Research Activities Involving Human Subjects, Human Tissue, Data or Recordings Involving Human Subjects Including Software Testing.

Any application that includes research activities involving human subjects, human tissue/cells, or data or recordings from or about human subjects, must satisfy the requirements of the Common Rule for the Protection of Human Subjects ("Common Rule"), codified for the Department of Commerce at 15 C.F.R. Part 27. Research activities involving human subjects that fall within one or more of the classes of vulnerable subjects found in 45 C.F.R. Part 46, Subparts B, C and D must satisfy the requirements of the applicable subpart(s). In addition, any such application that includes research activities on these subjects must be in compliance with all applicable statutory requirements imposed upon the Department of Health and Human Services (DHHS) and other Federal agencies, all regulations, policies and guidance adopted by DHHS, the Food and Drug Administration (FDA), and other Federal agencies on these topics, and all Executive Orders and Presidential statements of policy on applicable topics. (Regulatory Resources: http://www.hhs.gov/ohrp/humansubjects/index.html which includes links to FDA regulations, but may not include all applicable regulations and policies).

NIST uses the following Common Rule definitions for research and human subjects research:

Research: A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities.

Human Subject: A living individual about whom an investigator (whether professional or student) conducting research: (i) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or (ii) Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.

(1) *Intervention* includes both physical procedures by which information or biospecimens are gathered and manipulations of the subject or the subject's environment that are performed for research purposes.

(2) *Interaction* includes communication or interpersonal contact between investigator and subject.

(3) *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 that 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 associated with the information) in order for obtaining the information to constitute research involving human subjects.

(4) *Identifiable biospecimen* includes a biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimen.

See 15 C.F.R. § 27.102 (Definitions).

1) **Requirement for Federalwide Assurance.** If the application is accepted for [or awarded] funding, organizations that have an Institutional Review Board (IRB) are required to follow the procedures of their organization for approval of exempt and non-exempt research activities that involve human subjects. Both domestic and foreign organizations performing exempt research requiring limited IRB review or non-exempt research activities involving human subjects will be required to have protocols approved by a cognizant, active IRB currently registered with the Office for Human Research Protections (OHRP) within the DHHS that is linked to the engaged organizations. All engaged organizations must possess a currently valid Federalwide Assurance (FWA) on file from OHRP. Information regarding how to apply for an FWA and register an IRB with OHRP can be found at http://www.hhs.gov/ohrp/assurances/index.html. *See* 15 C.F.R. § 27.103. NIST relies only on OHRP-issued FWAs and IRB Registrations for both domestic and foreign organizations for NIST supported research involving human subjects. NIST will not issue its own FWAs or IRB Registrations for domestic or foreign organizations.

2) **Administrative Review.** The NIST Research Protections Office (RPO) reserves the right to conduct an administrative review[1] of all

[1] Conducting an "administrative review" means that the NIST RPO will review and verify the performing institution's determination for research not involving human subjects or exempt human subjects research. In addition, for exempt research requiring limited IRB review and non-exempt human subjects research, the NIST RPO will review and confirm that the research and performing institution(s) are in compliance with 15 C.F.R. Part 27, which means RPO will 1) confirm the engaged institution(s) possess, or are covered under a Federalwide Assurance, 2) review the research study documentation submitted to the IRB and verify the IRB's determination of level of risk and approval of the study for compliance with 15 C.F.R. Part 27, 3) review and verify IRB-approved substantive changes to an approved research study

applications that potentially include research involving human subjects and were approved by an authorized non-NIST institutional entity (an IRB or entity analogous to the NIST RPO) under 15 C.F.R. § 27.112 (Review by Institution). If the NIST RPO determines that an application includes research activities that potentially involve human subjects, the applicant will be required to provide additional information to NIST for review and approval. The documents required for funded proposals are listed in each section below. Most documents will need to be produced during the proposal review process; however, the Grants Officer may allow final versions of certain required documents to be produced at an appropriate designated time post-award. Research involving human subjects may not start until the NIST Grants Officer issues an award explicitly authorizing such research. In addition, all amendments, modifications, or changes to approved research and requests for continuing review and closure will be reviewed by the NIST RPO.

