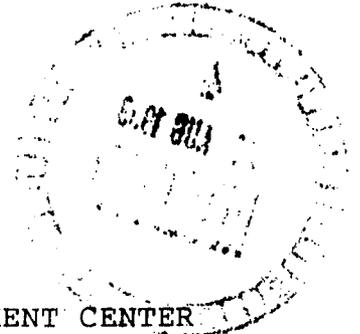




OFFICE OF THE DIRECTOR OF  
DEFENSE RESEARCH AND ENGINEERING

WASHINGTON, DC 20301-3030



MEMORANDUM FOR THE COMMANDER, U.S ARMY MEDICAL DEPARTMENT CENTER  
AND SCHOOL ATTN: CHIEF, CLINICAL INVESTIGATION  
REGULATORY OFFICE

THROUGH: ~~SURGEON GENERAL OF THE ARMY~~  
COMMANDER, U.S. ARMY HEALTH SERVICES COMMAND

SUBJECT: Protection of Human Subjects Assurance Statement

Your memorandum of 13 May 1993 has been reviewed and approved. By this memorandum, the Surgeon General of the United States Army, or his designee, in accordance with Chapter 24 of Army Regulation 40-38 is delegated authority to grant approval to assurances provided by U.S. Army Health Services Command (HSC) and to issue assurance numbers to all organizations conducting clinical investigations which comply with the regulations for the protection of human subjects as contained in Title 32, Code of Federal Regulations, Part 219. The Surgeon General, or his designee, is delegated authority to issue approved assurances using numbered assurances DoD10002 through DoD19999. Assurance number DoD10000 is provided to the Office of The Surgeon General and its Human Subjects Research Review Board. Assurance number DoD10001 is provided to the U.S. Army Health Services Command and its assurance approval oversight office, the Clinical Investigation Regulatory Office, U.S. Army Medical Department Center and School. The Surgeon General, or his designee, by this delegated authority is responsible for ensuring that the regulations contained in Title 32, Code of Federal Regulations, Part 219, Army Regulation 70-25, "Use of Volunteers as Subjects of Research", and "Department of Defense Guidance for Assurances of Compliance with the Federal Policy for the Protection of Human Subjects" are implemented within Health Services Command and its subordinate commands as stated in Army Regulation 40-38.

*Joseph V. Osterman*  
Joseph V. Osterman, Ph.D.  
Director, Environmental  
and Life Sciences



OFFICE OF THE DIRECTOR OF  
DEFENSE RESEARCH AND ENGINEERING

WASHINGTON, DC 20301-3030

MEMORANDUM FOR THE SURGEON GENERAL OF THE ARMY

THROUGH: ~~ASSISTANT SECRETARY OF THE ARMY (MANPOWER AND RESERVE AFFAIRS) DES~~  
~~ASSISTANT SECRETARY OF THE ARMY (RESEARCH DEVELOPMENT ACQUISITION)~~ B-16

David E. Suttle, M.D. 1 AUG 1993  
Colonel GS  
Assistant Deputy for Health Policy

SUBJECT: Protection of Human Subjects Assurance Statement

The memorandum from the Assistant Surgeon General for Research and Development dated 25 May 1993, has been reviewed and approved. By this memorandum, the Surgeon General of the United States Army, or his designee, has authority to approve assurances provided by, and to issue assurance numbers to Army staff agencies, major Army Commands, their subordinate organizations and Army funded contractors/grantees which comply with the regulations for the protection of human subjects as contained in Title 32, Part 219, Code of Federal Regulations and the Department of Defense Guidance for Assurances of Compliance with the Federal Policy for the Protection of Human Subjects. Assurance number DoD10000 is reserved for the Office of The Surgeon General and its Human Subjects Research Review Board. Assurance Number DoD20000 is provided to the U.S. Army Medical Research and Development Command designating its approved assurance status. The Human Use Review and Regulatory Affairs Office is the designated oversight Office for The Surgeon General and has the authority to issue approved assurance numbers DoD20001 through DoD29999. The Human Use Review and Regulatory Affairs Office, in its capacity as the approval authority for the human use review process, as stated in Army Regulation 40-38 and Army Regulation 70-25, is responsible to advise and assist Department of the Army staff agencies, major Army Commanders and Commanders of research, development, test and evaluation organizations in ensuring that the Federal and Army regulations, and DoD guidance cited above are implemented.

*Joseph V. Osterman*  
Joseph V. Osterman, Ph.D.  
Director, Environmental and  
Life Sciences



REPLY TO  
ATTENTION OF

DEPARTMENT OF THE ARMY  
U.S. ARMY MEDICAL DEPARTMENT CENTER AND SCHOOL  
FORT SAM HOUSTON, TEXAS 78234-6100



HSHN-I

30 April 1993

MEMORANDUM FOR Acting Assistant Secretary of Defense  
(Health Affairs), Room 3E-346, the Pentagon,  
Washington, DC 20301-1200

SUBJECT: Department of Defense Guidance for Assurance of  
Compliance With the Federal Policy for the Protection of Human  
Subjects

1. The Clinical Investigation Program Division, Army Medical Department Center and School, Ft. Sam Houston, Texas, concurs with contents of draft document, and will comply with all implementation suspense dates as directed.
2. This office will serve as the designated approval and oversight office for Clinical Investigation laboratories in all Health Services Command (HSC) Medical Centers (MEDCENS)/Medical Department Activities (MEDDACs) IAW with AR 40-38. All subordinate HSC activities conducting non-exempted clinical research involving human subjects will submit an assurance statement to this office for approval prior to issuance of a DoD Assurance number.
3. The undersigned, or a designated representative, will represent Health Services Command and the Army Medical Department Center and School on the standing committee for the Protection of Human Subjects as established by the Director, Research and Life Sciences.
4. POC this action is LTC Steve Speights, DSN 471-2511 or commercial (210) 221-2511.

