U.S. Department of Energy
Washington, D.C.

ORDER

DOE O 443.1

Approved:05-15-00
Sunset Review: 05-15-02
Expires: 05-15-04

SUBJECT: PROTECTION OF HUMAN SUBJECTS

1. OBJECTIVE. To establish Department of Energy (DOE) procedures and responsibilities for implementing the policy and requirements set forth in 10 CFR Part 745, *Protection of Human Subjects*, and in DOE P 443.1, POLICY ON THE PROTECTION OF HUMAN SUBJECTS.

2. CANCELLATION. This Order cancels DOE Order 1300.3, PROTECTION OF HUMAN SUBJECTS, dated 8-23-90.

3. APPLICABILITY.

   a. DOE Elements. The provisions of this Order apply to all DOE elements.

   b. DOE Contractors/Financial Assistance Recipients. The provisions of this Order apply to DOE contractors including the National Nuclear Security Administration (NNSA), and financial assistance recipients, as provided by law and/or contract or financial assistance agreements, and as implemented by the cognizant contracting officer. The Contractor Requirements Document (CRD), Attachment 1, sets forth requirements to be applied to DOE managing and operating (M&O) contractors with respect to all human subjects research conducted *by anyone* under the M&O contract. DOE non-M&O contractors and financial assistance recipients performing DOE-funded research that is subject to 10 CFR Part 745 and/or 45 CFR Part 46 must also be made subject to requirements 4d through 4f of this Order.

4. REQUIREMENTS.

   a. Approvals. No research involving human subjects conducted with DOE funding, at DOE institutions, or by DOE personnel may be initiated without both a project assurance and approval by the cognizant Institutional Review Board (IRB) in accordance with 10 CFR 745.103. The assurance may be either an approved single project assurance (SPA) or multiple project assurance (MPA) obtained from the Department of Health and Human Services (DHHS) or the DOE Human Subjects Research Program Manager (SC-72).

   b. Solicitations. Any solicitation for research involving human subjects must indicate the requirement for compliance with this Order, 10 CFR PART 745, and 45 CFR PART 46.

c. Requirements Document. Any DOE contract or financial assistance agreement involving human subjects research must require compliance with this Order, 10 CFR PART 745, and 45 CFR PART 46. See also Contractor Requirements Document (Attachment 1).

d. Notification. SC-72 must be notified of any new solicitation or proposal involving human subjects research (including personally identifiable information or materials) that addresses–

(1) an institution without an established IRB;

(2) a foreign country;

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

(4) research subjects in a protected class; or

(5) the generation or use of classified or sensitive unclassified information.

e. Reporting. Human subjects research projects must be reported annually to the DOE Human Subjects Research Projects Database, in accordance with directions and schedules provided by SC-72.

f. Waivers. Requests for waivers from the requirements of 10 CFR Part 745 or this Order must be submitted to SC-72 in writing. A waiver may be granted provided that it is not prohibited by law and does not present an undue risk to the health and safety of workers or research volunteers. Waiver decisions must set forth in writing the basis for granting or denying the request.

g. Protected Classes. Research involving pregnant or lactating women, children, prisoners, or the mentally disabled must be conducted in accordance with 45 CFR Part 46 Subparts B, C, and D.

h. Non-compliance. SC-72 must be notified of any known or potential incidents of non-compliance with requirements of this Order, 10 CFR Part 745, 45 CFR Part 46, or any approved plan for correcting a non-compliance.

5. RESPONSIBILITIES.

a. Director of the Office of Science (SC-1).

(1) Implements 10 CFR Part 745 within the Department in accordance with policy established by the Secretary and DOE P 443.1.

(2) Determines what constitutes DOE-related human subjects research.

(3) Ensures implementation of human research subject protection.

b. DOE Human Subjects Research Program Manager (SC-72).

(1) Develops and implements procedures for the DOE human subjects research program.

(2) Prepares and updates guidance to be followed for obtaining approval for human subjects research.

(3) Approves human subjects research assurances.

(4) Reviews/approves local plans to correct any noncompliance with applicable human subjects research requirements, or to mitigate adverse study events.

(5) Provides advice and guidance on evolving DOE and national bioethics and regulatory issues regarding human research subjects protection and helps identify and resolve program/project concerns.

