U.S. Department of Energy
Washington, DC

ORDER

DOE O 443.1C, Chg. 1

Approved 11-26-2019
Chg.1 (LtdChg): 11-23-2024

SUBJECT: PROTECTION OF HUMAN RESEARCH SUBJECTS

1. PURPOSE. To establish Department of Energy (DOE)-specific policy and principles for the protection of human subjects involved in DOE research, and DOE procedures and responsibilities for implementing the policy and requirements set forth in Title 45 Code of Federal Regulations (CFR) Part 46, *Protection of Human Subjects*, and 10 CFR Part 745, *Protection of Human Subjects*, and the 1997 Presidential Memorandum, "Strengthened Protections for Human Subjects of Classified Research," dated March 27, 1997.

2. CANCELS/SUPERSEDES. This Order cancels DOE Order (O) 443.1C, *Protection of Human Subjects*, dated 11-26-2019.

   Cancellation of a directive does not, by itself, modify or otherwise affect any contractual or regulatory obligation to comply with the Order. Contractor Requirements Documents (CRDs) that have been incorporated into a contract remain in effect throughout the term of the contract unless and until the contract or regulatory commitment is modified to either eliminate requirements that are no longer applicable or substitute a new set of requirements.

3. APPLICABILITY.

   a. Departmental Applicability. Except for exemption in paragraph 3.c., this Order applies to all Departmental elements.

      (1) The Administrator of the National Nuclear Security Administration (NNSA) is responsible for ensuring that NNSA employees, contractors, and elements comply with their respective responsibilities under this directive. Nothing in this Order should be construed to interfere with the NNSA Administrator's authority under Section 3212(d) of Public Law (P.L.) 106-65 to establish Administration-specific policies, unless disapproved by the Secretary.

      (2) In accordance with the responsibilities and authorities assigned by Executive Order (E.O.) 12344, codified at 50 CFR Parts 2406 and 2511, and to ensure consistency throughout the joint Navy/DOE Naval Nuclear Propulsion Program, the Deputy Administrator for Naval Reactors (Director) will implement and oversee requirements and practices pertaining to this Directive for activities under the Director’s cognizance, as deemed appropriate.

b. DOE Contractors. Except for the exemption in paragraph 3.c., the CRD, Attachment 1, sets forth the requirements of this Order that apply to contracts that include the CRD. The CRD must be included in contracts (i.e., those contracts that include the clause at 48 CFR Part Department of Energy Acquisition Regulations (DEAR) 970.5204-2, Laws, Regulations, and DOE Directives) for the management or operation of a DOE-owned or –leased facility that involves human subjects research (HSR) as defined in paragraph 8.r., and comprehensively explained in paragraph 4.a., irrespective of the party conducting the HSR under the contract. For all other contracts that involve HSR, the applicable requirements set forth in this CRD must be included in the contract terms and conditions as appropriate.

c. Exemptions for DOE O 443.1C, Change (Chg.) 1 (LtdChg).

Any requests for partial or full exemptions by Departmental Elements from the requirements of this Order must be submitted in writing to the DOE Human Subjects Protection (HSP) Program Manager (and when an NNSA element is involved, the NNSA HSP Program Manager). An exemption may be recommended to the Secretary by the DOE HSP Program Manager (or by the NNSA HSP Program Manager when an NNSA element is involved) after concurrence by the DOE Institutional Official (IO) (see paragraph 8.8.l). The basis for granting or denying exemption requests must be set forth in writing.

Exemption. Bonneville Power Administration is exempt from the requirements of DOE O 443.1C, Chg. 1.

4. REQUIREMENTS. Research using human subjects provides important medical and scientific benefits to individuals and to society. The need for this research does not, however, outweigh the need to protect individual rights and interests. DOE requirements are established in the Federal Policy for the Protection of Human Subjects (45 CFR Part 46, *Protection of Human Subjects*), in 10 CFR Part 745 (DOE's implementation of Subpart A of 45 CFR Part 46, or the Common Rule), and in this Order.

a. Requirement Criteria.

(1) No HSR conducted with DOE funding, at DOE institutions (regardless of funding source)[1], or by DOE or DOE contractor personnel (regardless of funding source or location conducted), whether done domestically or in an international environment, including classified and proprietary research, may be initiated without both a Federalwide Assurance (FWA) or

[1] HSR conducted by researchers from outside institutions at/using DOE/NNSA user facility capabilities may only be initiated if the researchers have provided documentation of study-specific approval or exemption determination from the IRB/ethics board used by their institution.

If the outside institutions using DOE facility capabilities are not funded by DOE, partnering with any DOE or DOE contractor organizations, or using DOE or DOE contractor employees or employee data, their studies will not be expected to comply with all other requirements in this order unless the DOE/NNSA site responsible for the user facility requires such compliance.

comparable assurance (e.g., Department of Defense assurance) of compliance and approval by the cognizant Institutional Review Board (IRB) in accordance with 10 CFR Part 745.103.

(2) Informed consent will be documented or waived in accordance with 10 CFR Part 745.116-7.

(3) HSR involving multiple DOE sites (e.g., members of the research team from more than one DOE site and/or data or human subjects from more than one DOE site) must be reviewed and approved by one of the Central DOE IRBs prior to initiation, or if authorized by the DOE and/or NNSA HSP Program Manager, other appropriate IRB of record. In all cases, an IRB Authorization Agreement (IAA) or Memorandum of Understanding (MOU) must be in place between the organization(s) conducting the HSR and the organization responsible for IRB review.

(4) HSR that involves targeted inclusion of DOE Federal and/or contractor employees or their data must first be reviewed and approved by the appropriate DOE IRB (the DOE site IRB or one of the Central DOE IRBs), or if deemed more fitting by the Federally assured DOE site or Headquarters, other appropriate IRB of record, in accordance with an IAA or MOU negotiated between the DOE site or Headquarters and the organization responsible for IRB review.

(5) Research that uses social media data and/or other publicly available data about individuals or publicly available biospecimens, even the data or biospecimens appear(s) to be de-identified, must be submitted for HSR/not HSR determination through the appropriate IRB and/or IRB office. *Note: DOE follows the Health Insurance Portability and Accountability Act (HIPAA) and guidance issued by the National Institute of Standards and Technology, as a minimum, in determining identifiability.*

(6) Research that involves the study of humans in a systematically modified environment must be submitted to the appropriate IRB for HSR review and determination.

(7) Classified and unclassified intelligence and intelligence-related HSR, regardless of funding source (including, but not limited to, Strategic Intelligence Partnership Program (SIPP) funded studies, DOE Office of Intelligence and Counterintelligence (DOE-IN) funded studies, and/or studies funded by other DOE program offices that use intelligence datasets), must be reviewed and approved by the Central DOE IRB-Classified.

(8) Final HSR/not-HSR determinations for studies that may constitute HSR, including exempt HSR determinations, must be made through the appropriate IRB and/or IRB office. For sites that use one or both Central

DOE IRB(s) as their IRB(s) of record, the Central DOE IRB office is the responsible office and coordinates with the site HSR leads, as appropriate, to discuss project-specific information and convey study determinations.

(9) In order for a DOE IRB to vote on a new or amended protocol that requires full board review, there must be a minimum of five members present, including a scientist, a nonscientist, and an unaffiliated member.

(10) Personally identifiable information (PII) collected and/or used during HSR projects must be protected in accordance with the requirements of DOE Order 206.1, *Department of Energy Privacy Program*, current version.

(11) If applicable, Federally funded HSR must comply with the requirements of the Paperwork Reduction Act.

(12) If applicable, HSR involving visiting student researchers, researchers, and scholars from other countries as members of research teams must comply with Department of State requirements, e.g., those outlined in 22 CFR Part 62, *Exchange Visitor Program*, and *U.S. Department of State Guidance Directive 2024-01*, current version.