3) **Required documents for proposal review. All applications involving human subjects research must clearly indicate, by separable task, all research activities believed to be exempt or non-exempt research involving human subjects, the expected institution(s) where the research activities involving human subjects may be conducted, and the institution(s) expected to be engaged in the research activities.**

   a. **Not research determination.** If an activity/task involves human subjects as defined in the Common Rule, but the applicant participant(s) indicates to NIST that the activity/task is not research as defined in the Common Rule, the following information may be requested for that activity/task:

      (1) Justification, including the rationale for the determination and such additional documentation as may be deemed necessary by NIST to review and/or support a determination that the activity/task in the application is not research as defined in the Common Rule.
      (2) If the applicant participant(s) used a cognizant IRB that provided a determination that the activity/task is not research, a copy of that determination documentation must be provided to NIST. The applicant participant(s) is not required to establish a relationship with a cognizant IRB if they do not have one.

   NIST will review the information submitted and may coordinate further with the applicant before determining whether the activity/task will be

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before the changes are implemented, and 4) review and verify that the IRB conducts a continuing review at least annually, as appropriate.

defined as research under the Common Rule in the applicable NIST financial assistance program or project.

b. Research not involving human subjects. If an activity/task is determined to be research and involves human subjects, but is determined to be *not human subjects research* (or *research not involving human subjects*) under the Common Rule, the following information may be requested for that activity/task:

(1) Justification, including the rationale for the determination and such additional documentation as may be deemed necessary by NIST to review and/or support a determination that the activity/task in the application is not research as defined in the Common Rule.
(2) If the applicant participant(s) used a cognizant IRB that provided a determination that the activity/task is research not involving human subjects, a copy of that determination documentation must be provided to NIST. The applicant participant(s) is not required to establish a relationship with a cognizant IRB if they do not have one.

c. Exempt research determination with no IRB. If the application appears to NIST to include exempt research activities that do not meet the criteria for requiring a limited IRB review, and the performer of the activity or the supplier and/or the receiver of the information or biospecimens from human subjects **does not** have a cognizant IRB to provide an exemption determination, the following information may be requested during the review process so that NIST can evaluate whether an exemption under the Common Rule applies (*see* 15 C.F.R. § 27.104(b) and (d)):

(1) The name(s) of the institution(s) where the exempt research will be conducted.
(2) The name(s) of the institution(s) providing the biospecimens or information from human subjects.
(3) A copy of the protocol for the research to be conducted; and/or the biospecimens or information from human subjects to be collected/provided, not pre-existing samples (*i.e.,* will proposed research collect only information without personal identifiable information, will biospecimens or information be de-identified and when and by whom was the de-identification performed, how were the materials or data originally collected).
(4) For pre-existing biospecimens or information from human subjects, provide copies of the consent forms used for collection and a description of how the biospecimens or information were

originally collected and stripped of personal identifiers. If copies of consent forms are not available, explain.

(5) Any additional clarifying documentation that NIST may deem necessary in order to make a determination whether the activity/task or use of biospecimens or information from human subjects is exempt under the Common Rule.

d. Research review with an IRB. If the application appears to NIST to include research activities (exempt or non-exempt) involving human subjects, and the proposed performer of the activity has a cognizant IRB registered with OHRP, and linked to their Federalwide Assurance, the following information may be requested during the review process:

(1) The name(s) of the institution(s) where the research will be conducted.
(2) The name(s) and institution(s) of the cognizant IRB(s), and the IRB registration number(s).
(3) The FWA number of the applicant linked to the cognizant IRB(s).
(4) The FWAs associated with all organizations engaged in the planned research activity/task, linked to the cognizant IRB.
(5) If the IRB review(s) is pending, the estimated start date for research involving human subjects.
(6) The IRB approval date (if currently approved for exempt or non-exempt research).
(7) If any of the engaged organizations has applied for or will apply for an FWA or IRB registration, those details should be clearly provided for each engaged organization.

If the application includes research activities involving human subjects to be performed in the first year of an award, additional documentation may be requested by NIST during pre-award review for those performers, and may include the following for those research activities:

(1) A copy of each applicable final IRB-approved protocol.
(2) A signed and dated approval letter from the cognizant IRB(s) that includes the name of the institution housing each applicable IRB, provides the start and end dates for the approval of the research activities, and any IRB-required interim reporting or continuing review requirements.
(3) A copy of any IRB-required application information, such as documentation of approval of special clearances (*i.e.,* biohazard, HIPAA, etc.) conflict-of-interest letters, or special training requirements.