(6) Develops and implements educational programs on bioethics and human research subjects protection requirements, practices, and procedures for DOE, DOE contractor personnel, financial assistance recipients, and the public.

(7) Regularly conducts institutional performance reviews to assess compliance with human research subjects protection requirements.

(8) Serves as the Chair of the DOE Human Subjects Working Group and as the official DOE representative to groups with bioethics and human subjects research interests.

(9) Reviews and approves requests for waivers to requirements of 10 CFR Part 745 and satisfies the advance notice and publication requirements of 10 CFR Part 745.101(i) prior to granting any waiver.

(10) Concurs in human subjects research provisions in interagency agreements.

c. Program Secretarial Officers (PSOs), NNSA Administrators and Heads of Field Organizations (HFOs) 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. Refer any questions or uncertainties regarding the applicability of human research subjects protection requirements to such proposals to SC-72 for resolution and determination.

(2) Ensure that solicitations, contracts, and financial assistance agreements involving human subjects research include the appropriate human research subjects protection requirements and that the contracting officer is advised of projects involving such human subjects research. [It is recommended that the *OSC Face Sheet for Grant Applications* (DOE F 4650.2), Attachment 2, be used in place of the standard Federal face sheet (SF 424, *Application for Federal Assistance*) referenced in 10 CFR 600.10. DOE F 4650.2 contains questions for the applicant to answer on the involvement of human subjects in the DOE-funded research while SF 424 does not solicit such information.]

(3) Ensure their staffs and subordinate field elements comply with the requirements of this Order.

(4) Ensure their staffs and subordinate field elements implement the procedures established by SC-72.

(5) Promptly notify SC-72 of known or potential adverse events and issues of non-compliance with this Order, 10 CFR Part 745, and 45 CFR Part 46 Subparts B, C, and D. Submit proposed corrective action for approval to SC-72 and implement approved corrective actions.

(6) Promptly consult with SC-72 regarding human subjects research issues and concerns.

(7) Actively participate in human research subjects protection educational programs.

(8) Periodically conduct self-assessments to ensure compliance with the requirements of this Order.

(9) At their discretion, conduct further review and approve or disapprove research that has been approved by the IRB. (Note: PSOs, NNSA Administrators, HFOs, or their designees may not approve human subjects research that has not been approved by an IRB.) (See 10 CFR Part 745.112.)

(10) Oversee the administration of human research subjects protection programs of contractors and financial assistance recipients under their cognizance to ensure compliance with applicable human research subjects protection requirements.

(11) Involve SC-72 in negotiating those portions of interagency agreements that address human subjects research.

(12) Appoint a point of contact for interacting with SC-72 on program-related and/or Department-wide issues.

6. DEFINITIONS.

a. 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 or DHHS regulations for the protection of human research subjects. A single project assurance (SPA) is a commitment to comply with human research subjects protection requirements during the conduct of a specific project by a particular investigator. SPAs must be renewed annually. A multiple project assurance (MPA) is a compliance commitment by an institution covering all research involving human research subjects conducted at that institution, irrespective of the investigator. The institution's first DOE MPA will be awarded for a 3-year period. Subsequent renewals of the DOE MPA may be granted for 5-year periods. An institution's DHHS SPA or MPA will be accorded the same acceptance and responsibilities as those granted by DOE. (See 10 CFR Part 745.103 and the *DOE Human Subjects Research Handbook.)*

b. Adverse Effect. A direct result of an administered research protocol (e.g., negative or deleterious drug reaction, collateral damage to the human subject.)

c. Adverse Event. A result surrounding or indirectly related to the entire research process (e.g., mishaps, mistakes, incorrect dosage administered, reconsideration of human subject involvement.)

d. DOE Human Subjects Research Database. A compilation of summary information, which is available on the DOE website at: http://www.doe.eml.gov/hsrd/, updated annually, on every human subjects research project conducted by DOE personnel, with DOE funding, or at DOE institutions or facilities.

e. Human subjects. Living individual(s) about whom an investigator conducting research obtains (1) data through intervention or interaction with the individual or (2) personally identifiable information or materials.