(13) It is Departmental policy that Human Terrain Mapping (HTM), defined in paragraph 8.s., is managed as HSR and is subject to this Order.

(a) HTM projects, conducted with DOE funding, at DOE sites/institutions (regardless of funding source), or by DOE or DOE contractor personnel (regardless of funding source or location conducted), whether done domestically or in an international environment, including classified and proprietary research, must be strictly limited to only those projects involving the analysis and modeling of de-identified data.

(b) Statements of work for HTM projects must be submitted to the HSP Program Manager (and when an NNSA element is involved, the NNSA HSP Program Manager), for DOE Headquarters review and approval prior to initiation. If the project is to be conducted by or for the intelligence community, DOE-IN must also review and approve it prior to initiation. The HSP Program Manager(s) and DOE-IN must engage the recognized DOE site IRB, and as needed, the principal investigator (PI) and/or sponsor, in clarifying whether the proposed project is HTM and if so, that the data to be used will be de-identified. Additionally, the PI will be asked to provide written verification that only de-identified HTM data (as defined in paragraph 8.8.g.) will be used.

(c) The recognized DOE site IRB (or in the case of HSR funded through SIPP or other intelligence-related HSR, the Central DOE IRB-Classified) is the only entity authorized to determine whether

the HTM data received by the PI after project initiation meets DOE criteria for de-identification. If the DOE site does not have a designated site IRB, then the Central DOE IRB(s) must be the responsible IRB.

(d) All projects funded by other entities, including HTM activities, must comply with the applicable DOE O 481.1E, *Strategic Partnership Projects [Formerly Known as Work for Others (Non-Department of Energy Funded Work)]*, current version, or DOE O 484.1, *Reimbursable Work for the Department of Homeland Security,* current version.

(e) In a case where the sponsor requests assistance in the de-identification of HTM data prior to using the data and/or re-identification of the data following completion of the project, DOE sites may provide such services under a separate contract and/or task order with the sponsor by following the appropriate DOE standard operating procedure approved by the DOE IO.[2]

(14) International HSR: Researchers conducting HSR in any other country or on citizens or other individuals residing in that country must be cognizant of country specific HSR requirements and consult the IRB regarding applicability of such requirements.

(15) Classified HSR:

(a) All information related to classified HSR must be managed in accordance with applicable DOE directives and other requirements (E.O.s, laws, regulations), and researchers involved in the conduct of such HSR must have security clearances at the appropriate level to access such information.

(b) HSR that is classified, in whole or in part, must not be initiated without IRB approval, which must be followed by DOE IO approval. The DOE IO, in consultation with the HSP Program Managers, will determine whether he/she will approve/disapprove the project or brief the Secretary about the project prior to his/her approval/disapproval.

[2] It should be noted that: 1) only limited communications, if needed, may take place between the organization de-identifying and/or re-identifying the sponsor's data and the organization performing work on the sponsor's task; 2) the identified dataset shall not be shared with the individual who will perform work on the sponsor's task; and 3) the de-identified dataset shall be sent directly by the sponsor to the individual performing work on the sponsor's task and not by the organization at the DOE site that de-identified it.

(c) Informed consent may only be waived for classified HSR if the work meets one of the categories of the minimal risk HSR addressed at 10 CFR Part 745.104.

(d) The use of the expedited review process is prohibited. The fact that research meets a particular expedited category may be noted, but a full IRB review will be required.

(e) HSR exemptions (as per 10 CFR Part 745.104) will not be used. The fact that research meets a particular exemption category may be noted, but a full IRB review will be required.

(f) The identity of the sponsoring Federal agency must be disclosed to subjects, unless the sponsor requests it not be done. The only acceptable reason for non-disclosure is that disclosure could compromise intelligence sources or methods. Additionally, the research must be no more than minimal risk, and the IRB must determine that not disclosing the identity will not adversely affect the subjects.

(g) The informed consent document will state that the project is classified, what that means for the purposes of that project, and what part of the research that applies to. The IRB must determine whether the potential human subjects need access to classified information to make a valid informed consent decision.

(h) When reviewing classified HSR, the unaffiliated member of a DOE or DOE site IRB must be a non-governmental member (not currently a Federal employee or a DOE site contractor employee) with the appropriate security clearance.

(i) Any IRB member can appeal an IRB decision to approve a project to the DOE IO, and if not resolved to the IRB member's satisfaction, to the Secretary of Energy. If still dissatisfied, the IRB member can appeal that approval decision to the Director of the Office of Science and Technology Policy (OSTP) or that Director's designee, or the Director of National Intelligence (ODNI), or that Director's designee.[3] The Director of OSTP, or that Director's designee, or the ODNI, or that Director's designee will review and approve or disapprove the research, or will convene or designate an IRB that is, to the extent possible, made up of unaffiliated members with the appropriate qualifications and clearance to approve or disapprove the research.

[3] The Presidential Memorandum, *Strengthened Protections for Human Subjects of Classified Research*, dated March 27, 1997, requires such an appeal process.

(j) Information on each HSR project that is classified must be submitted annually, or in accordance with the directions and schedules provided by the appropriate HSP Program Manager. The HSP Program Managers will compile this information and prepare a summary document, for signature by the DOE IO and delivery to OSTP and/or ODNI, in accordance with E.O.s (see Reference 7.g.) and other Federal requirements.

(k) An IRB that believes that an HSR project which is classified, in whole or in part, can be thoroughly reviewed in an unclassified manner, may submit a request for a waiver from some or all of the requirements of this section (specific to classified HSR) for the purpose of that particular study. The study-specific waiver request must be signed by the submitting IRB's Chair(s) and reviewed and approved by the appropriate HSP Program Manager. If the waiver request relates to an intelligence-related project, DOE-IN must also review and approve the waiver. A list of study-specific waiver requests and the actions taken will be provided monthly to the DOE IO.

b. Solicitations. Any solicitation issued by a DOE element for HSR must require compliance with the requirements of this Order, 10 CFR Part 745, and 45 CFR Part 46.

c. Contracts, Financial Assistance Agreements, and Other Agreements. Any DOE contract, financial assistance agreement, or other agreement involving HSR must require compliance with the requirements set forth in this Order and/or the CRD associated with this Order (Attachment 1), as well as with 10 CFR Part 745 and 45 CFR Part 46.

d. Notification. The HSP Program Manager (and when an NNSA element is involved, the NNSA HSP Program Manager) must be notified in writing[4] even if the project meets the regulatory definition of exempt HSR as outlined in 10 CFR Part 745.104:

(1) Prior to initiation of the HSR portion of a new project that involves:

(a) an institution without an established IRB;

(b) a foreign country;

(c) a potential for significant controversy (e.g., negative press or reaction from stakeholder or oversight groups);

[4] The notification requirements listed in paragraphs 4.d.(2), (3) and (4) are in addition to expectations of researchers, who must notify the IRB immediately upon learning of any of the issues identified in the subject paragraphs.

(d) research subjects in a protected class (including the populations identified in Subparts B, C, and D of 45 CFR Part 46), as well as others such as individuals with impaired decision making, or DOE/NNSA Federal or DOE/NNSA contractor employees as human subjects, who may be more vulnerable to coercion and undue influence to participate) that is outside of the reviewing IRB's typical range/scope; or

(e) the generation or use of classified information.

(2) Immediately upon a finding of a suspected or confirmed data breach involving PII in printed or electronic form, and the incident must also be reported to the Integrated Joint Cybersecurity Coordination Center (iJC3) in accordance with the requirements of DOE O 206.1. The appropriate HSP Program Manager must also be notified of any corrective actions taken and consulted regarding the plan for any remaining corrective actions.