(4) A brief description of which portions of the IRB submitted protocol are specifically included in the application submitted to NIST, if the protocol includes tasks not included in the application, or if the protocol is supported by multiple funding sources. For protocols with multiple funding sources, NIST will not approve the study without a non-duplication-of-funding letter indicating that no other federal funds will be used to support the tasks proposed under the proposed research or ongoing project.
(5) If a new protocol will only be submitted to an IRB if an award from NIST is issued, a draft of the proposed protocol.
(6) Any additional clarifying documentation that NIST may request during the review process to perform the NIST administrative review of research involving human subjects. (*See* 15 C.F.R. § 27.112 (Review by Institution)).

This clause reflects the existing NIST policy and requirements for Research Involving Human Subjects. Should the policy be revised prior to award, a clause reflecting the policy current at time of award may be incorporated into the award.

If the policy is revised after award, a clause reflecting the updated policy may be incorporated into the award.

For more information regarding research projects involving human subjects, contact Anne Andrews, Director, NIST Research Protections Office (e-mail: anne.andrews@nist.gov; phone: (301) 975-5445).

a. Research Activities Involving Live Vertebrate Animals or Pre-Existing Cell Lines/Tissues From Vertebrate Animals. Any application that proposes research activities involving live vertebrate animals that are to be cared for, euthanized, or used by award recipients to accomplish research goals, teaching, or testing must meet the requirements of the Animal Welfare Act (AWA) (7 U.S.C. § 2131 et seq.), and the AWA final rules (9 C.F.R. Parts 1, 2, and 3), and if appropriate, the Good Laboratory Practice for Nonclinical Laboratory Studies (21 C.F.R. Part 58). In addition, such research activities should be in compliance with the *"U.S. Government Principles for Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training"* (Principles). The Principles and guidance on these Principles are available in the National Research Council's "Guide for the Care and Use of Laboratory Animals," which can be obtained from National Academy Press, 500 5th Street, N.W., Department 285, Washington, DC 20055, or as a free PDF online at http://www.nap.edu/catalog/12910/guide-for-the-care-and-use-of-laboratory-animals-eighth.

1) **Administrative Review.** NIST reserves the right to conduct an administrative review[2] of all applications that potentially include research activities that involve live vertebrate animals, or custom samples from, or field studies with live vertebrate animals. If the application includes research activities, field studies, or custom samples involving live vertebrate animals, the applicant will be required to provide additional information for review and approval. In addition, NIST will verify the applicant's determination(s) of excluded samples from vertebrate animals. The documents required for funded proposals are listed in each section below. Some may be requested for a pre-review during the proposal review process; however, the Grants Officer may allow final versions of certain required documents to be produced at an appropriate designated time post-award. If an award is issued, no research activities involving live vertebrate animals shall be initiated or costs incurred for those activities under the award until the NIST Grants Officer issues written approval. In addition, all re-approvals, amendments, modifications, changes, annual reports and closure will be reviewed by NIST.

2) **Required documents for NIST proposal review.** ***The applicant should clearly indicate in the application, by separable task, all research activities believed to include research involving live vertebrate animals and the institution(s) where the research activities involving live vertebrate animals may be conducted. In addition, the applicant should indicate any activity/task that involves an excluded or custom collection from vertebrate animals, or a field study with animals.***

   a) **Excluded Collections from Vertebrate Animals:** The requirements for review and approval by an Institutional Animal Care and Use Committee (IACUC) do not apply to proposed research using preexisting images of animals or to research plans that do not include live animals. These regulations also do not apply to obtaining stock or pre-existing items from animal material suppliers (*e.g.,* tissue banks), such as pre-existing cell lines and tissue samples, or from commercial food processors, where the

[2] Conducting an "administrative review" means that the NIST RPO will review and verify the performing institution's IACUC's approval of research with live vertebrate animals, and confirm that the research and performing institution(s) have an appropriate assurance and are in compliance with applicable regulations. RPO will 1) confirm the engaged institution(s) possess, or are covered under an applicable assurance, 2) review the research study documentation submitted to the IACUC and verify the IACUC's determination of level of risk and approval of the study for compliance with applicable regulations, 3) review and verify IACUC-approved substantive changes to an approved research study before the changes are implemented, and 4) review and verify that the IACUC receives an annual report for the study and conducts an appropriate continuing review at least every three years.

vertebrate animal was euthanized for food purposes and not for the purpose of sample collection.

