduct of research involving human subjects, the CO includes such language in the contract. Contract proposals involving human subjects may proceed through the selection and award process if there are no human subjects concerns (Code 30) or if the CO, working with the offeror, resolved the concerns in consultation with OEP (Code 44 changed to Code 54). If the offeror proposes subcontracts that involve human subjects, the CO must document that all engaged institutions have a FWA and have submitted appropriate IRB approval or institutional determination of exemption. For those proposals that have received a Code 44 and are selected for negotiations for possible award, OEP must review and approve the resolutions of all concerns that gave rise to the assignment of a Code 44.

Periodic Review:
The CO is responsible for documenting that the research protocol(s) undergo IRB review and approval at intervals appropriate to the degree of risk, but not less than once per year. The contractor must submit a copy of an acceptable IRB approval annually.

Modifications that affect human subjects research in a contract:
The IC Director or designee establishes procedures and guidelines for review of contract modifications that have an impact on protection of human subjects in research. The Director or designee determines if any modifications (e.g., concerning procedures or characteristics of subject population groups) warrant referral for additional peer review or OEP review.

Early termination of research support:
NIH staff shall conduct early termination of research funding and evaluation of subsequent proposals in accordance with prevailing contract policy.

Records:
Research records are maintained by the contractor performing the research as discussed in the Statement of Work and contract, and in accordance with 45 CFR 46.115. COs, with assistance from the COR, maintain records on each contract involving human subjects that include: (1) the contractor's annual certification or memo indicating that the assurance has been approved by OHRP; (2) copies of the TER, memoranda, correspondence with investigators, and other documents identifying concerns for the welfare of subjects. The COR may request that the CO obtain documentation of IRB evaluations and recommendations given by advisory groups, including minutes of the contractor's clinical research committees, through OEP or the contractor when additional information is needed. The CO, with advice from the COR, must keep OEP informed on all matters regarding human subjects, such as changes in protocol, study design or research scope, which may affect the HS Code of the NIH supported research.

6. **Review of the Annual Grant Progress Reports:**

Grant project performance monitoring is required on an annual basis. Evaluation of progress must be made and forwarded to grants management in sufficient time to allow a continuation award to be issued prior to the committed budget period start date. Scientific progress of the grant must be determined to be satisfactory by a PO before additional funds can be awarded for continuation of the project (see NIH Manual Chapter 54444). Among the areas that must be addressed by POs in reviewing annual progress reports is determination of the acceptability of protections for human subjects.

Grantee institutions typically submit progress reports annually as the anniversary date of the grant nears. However, they may be asked to submit reports as often as quarterly. The assumption is that the Human Subjects involvement of the entire project period is documented at the time of the administrative and programmatic review of the competing application; however, policy requires that any IRB approval information be updated annually. NIH has streamlined progress reports for many of its programs. Awards issued under the Streamlined Non-Competing Award Process (SNAP) authorities no longer are required to provide to NIH updated IRB dates as part of the annual SNAP progress report. However, grantees still are required to conduct these reviews in accordance with Federal requirements and provide this data upon request. Non-SNAP progress reports require the updated IRB approval information as part of the submission. In all progress reports, SNAP and non-SNAP, grantees must specifically address any changes in Human Subjects involvement. Further they must also provide any additional certifications for Human Subjects Education for new Senior/Key Persons.

Unless Human Subjects involvement changes during one of the subsequent non-competing years, the grant record will continue to reflect the human subjects coding

(involvement-Yes/No, etc.) of the competing application. Grants Management staff will update the IMPAC II record to reflect the current IRB approval date, as applicable. Further Grants Management and POs will continue to review Human Subjects involvement as part of their programmatic and administrative reviews and document any issues on the checklist as appropriate. Policies and procedures for PO evaluation of progress reports are described in NIH Manual Chapter 54444.

If, in the grant progress report, a change in human subjects protections or activities is described, the PO will determine whether the change constitutes a change in scope of the project. In cases of change in scope, the PO will determine whether to apply restrictions on continued funding until the proposed change undergoes peer review, if necessary, is approved by the IC, and has the appropriate IRB approvals in place.