(3) Immediately upon learning of a serious adverse event. The appropriate HSP Program Manager must also be informed of any corrective actions taken and consulted regarding the plan for any remaining corrective actions.

(4) Within two business days of learning of the following, with a description of corrective actions taken. The appropriate HSP Program Manager must also be consulted regarding the plan for any remaining corrective actions, following other incidents not covered in (2) and (3) above:

(a) unanticipated problems, significant adverse events, and complaints about the research, as well as suspension or termination of IRB approval of research; and

(b) known or potential incidents of noncompliance with requirements of this Order, 10 CFR Part 745, or 45 CFR Part 46.

(5) Immediately upon the appointment of a new DOE or NNSA site IRB Chair, Co-Chair, or IO.

e. Human Subjects Research Database (HSRD) Reporting. All HSR projects (excluding classified and/or intelligence-related HSR) conducted with DOE funding, by DOE or DOE contractor researchers (regardless of funding source or location), or that involve targeted inclusion of current or former DOE site or contractor employees or their data must be reported annually to the HSRD in accordance with directions and schedules provided by the appropriate HSP Program Manager. Such annual reporting is also required when HSR is minimal risk (including exempt HSR) and when a DOE IRB is not the IRB of record. In cases where a DOE site IRB defers to an external IRB for the review of a study the DOE site is engaged in, the DOE site IRB will still be responsible for ensuring

HSRD reporting requirements are met. In cases where a DOE Headquarters program office funds outside institutions to conduct HSR, the program office will be responsible for ensuring HSRD reporting requirements are met.

f. Records. Project- and meeting-specific record keeping for all DOE/NNSA site and central IRBs must be done via the DOE Headquarters-provided electronic IRB protocol system and must be managed in accordance with National Archives and Records Administration approved records schedules. Additionally, all records related to IRB review/approval of classified HSR and key research records must be maintained permanently. During and following the completion of the research, copies of all signed classified consent forms must be stored in a separate but secure central location (e.g., security policy officer or IRB office), other than the researchers' office, and participants of such research must be notified during the consenting process regarding how to access a copy of their individual signed classified consent forms should they want to in the future.

g. Protected Classes. Research involving the vulnerable populations identified in Subparts B, C, and D of 45 CFR Part 46 must be conducted in accordance with those Subpart(s). Appropriate protections should be afforded to subjects who are vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons. Care must also be taken to ensure the proper protections are in place for DOE/NNSA Federal and/or contractor employees who become human subjects of research and may be subject to coercion or undue influence. An employee cannot be recruited or consented by a direct supervisor who is the PI and/or a member of the research team, except in unusual circumstances approved by the IRB.

h. IRB Registration. Each IRB that is designated by an institution under an assurance of compliance approved for Federal wide use by the Office for Human Research Protections (OHRP) under 45 CFR Part §46.103(a) and that reviews research involving human subjects conducted or supported by the Department of Health and Human Services (DHHS) must be registered with HHS in accordance with 45 CFR Part 46 Subpart E.

i. Training. Researchers who submit studies to the DOE central and DOE site IRBs and members of these IRBs must complete initial and periodic refresher training in human subjects' protection. Researchers who submit studies to the central DOE IRBs and members of the central DOE IRBs must additionally complete DOE-specific training that includes a module on recognizing and addressing bias in the design, review, and conduct of HSR.

j. Payment. Equitable payment of human subjects participating in HSR is allowable.

5. RESPONSIBILITIES.

All DOE employees, contractors, financial assistance recipients, and parties to other DOE agreements share the responsibility to protect the rights and welfare of human research subjects.

a. The Secretary of Energy.

(1) Responsible for oversight of DOE-supported and conducted HSR. Delegates this responsibility to a Senior DOE IO for HSR. For DOE, the IO is the Associate Director of Science, Office of Biological and Environmental Research (BER), or their designee at the Senior Executive Service (SES) level from BER.

(2) Approves, or defers to the DOE IO to approve, requests for partial or full exemptions from the requirements of this Order, when deemed appropriate by the DOE IO and the DOE HSP Program Manager (or the NNSA HSP Program Manager when an NNSA element is involved).

(3) If elevated to the Secretary of Energy, reviews and adjudicates IRB member appeals of IRB approval determinations for classified projects.

b. Under Secretary for Science and Innovation.

(1) Monitors compliance with this Order, 10 CFR Part 745, and 45 CFR Part 46, within DOE in accordance with policy established by the Secretary and in consultation with NNSA, as appropriate.

(2) Designates the DOE IO. For DOE, the IO is the Associate Director of Science for BER or their designee at the SES level from BER.

(3) Designates the DOE HSP Program Manager. For DOE, the HSP Program Manager resides within SC's BER.

(4) Delegates review and approval of statements of work for HTM projects submitted by DOE's non-NNSA sites to the DOE HSP Program Manager.

c. Under Secretary for Nuclear Security and Administrator of the National Nuclear Security Administration.

(1) Designates the NNSA HSP Program Manager and delegates review and approval of statements of work for HTM projects submitted by DOE's NNSA sites to the NNSA HSP Program Manager. The NNSA HSP Program Manager resides within the Office of Policy and Strategic Planning.

(2) In consultation with the Under Secretary for Science and Innovation, monitors compliance with this Order.

d. The DOE Institutional Official (IO).

(1) Resides within SC and serves both as the Associate Director of Science for BER and the Senior DOE Official responsible for overseeing and monitoring DOE-supported and conducted HSR (or for designating an SES-level manager from BER to do so). Specifically, the DOE IO oversees the Departmental implementation of the requirements of this Order, 10 CFR Part 745, 45 CFR Part 46, and related E.O.s, Presidential Memoranda, and other Presidential directives and international requirements, as applicable, in consultation with the NNSA, as appropriate.

(2) Reports to the Secretary of Energy for purposes of this function and determines what constitutes Departmental HSR, in consultation with the NNSA.

(3) Allocates resources for the DOE Human Subjects Protection Program (HSPP) and ensures that policies are in place that support research review processes that are independent and free of coercion or undue influence.

(4) Establishes a process to receive and act on complaints and allegations regarding the HSPP.

(5) Oversees the Central DOE IRBs and formally appoints all members of the Central IRBs.

(6) Approves classified research to be conducted at DOE sites/laboratories after IRB approval and prior to initiation.

(7) Reviews and adjudicates IRB member appeals of IRB approval determinations for classified projects.

(8) Must concur on all requests from Departmental Elements for partial or full exemptions from the requirements of this Order, in order for such requests to be considered for approval.

(9) Approves and rescinds authorization agreements with other DOE and outside organizations for IRB review.

e. DOE HSP Program Manager.

(1) Resides within DOE SC's BER and reports to the DOE IO.

(2) Develops procedures for the HSP program in consultation with the NNSA HSP Program Manager, as appropriate.

(3) Prepares and updates guidance to be followed for obtaining approval for HSR in consultation with the NNSA HSP Program Manager, as appropriate.

(4) Reviews and coordinates with DOE site Offices and site IRBs regarding plans to correct any noncompliance or to mitigate adverse study events, ensuring they comply with applicable HSP requirements.

(5) Reviews and approves statements of work for HTM projects submitted by DOE's non-NNSA sites. Ensures compliance with DOE requirements [see paragraph 4.a.(12)], and, for HTM projects that are Strategic Partnership Projects (SPPs) and SIPP projects, coordinates with appropriate Headquarters SPP/SIPP leads prior to approving such statements of work for initiation. Ensures site Offices and M&O contractors are aware of decisions concerning proposed HTM work.

(6) Provides advice and guidance on evolving Departmental and national bioethics and regulatory issues regarding human research subject protection and helps identify and resolve program/project concerns in consultation with the NNSA HSP Program Manager, as appropriate.