For pre-existing cell lines and tissue samples originating from vertebrate animals, NIST requires that the proposer provide documentation or the rationale for the determination that the cell line or tissue is pre-existing and not a custom collection from live vertebrate animals for an activity/task within the proposal. NIST may require additional documentation to review and/or support the determination that the cells and/or tissues from vertebrate animals are excluded from IACUC review.

b) **Custom Collections Harvested from Live Vertebrate Animals:** NIST requires documentation for obtaining custom samples from live vertebrate animals from animal material suppliers and other organizations (*i.e.,* universities, companies, and government laboratories, etc.). Custom samples includes samples from animal material suppliers, such as when a catalog item indicates that the researcher is to specify the characteristics of the live vertebrate animal to be used, or how a sample is to be collected from the live vertebrate animal.

c) **Field Studies of Animals:** Some field studies of animals may be exempt under the Animal Welfare Act from full review and approval by an animal care and use committee, as determined by each institution. Field study is defined as "*… a study conducted on free-living wild animals in their natural habitat...".* 9 C.F.R. § 1.1. However, this term excludes any study that involves an invasive procedure or that harms or materially alters the behavior of an animal under study. Field studies, with or without invasive procedures, may also require obtaining appropriate federal or local government permits (marine mammals, endangered species, etc.). If the applicant's institution requires review and approval by an animal care and use committee, NIST will require that documentation to be provided as described below.

d) **For custom collections or studies with live vertebrate animals that require review and approval by an animal care and use committee the following documentation is required:**

(1) **Requirement for Assurance.** An applicable assurance for the care and use of the live vertebrate animal(s) to be used in the proposed research is required. NIST may request documentation to confirm an assurance, if adequate confirmation is not available through an assuring organization's website. The cognizant IACUC where the research activity is located may hold

one or more assurances applicable to the research activity that are acceptable to NIST. These four assurances are:

i. Animal Welfare Assurance from the Office of Laboratory Animal Welfare (OLAW) indicated by the OLAW assurance number, *i.e.,* A-1234;
ii. USDA Animal Welfare Act certification indicated by the certification number, *i.e.,* 12-R-3456;
iii. Association for the Assessment and Accreditation of Laboratory Animal Care (AAALAC) indicated by providing the organization name accredited by AAALAC as listed in the AAALAC Directory of Accredited Organizations; and
iv. Letter of Assurance of compliance with the Animal Welfare Act, the U.S. Government Principles, and National Marine Fisheries Service (NFMS) IACUC policy that is valid for five years and provided by a NMFS Regional IACUC for activities with marine mammals or sea turtles (NMFS Policy Directive 04-112).

(2) **Documentation of Research Review by an IACUC:** If the applicant's application appears to include research activities, field studies, or custom sample collections involving live vertebrate animals the following information regarding review by an applicable IACUC may be requested during the application review process:

1. The name(s) of the institution(s) where the research involving live vertebrate animals will be conducted and/or custom samples collected.
2. The assurance type and number, as applicable, for the cognizant Institutional Animal Care and Use Committee (IACUC) where the research activity is located. [For example: Animal Welfare Assurance from the Office of Laboratory Animal Welfare (OLAW) should be indicated by the OLAW assurance number, i.e. A-1234; an USDA Animal Welfare Act certification should be indicated by the certification number i.e. 12-R-3456; and an Association for the Assessment and Accreditation of Laboratory Animal Care (AAALAC) should be indicated by AAALAC.]
3. The IACUC approval date for the Animal Study Protocol (ASP) (if currently approved).
4. If the review by the cognizant IACUC is pending, the estimated start date for research involving vertebrate animals.
5. If any assurances or IACUCs need to be obtained or established, that should be clearly stated.

6. If any special permits are required for field studies, those details should be clearly provided for each instance, or indicated as pending.

If the application includes research activities involving vertebrate animals to be performed in the first year of an award, additional documentation may be requested by NIST during pre-award review for those performers, and may include the following for those research activities, which may also include field studies, custom sample collections involving live vertebrate animals:

1. A copy of the IACUC approved ASP.
2. Documentation of the IACUC approval indicating the approval and expiration dates of the ASP.
3. If applicable, a non-duplication-of-funding letter if the ASP is funded from several sources.
4. If a new ASP will only be submitted to an IACUC if an award from NIST is issued, a draft of the proposed ASP may be requested.
5. Any additional clarifying documentation that NIST may request during review of applications to perform the NIST administrative review of research involving live vertebrate animals.

This clause reflects the existing NIST policy for Research Involving Live Vertebrate Animals. Should the policy be revised prior to award, a clause reflecting the policy current at time of award may be incorporated into the award.

If the policy is revised after award, a clause reflecting the updated policy may be incorporated into the award.

For more information regarding research projects involving live vertebrate animals, contact Linda Beth Schilling, Senior Analyst (e-mail: linda.schilling@nist.gov; phone: 301-975-2887