G. Primary References

1. Public Health Service Act as amended, 42 USC 289,http://uscode.house.gov/download/pls/Title_42.txt
2. Code of Federal Regulations, Title 45, Part 46, Protection Of Human Subjects
3. Code of Federal Regulations, Title 45, Part 74.13, Uniform Administrative Requirements For Awards And Subawards To Institutions Of Higher Education, Hospitals, Other Nonprofit Organizations, And Commercial Organizations, Debarment and suspension.
4. Chapter I--Public Health Service, HHS, Part 52h—Scientific Peer Review of Research Grant Applications and Research and Development Contract Projectshttp://www.access.gpo.gov/nara/cfr/waisidx_03/42cfr52h_03.html
5. Code of Federal Regulations, Title 21, Subchapters D, F, and H; Food and Drug Administration http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm.
6. Office for Human Research Protections (OHRP) Database for Registered IORGs & IRBs, Approved FWAs, and Documents Received in Last 60 Days: http://ohrp.cit.nih.gov/search/
7. Federal Acquisition Regulation (FAR) Subpart 9.4—Debarment, Suspension, and Ineligibility
8. Evaluation of NIH Implementation of Section 491 of the Public Health Service Act, Mandating a Program of Protection for Research Subjects:http://www.hhs.gov/ohrp/archive/policy/hsp_final_rpt.pdf
9. OHRP Guidance, Engagement of Institutions in Human Subjects Research
10. OHRP Guidance, Exempt Research and Research That May Undergo Expedited Review
11. OHRP Guidance, Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events
12. OHRP Policy Announcement, IRB Review of Applications for HHS Support
13. NIH Grants Policy Statement, http://grants.nih.gov/grants/policy/nihgps_2011/
14. NIH Manual Chapter 3014, NIH Human Research Protection Program

15. NIH Manual Chapter 6315-1, Initiation, Review, Evaluation, and Award of Research & Development (R&D) Contracts
16. NIH Manual Chapter 54444, NIH Program Official Evaluation of Progress Reports.
17. NIH Manual Chapter 54104, NIH Research Grants to Foreign Institutions and International Organizations.
18. NIH Manual Chapter 54805, Research Grants Awarded to Non-Affiliated Individuals.
19. NIH Manual Chapter 1805, Use of Advisors in Program and Project Review and Management
20. OER Policy Announcement 2000-06: FY 2000 End of Year Procedures For Awarding Applications Involving Human Subjects (http://odoerdb2.od.nih.gov/oer/policies/oer_announce_2000_06.htm)
21. NIH Manual Chapter 4204-204B**,** Peer Review Process
22. NIH Manual Chapter 54513, Management and Procedures of NIH National Advisory Councils and Boards in Their Review of Extramural Activities
23. NIH Manual Chapter 1743, Keeping and Destroying Records, Appendix 1, NIH Records Control Schedule
24. NIH Policy Announcement, FURTHER GUIDANCE ON A DATA AND SAFETY MONITORING FOR PHASE I AND PHASE II TRIALS
25. NIH Policy Announcement, NIH POLICY FOR DATA AND SAFETY MONITORING
26. NIH Policy Announcement, REQUIRED EDUCATION IN THE PROTECTION OF HUMAN RESEARCH PARTICIPANTS
27. NIH Policy Announcement, GUIDANCE ON REPORTING ADVERSE EVENTS TO INSTITUTIONAL REVIEW BOARDS FOR NIH-SUPPORTED MULTICENTER CLINICAL TRIALS

H. Records Retention and Disposal

All records (e-mail and non-e-mail) pertaining to the processes described in this chapter must be maintained (e.g., retained and/or disposed of) under the authority of NIH Manual 1743, "Keeping and Destroying Records", NIH Records Control Schedule, Section 1100 - General Administration and Section 4000 Grants and Awards and according to the FAR.

NIH e-mail messages, including attachments that are created on NIH computer systems or transmitted over NIH networks that are evidence of the activities of the agency or have informational value are considered Federal records. These records must be maintained in accordance with current NIH Records Management guidelines. Contact your IC Records Liaison for additional information.

All e-mail messages are considered Government property, and, if requested for a legitimate Government purpose, must be provided to the requester. Employees' supervisors, NIH staff conducting official reviews or investigations, and the Office of the Inspector General may request access to or copies of the e-mail messages. E-mail messages must also be provided to Congressional oversight committees if requested and are subject to Freedom of Information

Act requests. Back-up files are subject to the same requests as the original messages.

I. Internal Controls

The purpose of this section is to provide guidance to OEP for the implementation and review of the policies on grants involving human subjects described in this chapter.