(7) Develops and conducts educational programs on bioethics and human research subjects' protection requirements, practices, and procedures relevant to DOE employees, DOE contractor personnel, financial assistance recipients, and the public in consultation with the NNSA HSP Program Manager, as appropriate.

(8) Regularly (at least every three years, or every two years for sites that perform classified HSR), conducts institutional performance reviews, or quality assurance (QA) consultations, to assess compliance with human research subject protection requirements, in consultation with the NNSA HSP Program Manager, as appropriate.

(9) Serves as the Chair of the DOE Human Subjects Working Group and as official DOE representative to groups with bioethics and HSP interests. The NNSA HSP Program Manager shall be invited to attend all such meetings and to co-chair meetings, as appropriate.

(10) Reviews and, in coordination with the NNSA HSP Program Manager and DOE-IN, approves requests for waivers, on a project by project basis, from the requirements for classified research (Section 4.a.(14)), if the reviewing IRB determines that a project that is classified, in whole or in part, can be reviewed in an unclassified manner.

(11) Makes recommendations to the Secretary, after concurrence from, and through the IO, regarding requests for exemptions from any other requirements of this Order and satisfies the advance notice and publication requirements of 10 CFR Part 745.101(i) prior to the granting of any

exemption (in consultation with the NNSA HSP Program Manager, as appropriate).

(12) Concurs on HSP provisions in interagency agreements, in consultation with the NNSA HSP Program Manager, as appropriate.

(13) Maintains the HSRD, the list of unclassified intelligence-related HSR projects, and the unclassified list of classified HSR projects for DOE.

(14) Serves as one of the Co-Chairs of the Central DOE IRB-C.

f. NNSA HSP Program Manager.

(1) Resides within NA-1.1, the Office of Policy and Strategic Planning and reports functionally to the DOE IO.

(2) When an NNSA element or project is involved, the responsibilities of the NNSA HSP Program Manager are identical to those of the DOE HSP Program Manager.

(3) Ensures compliance with the DOE/NNSA requirements.

(4) Works with the DOE HSP Program Manager, as outlined in Section 5.e.

(5) Serves as one of the Co-Chairs of the Central DOE IRB-C.

g. DOE Office of Intelligence and Counterintelligence (DOE-IN).

(1) Reviews and approves, prior to initiation, statements of work for HSR and HTM projects received from members of the intelligence community.

(2) Collaborates with the DOE IO, and with the DOE and NNSA HSP Program Managers, in overseeing the Central DOE IRB-Classified, and provides the Vice Chair and the Administrator for this IRB.

(3) Reviews and, in coordination with the DOE and NNSA HSP Program Managers, approves requests for waivers, on a project-by-project basis, from the additional requirements for classified research (Section 4.a.(14)), if the Central DOE IRB-Classified determines that an intelligence-related HSR project that is classified, in whole or in part, can be reviewed in an unclassified manner.

h. Secretarial Officers or their Designees.

(1) Ensure that all proposals for research, studies, tests, surveys, surveillance, or other data collection are reviewed to identify research involving human subjects.

(2) Ensure that any questions or uncertainties regarding the applicability of human research subjects protection requirements to such proposals, and any other issues and concerns regarding the requirements of this Order, are promptly referred to the appropriate HSP Program Manager for resolution.

(3) Ensure that the contracting officer is advised when work statements for proposed agreements include HSR to ensure that the CRD or its requirements (as appropriate) will be applied to HSR conducted with DOE/NNSA funding, at DOE/NNSA institutions, or by DOE/NNSA personnel under agreements other than site/facility management contracts, such as support services contracts, grants, cooperative agreements, SPP/SIPP agreements, and interagency agreements.

(4) Ensure that the contracting officer, after being notified of the affected contracts, incorporates the CRD into the affected contracts by way of the DEAR Laws, regulations, and directives clauses included in those contracts. In the case of contracts or other agreements requiring contractor performance of activities covered by the CRD, but which do not contain the Laws, regulations, and DOE directives clause, the contracting officer will work to include the requirements as appropriate.

(5) Ensure their staffs and field elements comply with the requirements of this Order, including the notification requirements in paragraph 4.d.

(6) Ensure relevant personnel actively participate in human research subjects' protection training and educational programs.

(7) Ensure that routine informal reviews are conducted to verify compliance with the requirements of this Order. Support, as needed, HSP Program Managers' triennial (or biennial for sites that perform classified HSR) QA consultations.

(8) At their discretion, conduct further review and approve or disapprove research that has been approved by the IRB. (Note: Secretarial Officers or their designees may not approve HSR that has not been approved by an IRB. See 10 CFR Part 745.112.)

(9) Ensure appropriate oversight of the administration of research subjects protection programs of contractors and financial assistance recipients under their cognizance, and other parties to DOE agreements, to ensure compliance with applicable human research subjects protection requirements, including HSRD reporting.

(10) Ensure that the DOE HSP Program Manager and the NNSA HSP Program Manager are involved in negotiating those portions of interagency agreements that address HSR.

(11) Appoint a point of contact for interacting with the appropriate HSP Program Manager on program-related and/or Department-wide issues.

i. DOE Field/Site Offices.

(1) Ensure contracts and other agreements involving HSR require compliance with the requirements set forth in the CRD associated with this Order (Attachment 1), 10 CFR Part 745, and 45 CFR Part 46 (all subparts).

(2) Ensure that contractors establish and maintain a process for:

(a) Identifying, reporting, and managing HTM work in accordance with the requirements in the CRD (Attachment 1, paragraph 10) associated with this Order.

(b) Managing classified HSR in accordance with the requirements in the CRD (Attachment 1, paragraph 11) associated with this Order.

(c) Maintaining records in accordance with the requirements in the CRD (Attachment 1, paragraph 21) associated with this Order.

(d) Notifying the HSP Program Manager(s) as required in paragraph 1 of the CRD associated with this Order.

(e) Ensuring that HSR involving targeted inclusion of site Federal and/or contractor employees or their data is reviewed by the appropriate DOE IRB (the DOE site IRB or one of the Central IRBs) or, if deemed more fitting by the Federally assured DOE site or Headquarters, other appropriate IRB of record, in accordance with an IAA or MOU negotiated between the DOE site or Headquarters and the organization responsible for IRB review.

(f) Ensuring that classified and unclassified intelligence and intelligence-related HSR, regardless of funding source (including, but not limited to, SIPP-funded studies, DOE-IN-funded studies and/or studies funded by other DOE program offices that use intelligence datasets) is reviewed by the Central DOE IRB-Classified.

(g) Sending HSR involving multiple DOE sites (members of the research team from more than one DOE site and/or human subjects from more than one DOE site) to the appropriate Central DOE IRB for review and approval prior to initiation, or, if authorized by the DOE and/or NNSA HSP Program Manager, other appropriate IRB of record. In all cases, an IAA or MOU must be in place between the organization(s) conducting the HSR and the organization responsible for IRB review.

(h) Training relevant personnel in HSP requirements.

(i) Conducting routine informal internal reviews of the HSP Program or portions of the Program.

(3) Attend the triennial (or biennial for sites that perform classified HSR) Headquarters-led QA consultations.

6. INVOKED TECHNICAL STANDARDS. This Order does not invoke any DOE technical standards or industry standards as required methods. Note: DOE O 251.1D Chg 1 (or current version), Appendix J provides a definition for "invoked technical standard."