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

g. Institutional Review Board (IRB). A committee or board instituted by the institution, approved by DOE or DHHS under an SPA or MPA, and charged with the responsibility for review of research activities involving human subjects in accordance with 10 CFR Part 745.

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

7. REFERENCES.

a. DOE P 443.1, POLICY ON THE PROTECTION OF HUMAN SUBJECTS, dated 05-15-00, which defines the DOE policy for the protection of human subjects in research activities.

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

c. DOE Human Subjects Research Handbook, Office of Health and Environmental Research, Second Edition, 1996.

d. 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.

e. 5 United States Code 552, *The Freedom of Information Act* (Public Law 89-487 as amended), which establishes the right of citizens to request information from Federal agencies and establishes a framework of procedures to implement this right.

f. 5 United States Code 552a, *Privacy Act of 1974* (Public Law 93-549), as amended, which establishes requirements for the collection, maintenance, and dissemination of personal information by Federal agencies.

g. DOE O 481.1, WORK FOR OTHERS (Non-Department of Energy Funded Work), dated 9-30-96, which establishes the policy, responsibilities, and procedures for authorizing and administering non-DOE funded work performed under DOE contracts.

h. DOE M 481.1-1, REIMBURSABLE WORK FOR NON-FEDERAL SPONSORS PROCESSES MANUAL, dated 9-30-96, which describes the process to be used in performing Work for Others projects for non-Federal sponsors.

i. DOE O 412.1, WORK AUTHORIZATION SYSTEM, dated 4-20-99, which provides the policy, responsibilities, and procedures for authorizing and administering DOE-funded work performed under DOE contracts.

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

k. 10 CFR Part 602, *Epidemiology and Other Health Studies Financial Assistance*, 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.

l. 10 CFR Part 605, *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 the Office of Science.

8. CONTACT. Questions regarding this Order should be addressed to the Program Manager, DOE Human Subjects Research Program, at the Office of Science, telephone 301-903-4731. Information about the DOE human subjects research protection program may be found at http://www.er.doe.gov/production/ober/humsubj/.

BY ORDER OF THE SECRETARY OF ENERGY:

T.J. GLAUTHIER
Deputy Secretary

CONTRACTOR REQUIREMENTS DOCUMENT

DOE O 443.1, PROTECTION OF HUMAN SUBJECTS

The following requirements must be incorporated by reference into management and operating (M&O) contracts with the potential to involve human subjects research.

1. Ensure that the DOE Human Subjects Research Program Manager (SC-72) is notified of any new human subjects research project involving–

   a. an institution without an established IRB;

   b. a foreign country;

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

   d. research subjects in a protected class; or

   e. the generation or use of classified or sensitive unclassified information.

2. Ensure that research involving human subjects conducted at the contractor-operated institution, with the contractor's DOE-contract funding, or by contractor personnel is conducted in accordance with the applicable requirements of 10 CFR Part 745 and 45 CFR Part 46.

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.

4. Ensure no research involving human subjects conducted at the contractor-operated institution, with the contractor's DOE-contract funding, or by contractor personnel is initiated without prior institutional review board (IRB) approval under the terms of an approved assurance covering the research. For research involving current or former DOE employees or DOE contractor employees at DOE sites or facilities, either the IRB or the assurance must be approved by SC-72.

5. Apply for SC-72 approval of any single project assurance (SPA) or multiple project assurance (MPA), with notice to the cognizant DOE Program Secretarial Officer (PSO), NNSA Administrators or Head of Field Organization (HFO).

6. Ensure research is reviewed at intervals appropriate to the degree of risk, but not less than once per year, to determine whether test subjects are at risk and if they are, whether the risk is reasonable in relation to anticipated benefits.

7. Periodically conduct self-assessments to ensure compliance with the Human Subjects Research Program procedures and other requirements.

8. Prepare and submit an annual report for the DOE Human Subjects Research Database in accordance with directions and schedules provided by SC-72 and the contracting officer.

9. Report the following to SC-72 (and any designated PSO, NNSA Administrators or HFO point of contact):

   a. any adverse events, unanticipated risks, or complaints about the research, and a description of any corrective actions taken and/or to be taken;

   b. any changes in the IRB membership;

   c. any suspension or termination of IRB approval of research;

   d. any significant non-compliance with Human Subjects Research Program procedures or other requirements.