1. **Office Responsible for Reviewing Internal Controls Related to this Chapter:** Responsibility for monitoring compliance with this chapter resides with the OEP/OER. Consult the Office of Policy for Extramural Research Administration (OPERA) with respect to internal controls relative to the grants management issues involved in this chapter. Consult the Office of Acquisitions and Logistics Management (OALM) with respect to internal controls in connection with contracts.
2. **Frequency of Review:** On-going review of this document, no less than every five years.
3. **Method of Review:** OEP will use several methods of review in which new issues may arise that need to be incorporated into the chapter, and in which feedback from IC Officials on current procedures is obtained. Methods may include:
    a. periodic sampling of funded grant applications and contracts via NIH grants and contract databases (e.g., IMPAC II);
    b. feedback from extramural staff training programs;
    c. feedback from the Review Policy Committee (RPC)
    d. the Program Leadership Committee (PLC)
    e. the Grants Management Advisory Committee (GMAC)
    f. the Acquisition Management Committee (AMC)
    g. Extramural Program Management Committee (EPMC).

    In addition, OPERA will be routinely apprised of any difficulties in the implementation of this policy.

    Reports of findings and recommendations resulting from these types of reviews will be issued to assess compliance with the policy stated in this chapter. Common issues will be brought to the PLC, RPC, GMAC, AMC and the EPMC for resolution and corrective action. Depending upon the nature and the extent of problems found, if any, the Deputy Director for Extramural Research (DDER) or the Deputy Director of OALM may recommend additional review, policy guidance, and/or training of staff.

4. **Review Reports:** Review reports are sent to the DDER, the Deputy Director of OALM and OPERA. Reports should indicate that controls are in place and working well or indicate any internal control issues that should be brought to the attention of the report recipient(s).

Appendix A

SAMPLE TEXTS FOR POSSIBLE USE IN FINAL CONTRACT DOCUMENTS

ARTICLE H.1. HUMAN SUBJECTS

It is hereby understood and agreed that research involving human subjects shall not be conducted under this contract and that no material developed, modified, or delivered by or to the Government under this contract, or any subsequent modification of such material, will be used by the Contractor or made available by the Contractor for use by anyone other than the Government, for experimental or therapeutic use involving humans without the prior written approval of the Contracting Officer.

ARTICLE H.2. HUMAN MATERIALS (ASSURANCE OF OHRP COMPLIANCE)

The acquisition and supply of all human specimen material (including fetal material) used under this contract shall be obtained by the Contractor in full compliance with applicable State and Local laws and the provisions of the Uniform Anatomical Gift Act in the United States, and no undue inducements, monetary or otherwise, will be offered to any person to influence their donation of human material.

The Contractor shall provide written documentation that all human materials obtained as a result of research involving human subjects conducted under this contract, by collaborating sites, or by subcontractors identified under this contract, were obtained with prior approval by the Office for Human Research Protections (OHRP) of an Assurance to comply with the requirements of 45 CFR 46 to protect human research subjects. This restriction applies to all collaborating sites without OHRP-approved Assurances, whether domestic or foreign, and compliance must be ensured by the Contractor.
Provision by the Contractor to the Contracting Officer of a properly completed "Protection of Human Subjects Assurance Identification/IRB Certification/Declaration of Exemption", Form OMB No. 0990-0263(formerly Optional Form 310), certifying IRB review and approval of the protocol from which the human materials were obtained constitutes the written documentation required. The human subject certification can be met by submission of a self designated form, provided that it contains the information required by the "Protection of Human Subjects Assurance Identification/IRB Certification/Declaration of Exemption", Form OMB No. 0990-0263(formerly Optional Form 310).

Appendix B

REVIEW OF CONTRACT PROPOSALS INVOLVING HUMAN SUBJECTS (HS)

In this document, the term, ‘contract proposals’ means proposals submitted in response to solicitations for R&D Contract proposals.

Proposals in response to all solicitations involving HS must undergo peer review that includes review of the offeror’s plans and provisions for the protections of HS as specified in the solicitation. Per regulation and policy, if the SRG (TEP) raises concerns in connection with protections of HS, prior to contract award, the CO, working with the offeror, must resolve

these concerns with the review and concurrence of the OEP. Also, the CO, in consultation with OEP, the COR and appropriate personnel of the IC, should communicate in writing to the PD/PI and the AOR, information regarding all suggested restrictions, contingencies, or expressions of concern for the involvement of human subjects. Copies of all relevant documents, or instruction for their access via the internet, should be sent to OEP. If changes resulting from resolution of human subjects concerns were made by OEP, these should be transmitted to the offeror and recorded in the appropriate contract files.