7. REFERENCES.

a. 10 CFR Part 600, *Financial Assistance Rules*, which provides the policies and procedures for administration and management of all DOE financial assistance activities.

b. 10 CFR Part 602, *Epidemiology and Other Health Studies Financial Assistance Program*, which sets forth the policies and procedures applicable to the award and administration of financial assistance agreements and cooperative agreements for health-related research, education/training, conferences, communication, and related activities.

c. 10 CFR Part 605, *Office of Science (formerly Office of Energy Research) Financial Assistance Program*, as explained at eCFR :: 10 CFR Part 605 -- The Office of Science Financial Assistance Program, which provides policies and procedures for the administration and management of basic and applied research financial award agreements awarded by SC.

d. 10 CFR Part 745, *Protection of Human Subjects*, which set Federal requirements for DOE for the protection of human subjects involved in research activities.

e. 10 CFR Part 1008, *Records Maintained on Individuals (Privacy Act*), which establishes the procedures to implement the Privacy Act of 1974 (PL. 93-579, 5 U.S.C. 552a) within DOE.

f. 45 CFR Part 46, *Protection of Human Subjects, Subparts B, C, and D*, which sets out DOE prescribed DHHS requirements for protected classes of human research subjects and Subpart E for IRB registration.

g. *The Belmont Report*, dated April 18, 1979, and written by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, identifies the three basic ethical principles (respect for persons, beneficence, and justice) and guidelines for the conduct of research with human subjects. The Belmont Report is the foundational report upon which the current U.S. regulations for the protection of human research subjects are based.

h. *Presidential Memorandum, Strengthened Protections for Human Subjects of Classified Research*, dated March 27, 1997, and published in the Federal Register on May 13, 1997 (62 Fed. Reg. 26369).

i. *The Freedom of Information Act*, 5 USC Section 552, as amended, which establishes the right of citizens to request information from Federal agencies and establishes a framework of procedures to implement this right.

j. The *National Nuclear Security Administration Act*, Title 32 of the National Defense Authorization Act for Fiscal Year 2000, Public Law No. 106-65; 50 USC 2401 et seq.

k. *European Union (EU) General Data Protection Regulation (GDPR)*, dated 04-14-2016. The GDPR not only applies to organizations located within the EU but also may apply to organizations located outside of the EU if they offer goods or services to, or monitor the behavior of, EU data subjects. It may apply to U.S. organizations processing and holding the personal data of data subjects residing in the EU, regardless of the company's location.

l. *21st Century Cures Act*, dated December 13, 2016, expands researchers' ability to obtain a Certificate of Confidentiality by making the issuance of a Certificate of Confidentiality mandatory for investigators engaged in Federally funded research involving certain sensitive, identifiable information about research subjects.

m. *DOE Policy Memorandum on Research Involving Intentional Modification of the Human Environment*, dated 4-25-13.

n. DOE O 206.1, *Department of Energy Privacy Program*, current version, which ensures compliance with privacy requirements;-establishes a Departmental training and awareness program for all DOE Federal and contractor employees to ensure personnel are cognizant of their responsibilities for safeguarding PII and complying with the Privacy Act; and provides Departmental oversight to ensure compliance.

o. DOE P 481.1, *DOE's Policy Regarding Laboratories, Plants, and Sites Engaging in Strategic Partnership Projects with Other Federal Agencies, Independent Organizations, and the Private Sector*, current version, which sets the context in which DOE and its laboratories, plants, and sites should pursue SPPs with other Federal government agencies, state and local institutions, universities, foreign entities and/or private companies. The Policy is applicable to the DOE laboratories, plants, and sites, and to the DOE programs that own them and facilitate their work.

p. DOE O 481.1E, *Strategic Partnership Projects [Formerly Known as Work for Others (Non-Department of Energy Funded Work)]*, current version, which establishes the policy, requirements, responsibilities, and procedures for authorizing, administering, and performing work for non-DOE entities by

DOE/NNSA and/or their respective contractor personnel or the use of DOE/NNSA facilities that is not directly funded by DOE appropriations.

q. DOE O 483.1B, *DOE Cooperative Research and Development Agreements*, current version, which establishes requirements for the performance of technology transfer through the use of Cooperative Research and Development Agreements.

r. DOE O 484.1, *Reimbursable Work for the Department of Homeland Security*, current version, establishes DOE policies and procedures for the acceptance, performance, and administration of reimbursable work directly funded by the Department of Homeland Security.

s. DOE O 475.2B, *Identifying Classified Information*, current version, establishes the program to identify information classified under the Atomic Energy Act [Restricted Data, Formerly Restricted Data, and Transclassified Foreign Nuclear Information] or E.O. 13526 [National Security Information], so that it can be protected against unauthorized dissemination in accordance with legal and Departmental requirements.

t. DOE O 471.7, *Controlled Unclassified Information*, current version, establishes the Department of Energy's (DOE) Controlled Unclassified Information (CUI) Program and documents a policy for designating and handling information that qualifies as CUI. The CUI Program standardizes the way DOE handles information that requires protection under laws, regulations, or Government-wide policies, but that does not qualify as classified under Executive Order (EO) 13526, Classified National Security Information, 12-29-2009 (3 CFR, 2010 Comp., p. 298-327), or any predecessor or successor order, or the Atomic Energy Act of 1954 (42 U.S.C. 2011, et seq.), as amended. This Directive implements the requirements in EO 13556, Controlled Unclassified Information, and 32 CFR part 2002, Controlled Unclassified Information.

u. 22 CFR Part 62, *Exchange Visitor Program*, current version, which addresses certain exclusions when the U.S. is hosting student researchers, researchers, and scholars, from other countries. U.S. Department of State Guidance Directive 2024-01*, current version, College and University Student, Professor, Research Scholar, Short -Term Scholar, and Specialist*: *Permissible contact with human participants and/or animal subjects in academic training, research, classroom-based, teaching, laboratory work, and other supervised learning environments.*

v. NIST SP 800-188, *De-identifying Government Datasets: Techniques and Governance.*

8. DEFINITIONS.

a. Adverse Event. Any unfavorable medical occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject's participation in the research, whether or not considered related to the subject's

participation in the research (Unanticipated Problems Involving Risk and Adverse Events Guidance, OHRP, 2007).

A significant adverse event is an adverse event that is unexpected and substantively impacts the human subjects.

A serious adverse event (Unanticipated Problems Involving Risk Adverse Events Guidance, OHRP, 2007) is any adverse event temporally associated with the subject's participation in research that meets any of the following criteria:

(1) results in death;

(2) is life-threatening;

(3) requires inpatient hospitalization or prolongation of existing hospitalization;

(4) results in a persistent or significant disability/incapacity;

(5) results in a congenital anomaly/birth defect; or

(6) based upon appropriate medical judgment, may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition.

b. Appropriate HSP Program Manager. The DOE HSP Program Manager (and when an NNSA element is involved, the NNSA HSP Program Manager).

c. Assurance. The written documentation, satisfactory to the Secretary of Energy, required from the prospective performing institution, that ensures institutional compliance with and implementation of DOE and DHHS regulations for the protection of human research subjects. The only documentation currently meeting this requirement is an FWA. See: http://ohrp.cit.nih.gov/efile/FwaStart.aspx. Also see definition of FWA in this section.

d. Certificate of Confidentiality. Authorizes persons engaged in Federally funded biomedical, behavioral, or clinical research to protect information, documents, and/or biospecimens that contain identifiable, sensitive information related to participants against compulsory disclosure in any Federal, State, or local judicial, administrative, or legislative proceeding.

e. Classified Human Subjects Research. Research involving human subjects that is classified, in whole or in part, in accordance with the Federal sponsor and/or DOE criteria.

f. Clinical trial. Research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo

or other control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes.

g. De-identified Data. Records that have had enough personally identifiable data removed or obscured such that the remaining information does not identify an individual and there is no reasonable basis to believe that the information can be used to identify an individual.

h. Direct Supervisor(s). The technical and/or administrative individual(s) or line management who direct(s) an individual's work and/or are responsible for performance evaluation of that individual.