   (The *adverse effects* of any study are to be reported to the IRB for evaluation for further action with SC-72, the PSO, the NNSA Administrators and the HFO, if necessary.)

10. Submit requests for waivers from these requirements in writing, through the designated cognizant PSO, NNSA Administrators or HFO point of contact) to SC-72, with appropriate justification.

11. Actively participate in human subjects research educational programs.

NOTE: This is not true to form, to get an actual copy go to url:
http://www.sc.doe.gov/production/grants/forms.html
or contact the Office of Science

DOE F 4650.2
(10-99)
(All Other Editions Are Obsolete)

Department of Energy
Office of Science (SC)

Face Page

OMB Control No.
1910-1400
(OMB Burden Disclosur
Statement on Back)

TITLE OF PROPOSED RESEARCH:

1. CATALOG OF FEDERAL DOMESTIC ASSISTANCE #:
   81.049

2. CONGRESSIONAL DISTRICT:
   Applicant Organization's District:
   Project Site's District:

3. I.R.S. ENTITY IDENTIFICATION OR SSN:

4. AREA OF RESEARCH OR ANNOUNCEMENT TITLE/#:

5. HAS THIS RESEARCH PROPOSAL BEEN SUBMITTED TO ANY OTHER FEDERAL AGENCY?
   Yes ____ No ____
   PLEASE LIST:

6. DOE/SC PROGRAM STAFF CONTACT (if known):

7. TYPE OF APPLICATION:
   New ____ Renewal
   Continuation Revision
   Supplement

8. ORGANIZATION TYPE:
   Local Govt. ____ State Govt. ____
   Non-Profit ____ Hospital ____
   Indian Tribal Govt. Individual ____
   Other ____ Inst. of Higher Educ. ____
   For-Profit ____
   Small Business Disadvan. Business
   Women-Owned ____ 8(a) ____

9. CURRENT DOE AWARD # (IF APPLICABLE):

10. WILL THIS RESEARCH INVOLVE:
    10A Human Subjects No ____ If yes, ____
    Exemption No. ____ or
    IRB Approval Date ____
    Assurance of Compliance No:
    10B Vertebrate Animals No ____ If yes, ____
    IACUC Approval Date ____
    Animal Welfare Assurance No:

11. AMOUNT REQUESTED FROM DOE FOR ENTIRE PROJECT PERIOD $ ____

12. DURATION OF ENTIRE PROJECT PERIOD:
    ____ to ____
    Mo/day/yr. Mo/day/yr.

13. REQUESTED AWARD START DATE
    ____ (Mo/day/yr.)

14. IS APPLICANT DELINQUENT ON ANY FEDERAL DEBT?
    Yes (attach an explanation) ____ No ____

15. PRINCIPAL INVESTIGATOR/PROGRAM DIRECTOR NAME, TITLE, ADDRESS, AND PHONE NUMBER

16. ORGANIZATION'S NAME, ADDRESS AND CERTIFYING REPRESENTATIVE'S NAME, TITLE, AND PHONE NUMBER

SIGNATURE OF PRINCIPAL INVESTIGATOR/ PROGRAM DIRECTOR

Date

PI/PD ASSURANCE: I agree to accept responsibility for the scientific conduct of the project and to provide the required progress reports if an award is made as a result of this submission. Willful provision of false information is a criminal offense. (U.S. Code, Title 18, Section 1001).

SIGNATURE OF ORGANIZATION'S CERTIFYING REPRESENTATIVE

Date

CERTIFICATION & ACCEPTANCE: I certify that the statements herein are true and complete to the best of my knowledge, and accept the obligation to comply with DOE terms and conditions if an award is made as the result of this submission. A willfully false certification is a criminal offense. (U.S. Code, Title 18, Section 1001).

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PRIVACY ACT STATEMENT

If applicable, you are requested, in accordance with 5 U.S.C., Sec. 562A, to voluntarily provide your Social Security Number (SSN). However, you will not be denied any right, benefit, or privilege provided by law because of a refusal to disclose your SSN. We request your SSN to aid in accurate identification, referral and review of applications for research/training support for efficient management of Office of Energy Research grant/contract programs.