Compliance with this Manual Chapter will entail the following provisions and actions:

1) Contract proposals need to be evaluated for human subjects protections in a manner that is appropriate for the contract, i.e., (a) If a Technical Evaluation Plan for a solicitation includes peer review of proposals, the members of the peer review panel will perform the evaluation of human subjects protections. (b) For all other R&D contracts, officers and employees of the department or agency and such experts and consultants as the department/agency determines to be appropriate will evaluate human subjects protections within the proposals.

2) For every individual contract proposal, the SRO who organizes and oversees the peer review should be informed as to the offeror's pre-review human subjects code. This code may be self-selected by the offeror or assigned by the CO. The following is a list of possible pre-review human subjects codes:

Code 10 – No human subjects involved
Code 20 – Human subjects involved – No exemption designated
Code E1 – Human subjects involved – Exemption category 1
Code E2 – Human subjects involved – Exemption category 2
Code E3 – Human subjects involved – Exemption category 3
Code E4 – Human subjects involved – Exemption category 4
Code E5 – Human subjects involved – Exemption category 5
Code E6 – Human subjects involved – Exemption category 6

The offeror's pre-review human subjects code may be conveyed to the SRO by means of (a) face sheet completed by the offeror according to instructions specified in the solicitation, (b) cover letter from the CO to the SRO, or (c) other agreed-upon method. It is understood that after each contract proposal undergoes peer review, the same or a different human subjects code may be assigned by the TEP. Codes that may be assigned after peer review are as follows:

Code 10 – No human subjects involved as indicated by the TEP
Code 30 – Human subjects involved – Certified, no TEP concerns
Code 44 – Human subjects involved – TEP concerns
Code E1 – Human subjects involved – Exemption category 1
Code E2 – Human subjects involved – Exemption category 2
Code E3 – Human subjects involved – Exemption category 3
Code E4 – Human subjects involved – Exemption category 4

Code E5 – Human subjects involved – Exemption category 5
Code E6 – Human subjects involved – Exemption category 6
Code E7 – Human subjects involved – Multiple exemptions

3) Technical evaluation of HS protections is performed in accordance with 45 CFR 46.120 (http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#46.120) and 42 CFR 52h (http://www.access.gpo.gov/nara/cfr/waisidx_03/42cfr52h_03.html). Review takes into consideration:

- Risks to subjects
- Adequacy of protection against these risks
- Potential benefits of the research to the subjects and others
- Importance of the knowledge gained or to be gained

4) The Technical Evaluation Report (TER) must include discussion of protections for HS in research as well as the appropriateness of any exemption claimed.

5) The discussions of technical merit and discussions of protections are conducted in a manner so that the TEP votes separately on the score of the proposal and on the adequacy of protections for human subjects. The SRO codes each proposal based on the technical evaluation and creates summary of discussion on HS using NIH codes (i.e., HSs not involved: 10, HS involved, no concerns: 30, HS involved, unacceptable protections: 44, or Exemption E1 – E7).

6) A proposal coded 44 cannot be awarded without further review by OEP (end of year procedures may be applied, if needed).

7) OEP receives from the CO or designee excerpts of the TER pertaining to HS concerns for proposals scored within the competitive range.

8) OEP advises the IC's CO as to any HS concerns that must be resolved before an award is made. Through this process and after discussions with the offeror(s), proposed resolution to HS concerns must be approved by OEP.

9) Records of the HS concerns, findings and resolutions are kept at OEP using its security-protected database tools.

10) Contracting Officers shall include language in the solicitation and contract as appropriate to the requirement.

Appendix C

SAMPLE FORMAT FOR A FACE SHEET OF THE TECHNICAL EVALUATION REPORT FOR CONTRACT PROPOSALS THAT INVOLVE HUMAN SUBJECTS

TECHICNAL EVALUATION REPORT FACE SHEET

Review Meeting Date:

Solicitation (Number and Title):

(Use either the paragraph below or the subsequent paragraph as appropriate.)

All of the technically acceptable proposals that involve human subjects include adequate protections for human subjects. None were designated Code 44.

(or)

The following technically acceptable proposals were designated, Code 44, which denotes inadequate protections for human subjects or a human subjects section that was not complete. A Code 44 is a bar to funding. An award cannot be made to an offeror that receives a Code 44 until the concerns on which the Code 44 are based are resolved in cooperation with OEP.

Offeror	PI	Offeror Identifying Number
A		
B		
C		
.		
.		
.		