i. DOE Human Subjects Research Projects Database (HSRD). An unclassified compilation of summary information, which is available on the DOE HSP website and updated annually, on HSR projects funded by DOE, conducted at DOE institutions or facilities, or performed with DOE or contractor personnel.

j. DOE IRB. One of the DOE (or NNSA) site IRBs or Central DOE IRBs.

k. DOE IRB Office. The team that administers the IRB. Within the DOE/NNSA complex, the IRB office typically includes the IRB chair, vice chair, administrator, and any IRB staff. For sites that use one or both Central DOE IRB(s) as the IRB of record, the Central DOE IRB office is the responsible IRB office and coordinates with the site HSR leads, as appropriate, to discuss project-specific information and convey study determinations.

l. DOE Institutional Official (IO). The Senior DOE Official responsible for overseeing and monitoring Departmental implementation of the requirements of 45 CFR Part 46, 10 CFR 745, Protection of Human Subjects, and this Order, in consultation with NNSA, as appropriate.

m. Exemption from the Requirements of DOE Order 443.1C, Chg.1. A request for partial or full exemption from the requirements outlined in this Order (see Section 3.c.). Must be submitted to the DOE HSP Program Manager, or when an NNSA element is involved, the NNSA HSP Program Manager. Requires DOE IO concurrence and Secretarial or Secretarial designee (DOE IO) approval.

n. Exempt Human Subjects Research (HSR). HSR in which the only involvement of human subjects will be in one or more of the categories outlined in 10 CFR Part 745.104. Within DOE, the initial exemption determination is made through the appropriate central DOE or DOE site IRB or IRB office. Note that exempt HSR is a category of HSR and has nothing to do with a request for an exemption from the requirements of this Order (as described in definition l. above).

o. Federalwide Assurance (FWA). The written documentation, satisfactory to the Secretary of Energy, required from the prospective performing institution, that ensures institutional compliance with and implementation of DOE and DHHS

regulations for the protection of human research subjects. See: http://ohrp.cit.nih.gov/efile/FwaStart.aspx.

p. Generalizable. Information/research findings that are intended to be applied to populations or situations beyond that studied/will have meaning and impact outside of the single immediate activity itself.

q. Human Subject. A living individual about whom an investigator (whether professional or student) conducting research:

(1) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or

(2) Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.

Intervention includes both physical procedures by which information or biospecimens 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 that 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).

Identifiable private information is private information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information.

An *identifiable biospecimen* is a biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimen.

r. Human Subjects Research (HSR). Any activity meeting the definitions of both: 1) research, and 2) human subject, as defined in this section.

s. Human Terrain Mapping (HTM). Research and data gathering activities primarily conducted for military or intelligence purposes to understand the "human terrain,"—the social, ethnographic, cultural, and political elements of the people among whom the U.S. Armed Forces are operating and/or in countries prone to political instability. This work includes observations, questionnaires, and interviews of groups of individuals, as well as modeling and analysis of collected data, and may become the basis for U.S. military actions in such locations. In

addition to HTM, such activities are often referred to as human social culture behavior studies. It is DOE policy that HTM activities will be managed as HSR.

t. HTM Data. Data collected or used as part of HTM efforts, as described above, as well as any auxiliary data on the same group(s) of individuals.

u. Immediate Reporting. Reporting as soon as feasible upon learning of an event. Sequential reporting may be needed in certain cases, e.g., loss/breach of PII should be reported to the iJC3 first, and then to the IRB. In all cases it is expected that required reporting would be completed within a few hours of the PI learning of an HSR-related event.

v. Institution. Any public or private entity or agency (including Federal, State, and other agencies). This term refers to laboratories and other facilities managed by DOE, DOE contractors, or DOE financial assistance recipients.

w. Institutional Review Board (IRB). A committee or board established by an institution that performs initial and continuing reviews of research involving human subjects and is registered with the OHRP and designated on an FWA.

x. Minimal Risk. 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.

y. Modification of the Human Environment. Research:

(1) in which people have their environment intentionally changed or manipulated for the purposes of the research, with or without their knowledge; and/or

(2) that cannot be validly conducted without people present (other than those conducting the research), regardless of whether identifiable private information is collected about them. Before such research begins, the potential risks to those individuals must be considered by the appropriate DOE IRB.

z. NNSA Human Subjects Protection Designee (NNSA HSP Program Manager). The program manager responsible for overseeing the HSPP for NNSA elements.

aa. Personally Identifiable Information. Any information collected or maintained about an individual, including but not limited to, education, financial transactions, medical history, criminal or employment history, and information that can be used to distinguish or trace an individual's identity, such as his/her name, Social Security number, date and place of birth, mother's maiden name, biometric data, and any other personal information that is linked or linkable to a specific individual.

bb. Protected Class of Human Subjects. Populations who may be more vulnerable to coercion or undue influence when participating as research subjects, such as children, prisoners, individuals with impaired decision-making capacity, economically or educationally disadvantaged persons, and other vulnerable populations, who are thus afforded additional protections by the Federal regulations (see additional subparts of 45 CFR Part 46) and/or the IRB. DOE and DOE site employees are considered vulnerable subjects when participating in research and additional care must be taken to ensure their participation is truly voluntary (e.g., by ensuring they do not report to members of the research team) and that data collected about them is kept confidential.

cc. Research. A systematic investigation, including research development, testing and evaluation, designed to contribute to generalizable knowledge. Activities which meet this definition constitute research for purposes of this policy, 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. For purposes of this part, the following activities are deemed not to be research:

(1) Scholarly or journalistic activities (e.g., oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information, that focus directly on the specific individuals about whom the information is collected.

(2) Public health surveillance activities, including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority. Such activities are limited to those necessary to allow a public health authority to identify, monitory, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance (including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products). Such activities include those associated with providing timely situational awareness and priority setting during an event or crisis that threatens public health (including natural or man-made disasters).

(3) Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes.

(4) Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions.

dd. Strategic Intelligence Partnership Program (SIPP). SIPP, formerly the Intelligence Work for Others program, is the mechanism by which DOE provides highly-specialized scientific and technical services and products to

non-DOE Intelligence Community (IC) and other agencies for intelligence and intelligence-related activities carried out under unique IC authorities held by DOE-IN and sponsoring IC agencies.

ee. Strategic Partnership Projects (SPPs). SPP, formerly the Work for Others (WFO) program, is the mechanism by which non-DOE entities fund DOE/NNSA and/or their contractors or use DOE/NNSA facilities for work that is not directly funded by DOE/NNSA appropriations.

ff. Unaffiliated IRB Member. For review of unclassified protocols, must not have a direct affiliation (employee, contractor, student in a fellowship, volunteer at the institution, or business related to the IRB, and must not have an immediate family member who is affiliated with the institution). For review of classified protocols, must be a nongovernmental member (not currently a Federal employee or a DOE site contractor employee) with the appropriate security clearance.

gg. Unanticipated Problem. In general, to be classified as an unanticipated problem, any incident, experience, or outcome should meet **all three** of the following criteria:

(1) Unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied.

(2) Related or possibly related to participation in the research (*possibly related* means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research).

(3) Likely to place subjects or others at greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

hh. Waiver from the Additional Requirements for Classified HSR. In certain cases, when classified projects can be fully reviewed in an unclassified form (e.g., because the protocol and consent form are unclassified), the IRB may submit, for consideration by the appropriate HSP Program Manager (and for intelligence-related HSR, also in consultation with DOE-IN), a request for a project-specific waiver from some or all of the additional requirements for classified HSR specified in Section 4.a.(14) of this Order. Such a waiver might be approved, for example, if only the sponsor or the ultimate use of a particular technology were classified, but everything else about the study were not. Note that even if a waiver from the additional requirements of classified HSR is

approved for a particular project, all other Federal and DOE-specific HSR requirements must still be met.

9. CONTACT. Questions regarding this Order should be addressed to the DOE Program Manager, HSP Program, SC, BER, telephone (301) 903-3213; or the DOE NNSA HSP Program Manager, as appropriate. Information about the DOE HSP program may be found at https://science.osti.gov/ber/human-subjects.

BY ORDER OF THE SECRETARY OF ENERGY:

DAVID M. TURK
Deputy Secretary

ATTACHMENT I
CONTRACTOR REQUIREMENTS DOCUMENT
DOE O 443.1C, CHG.1*, PROTECTION OF HUMAN RESEARCH SUBJECTS*

Regardless of the performer of the work, the contractor is responsible for compliance with the requirements of this Contractor Requirements Document (CRD).

The contractor is responsible for flowing down the requirements of this CRD to subcontracts at any tier to the extent necessary to ensure the contractor's compliance with the requirements.

Note: Throughout this CRD, the term "Human Subjects Protection Program Manager (HSP Program Manager)" refers either to the Department of Energy (DOE) HSP Program Manager or to the National Nuclear Security Administration (NNSA) HSP Program Manager except where otherwise noted.

As directed by the contracting officer, the contractor must—

1. Notify the DOE HSP Program Manager (and, when an NNSA element is involved, the NNSA HSP Program Manager)[1], even for human subject research (HSR) that meets the regulatory definition of exempt HSR as outlined in 10 Code of Federal Regulations (CFR) Part 745.104:

    a. Prior to initiation of any new HSR involving:

        (1) an institution without an established Institutional Review Board (IRB);

        (2) a foreign country;

        (3) the potential for significant controversy (e.g., negative press or reaction from stakeholder or oversight groups);

        (4) research subjects in a protected class (including the populations identified in Subparts B, C, and D of 45 CFR Part 46), as well as others such as individuals with impaired decision making capability and DOE/NNSA Federal or DOE/NNSA contractor employees as human subjects, who may be more vulnerable to coercion and undue influence to participate, that is outside of the reviewing IRB’s typical range/scope; or

        (5) generation or use of classified information.

    b. Immediately upon finding of a suspected or confirmed data breach involving Personally Identifiable Information (PII) in printed or electronic form, and additionally immediately notify the Integrated Joint Cybersecurity Coordination Center (iJC3), in accordance with the requirements of the CRD associated with

[1] Note: The notification requirements listed in paragraphs 1.b.(1)-(3), 1.c., and 1.d. are in addition to expectations for researchers, who must notify the IRB of record immediately upon learning of any of the issues identified in the subject paragraphs.

DOE O 206.1. The HSP Program Manager(s) shall also be notified of any corrective actions taken and consulted regarding the plan for any remaining corrective actions.

c. Immediately upon learning of a serious adverse event. The HSP Program Manager(s) shall also be informed of any corrective actions taken and consulted regarding the plan for any remaining corrective actions.

d. Within two business days of learning of the following, and provide a description of corrective actions taken immediately following the incident and consult with the HSP Program Manager(s) regarding additional corrective actions to be taken in the case of:

(1) any significant adverse events, unanticipated problems, and complaints about the research;

(2) any suspension or termination of IRB approval of research; and/or

(3) any known or potential noncompliance with the requirements of this Order, 10 CFR Part 745, or 45 CFR Part 46.

e. Upon appointment of a new DOE or NNSA site IRB Chair, Co-Chair, or Institutional Official (IO).

2. Ensure that research involving human subjects, regardless of source of funding, is conducted in accordance with the principles outlined in the Belmont Report and all applicable Federal, DOE-specific, sponsor-specific, and other applicable requirements, including relevant international requirements. (See also 10 CFR Part 745 and 45 CFR Part 46.)[2]

3. Ensure that contractor-issued solicitations or proposals for research, studies, tests, surveys, surveillance, or other data collection are reviewed to identify research involving human subjects and that any resulting agreements include the substance of the requirements in this CRD.

4. Ensure that no research involving human subjects, regardless of funding source, is initiated without prior IRB approval under the terms of an approved assurance covering the research.

[2] Ensure that research is reviewed by the IRB at intervals appropriate to the degree of risk and in accordance with DOE requirements, but not less than once per year for greater than minimal risk studies initiated under the 2018 Common Rule.

5. Ensure that final HSR/not HSR determinations for studies that may constitute HSR, including exempt HSR determinations, are made through the appropriate IRB and/or IRB office. For sites that use one or both Central DOE IRB(s) as their IRB(s) of record, the Central DOE IRB office is the responsible office and coordinates with the site HSR leads, as appropriate, to discuss project-specific information and convey study determinations.

6. Ensure that informed consent is documented or waived in accordance with 10 CFR Parts 745.116-7.

7. Ensure that HSR involving multiple DOE sites (e.g., members of the research team from more than one DOE site and/or data or human subjects from more than one DOE site) is reviewed and approved by one of the Central DOE IRBs prior to initiation, or if authorized by the DOE and/or NNSA HSP Program Manager, other appropriate IRB of record. In all cases, an IRB Authorization Agreement (IAA) or Memorandum of Understanding (MOU) must be in place between the organization(s) conducting the HSR and the organization responsible for IRB review.

8. Ensure that HSR that involves targeted inclusion of DOE Federal and/or contractor employees or their data is first reviewed and approved by the appropriate DOE IRB (the DOE site IRB or one of the Central DOE IRBs), or if deemed more fitting by the Federally assured DOE site or Headquarters, other appropriate IRB of record, in accordance with an IAA or MOU negotiated between the DOE site or Headquarters and the organization responsible for IRB review.

9. Ensure that classified and unclassified intelligence and intelligence-related HSR, regardless of funding source (including, but not limited to, Strategic Intelligence Partnership Program (SIPP) funded studies, DOE-IN funded studies, and/or studies funded by other DOE program offices that use intelligence datasets), is reviewed and approved by the Central DOE IRB-Classified.

10. Ensure that any Human Terrain Mapping (HTM) work is managed as HSR and complies with DOE requirements specified below:

    a. HTM projects, conducted with DOE funding, at DOE sites/institutions (regardless of funding source), or by DOE or DOE contractor personnel (regardless of funding source or location conducted), whether done domestically or in an international environment, including classified and proprietary research, must be strictly limited to only those projects involving the analysis and modeling of de-identified data.

    b. Statements of work for HTM projects must be submitted to the HSP Program Manager (and when an NNSA element is involved, the NNSA HSP Program Manager), for DOE Headquarters review and approval prior to initiation. If the project is to be conducted by or for the intelligence community, DOE-IN must also review and approve it prior to initiation. The HSP Program Manager(s) and DOE-IN must engage the recognized DOE site IRB, and as needed, the principal investigator (PI) and/or sponsor, in clarifying whether the proposed project is

HTM and if so, that the data to be used will be de-identified. Additionally, the PI will be asked to provide written verification that only de-identified HTM data (as defined in paragraph 8.g.) will be used.

c. The recognized DOE site IRB (or in the case of SIPP-funded or other intelligence-related HSR, the Central DOE IRB-Classified) is the only entity authorized to determine whether the HTM data received by the PI after project initiation meets DOE criteria for de-identification. If the DOE site does not have a designated site IRB, then the Central DOE IRB(s) must be the responsible IRB.

d. All projects funded by other entities, including HTM activities, must comply with the applicable DOE O 481.1E, *Strategic Partnership Projects [Formerly Known as Work for Others (Non-Department of Energy Funded Work)]*, current version, or DOE O 484.1, *Reimbursable Work for the Department of Homeland Security,* current version.

e. In a case where the sponsor requests assistance in the de-identification of HTM data prior to using the data and/or re-identification of the data following completion of the project, DOE sites may provide such services under a separate contract and/or task order with the sponsor by following the appropriate DOE standard operating procedure approved by the DOE IO, DOE Office of Science (SC).[3]

11. Ensure that any classified HSR complies with the additional requirements specified below:

a. All information related to classified HSR must be managed in accordance with applicable DOE directives and other requirements (Executive Orders (E.O.s), laws, regulations) and researchers involved in the conduct of such HSR must have security clearances at the appropriate level to access such information.

b. HSR that is classified, in whole or in part, must not be initiated without IRB approval, which must be followed by DOE IO approval. The DOE IO, in consultation with the Human Subjects Protection Program (HSPP) Managers, will determine whether he/she will approve/disapprove the project or brief the Secretary about the project prior to his/her approval/disapproval.

c. Informed consent may only be waived for classified HSR if the work meets one of the categories of minimal risk HSR addressed at 10 CFR Part 745.104.

[3] It should be noted that: 1) only limited communications, if needed, may take place between the organization de-identifying and/or re-identifying the sponsor's data and the organization performing work on the sponsor's task; 2) the identified dataset shall not be shared with the individual who will perform work on the sponsor's task; and 3) the de-identified dataset shall be sent directly by the sponsor to the individual performing work on the sponsor's task and not by the organization at the DOE site that de-identified it.

d. The use of the expedited review process is prohibited. The fact that research meets a particular expedited category may be noted, but a full IRB review will be required.

e. HSR exemptions (as per 10 CFR Part 745.104) will not be used. The fact that research meets a particular exemption category may be noted, but a full IRB review will be required.

f. The identity of the sponsoring Federal agency must be disclosed to subjects, unless the sponsor requests it not be done. The only acceptable reason for non-disclosure is that disclosure could compromise intelligence sources or methods. Additionally, the research must be no more than minimal risk, and the IRB must determine that not disclosing the identity will not adversely affect the subjects.

g. The informed consent document will state that the project is classified, what that means for the purposes of that project, and what part of the research that applies to. The IRB must determine whether the potential human subjects need access to classified information in order to make a valid informed consent decision.

h. When reviewing classified HSR, the unaffiliated member of a DOE or DOE site IRB must be a nongovernmental member (not currently a Federal employee or a DOE site contractor employee) with the appropriate security clearance.

i. Any IRB member can appeal an IRB decision to approve a project to the DOE IO, and if not resolved to the IRB member's satisfaction, to the Secretary of Energy. If still dissatisfied, the IRB member can appeal that approval decision to the Director of the Office of Science and Technology Policy (OSTP) or that Director's designee, or the Director of National Intelligence (ODNI), or that Director's designee.[4] The Director of OSTP, or that Director's designee, or the ODNI, or that Director's designee will review and approve or disapprove the research, or will convene or designate an IRB that is, to the extent possible, made up of unaffiliated members with the appropriate qualifications and clearance to approve or disapprove the research.

j. Information on each HSR project that is classified must be submitted annually, or in accordance with the directions and schedules provided by the appropriate HSP program manager. The HSP program managers will compile this information and prepare a summary document, for signature by the DOE IO and delivery to OSTP and/or ODNI, in accordance with E.O.s (see the *Presidential Memorandum, Strengthened Protections for Human Subjects of Classified Research*, dated March 27, 1997, and published in the Federal Register on May 13, 1997, (62 Federal Register 26369)) and other Federal requirements.

k. An IRB that believes that an HSR project which is classified, in whole or in part, can be thoroughly reviewed in an unclassified manner, may submit a request for a

[4] The Presidential Memorandum, Strengthened Protections for Human Subjects of Classified Research, dated March 27, 1997, requires such an appeal process.

waiver from some or all of the requirements of this section (specific to classified HSR) for the purpose of that particular study. The study-specific waiver request must be signed by the submitting IRB's Chair(s) and reviewed and approved by the appropriate HSP Program Manager. If the waiver request relates to an intelligence-related project, DOE-IN must also review and approve the waiver. A list of study-specific waiver requests and the actions taken will be provided monthly to the DOE IO.

12. Ensure that research that uses social media data and/or other publicly available data about individuals or publicly available biospecimens, even if the data or biospecimens appear(s) to be de-identified, is submitted for HSR/not HSR determination through the appropriate IRB and/or IRB office. *Note: DOE follows Health Insurance Portability and Accountability Act and guidance issued by National Institute for Standards and Technology, at a minimum, in determining identifiability.*

13. Ensure that research involving the study of humans in a systematically modified environment is submitted to the appropriate IRB for HSR review and determination.

14. In order for a DOE site IRB to vote on a new or amended protocol that requires full board review, there must be a minimum of five members present, including a scientist, a nonscientist, and an unaffiliated member.

15. Ensure that PII collected and/or used during HSR projects is protected in accordance with the requirements of DOE Order 206.1.

16. If applicable, ensure that Federally funded HSR complies with the requirements of the Paperwork Reduction Act.

17. If applicable, ensure that visiting student researchers, researchers, and scholars from other countries conduct HSR in accordance with Department of State requirements, e.g., those outlined in 22 CFR Part 62, *Exchange Visitor Program, and U.S. Department of State Guidance Directive 2024-01*, current versions.

18. Submit an application for a Federalwide Assurance (FWA) to the Office of Human Research Protections with Department of Health and Human Services (DHHS) and once approved by DHHS, maintain this FWA covering proposed and ongoing HSR and provide a copy to the appropriate HSP Program Manager. The Secretary of Energy uses the approved FWA as appropriate written documentation from DOE sites committing to institutional compliance with and implementation of DOE and DHHS regulations for the protection of human research subjects. See and/or contact the DOE HSP Program Manager, Office of Science, Office of Biological and Environmental Research, or the NNSA HSP Program Manager, as appropriate. Information about the DOE HSP program may be found at https://science.osti.gov/ber/human-subjects.

19. Perform informal internal review(s) of the HSP Program, or portions of the HSP Program, at least annually, consulting with the site office as appropriate. Participate in triennial (or biennial for sites that perform classified HSR) quality assurance consultations led by the appropriate DOE HSP program manager, which will be designed

to provide each site with useful information and understanding of HSP program requirements, including any changes in those requirements and recommendations for continuous improvement.

20. Provide data for the HSR Projects Database (HSRD), and separately transmit data on unclassified intelligence projects and, in accordance with directions and schedules provided by the appropriate HSP Program Manager. Such reporting is also required when HSR is minimal risk (including exempt HSR) and for studies for which a DOE IRB is not the IRB of record. In cases where a DOE site IRB defers to an external IRB for the review of a study the DOE site is engaged in, the DOE site IRB will still be responsible for ensuring HSRD reporting requirements are met. In cases where a DOE Headquarters program office funds outside institutions to conduct HSR, the program office will be responsible for ensuring HSRD reporting requirements are met.

21. DOE/NNSA site and central IRBs must keep key project- specific and meeting-specific records in the DOE Headquarters-provided electronic IRB protocol system and they must be managed in accordance with National Archives and Records Administration-approved records schedules. Additionally, all records related to IRB review/approval of classified HSR as well as key researcher records must be maintained permanently. During and following the completion of classified research, copies of all signed classified consent forms must be stored in a separate but secure central location (e.g., security policy officer or IRB office), other than the researchers' office, and participants of such research must be notified during the consenting process regarding how to access a copy of their individual signed classified consent forms should they want to in the future.

22. Ensure that researchers who submit studies to the DOE central and DOE site IRBs and members of these IRBs complete initial and periodic refresher training in human subjects' protection. Researchers submitting studies to the central DOE IRBs must also complete additional DOE-specific training that includes a module on recognizing and addressing bias in the design, review and conduct of HSR.

23. Submit requests for exemptions from the requirements of this Order in writing through the contracting officer to the appropriate HSP Program Manager.

24. Equitable payment of human subjects participating in HSR is allowable.