FOR THE COMMANDER:

SHANNON M. HARRISON, M.D.  
Colonel, Medical Corps  
Chief, Clinical Investigation  
Program Division



DEPARTMENT OF THE ARMY  
OFFICE OF THE ASSISTANT SECRETARY  
WASHINGTON, DC 20310-0103



SARD-TM

26 APR 1993

MEMORANDUM FOR ACTING ASSISTANT SECRETARY OF DEFENSE  
(HEALTH AFFAIRS)

SUBJECT: Department of Defense Guidance for Assurance  
of Compliance With the Federal Policy for the  
Protection of Human Subjects

The Army fully supports the Department of Defense Guidance and will ensure that all Department of the Army research, both clinical investigations and research, development, test and evaluation, involving human subjects, shall be in full compliance with the Common Federal Policy.

George T. Singley III  
Deputy Assistant Secretary  
For Research and Technology



OFFICE OF THE SECRETARY OF DEFENSE

WASHINGTON, D.C. 20301

MAR 30 1993

MEMORANDUM FOR ASSISTANT SECRETARY OF THE ARMY (M&RA)  
ASSISTANT SECRETARY OF THE ARMY (RDA) ←  
ASSISTANT SECRETARY OF THE NAVY (M&RA)  
ASSISTANT SECRETARY OF THE NAVY (RDA)  
ASSISTANT SECRETARY OF THE AIR FORCE (MRAI&E)  
ASSISTANT SECRETARY OF THE AIR FORCE (SAF/AQ)  
PRESIDENT, UNIFORMED SERVICES UNIVERSITY OF THE  
HEALTH SCIENCES  
DIRECTOR, ARMED FORCES RADIOBIOLOGY RESEARCH  
INSTITUTE

SUBJECT: Department of Defense Guidance for Assurance of  
Compliance with the Federal Policy for the Protection  
of Human Subjects

On August 19, 1991, all Federal Agencies issued a set of regulations regarding the protection of human subjects in research that has come to be regarded as the "Common Rule." All DoD sponsored research, including collaborative research, which involves the use of human subjects must follow the "Common Rule" as found in Title 32 of the Code of Federal Regulations, Part 219.

The issuance of Assurance Documentation for all DoD sponsored research, including collaborative research is a fundamental part of this regulation. Service representatives from both the clinical investigations program offices, and the human use and review program offices were requested to participate in the development of a DoD Assurance Guidance applicable uniformly across all Military Departments. The Service component agencies whose representatives participated in the preparation of this guidance are found in pages 3-4 of the attached document.

The DoD Guidance of Assurance for the Protection of Human Subjects is being submitted to you for formal coordination. Please provide your comments on the attached document to the Office of the Assistant Secretary of Defense for Health Affairs (OASD(HA)) not later than 15 April 1993. It is imperative that all Service component agencies conducting research that involves human subjects not so identified in this document be brought to our attention. The OASD(HA) point of contact for this action is Captain John F. Jemionek, MSC, USN, Director, Scientific Activities. Captain Jemionek may be contacted at (703) 695-7116 or DSN 225-7116.

*VH*  
Victor H. Reis  
Director, Defense Research  
and Engineering

*Edward D. Martin*  
Edward D. Martin  
Acting Assistant Secretary  
of Defense (Health Affairs)



OFFICE OF THE SECRETARY OF DEFENSE

WASHINGTON, DC 20301-1000

JUN 10 1993

MEMORANDUM FOR ASSISTANT SECRETARY OF THE ARMY (M&RA)  
ASSISTANT SECRETARY OF THE ARMY (RDA)  
ASSISTANT SECRETARY OF THE NAVY (M&RA)  
ASSISTANT SECRETARY OF THE NAVY (RDA)  
ASSISTANT SECRETARY OF THE AIR FORCE (MRAI&E)  
ASSISTANT SECRETARY OF THE AIR FORCE (SAF/AQ)  
PRESIDENT, UNIFORMED SERVICES UNIVERSITY OF THE  
HEALTH SCIENCES  
DIRECTOR, ARMED FORCES RADIOBIOLOGY RESEARCH  
INSTITUTE

SUBJECT: Department of Defense (DoD) Guidance for Assurance of  
Compliance with the Federal Policy for the Protection of  
Human Subjects

References:

- a. Department of Defense, Title 32, Code of Federal Regulations, Part 219 (32 CFR 219), "Protection of Human Subjects" and "Protection of Human Subjects in DoD Supported Research," August 19, 1991.
- b. Department of Health and Human Services Regulation "Protection of Human Subjects," (45 CFR 46), August 19, 1991.
- c. DoD Directive 3216.2, "Protection of Human Subjects in DoD Supported Research", January 7, 1983.

Definitions:

- a. Research means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities.
- b. Human subject means a living individual about whom an investigator (whether professional or student) conducting research obtains: (1) Data through intervention or interaction with the individual, or (2) Identifiable private information. Intervention includes both physical procedures by which data are gathered (for example,

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 an observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects.

c. Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

d. Certification means the official notification by the institution to the supporting department or agency, in accordance with the requirements of Reference (a), that a research project or activity involving human subjects has been reviewed and approved by an Institutional Review Board (IRB) with an approved assurance in accordance with Reference (a).

Reference (b) Subpart A has been accepted by the Department of Defense (DoD) as the Common Federal Policy for the Protection of Human Subjects. The DoD Common Federal Policy for the Protection of Human Subjects is promulgated in reference (a). Reference (b) also includes subparts which contain Department of Health and Human Services (DHHS) requirements for research which involves protected classes of human subjects. Subpart B addresses additional DHHS protections regulations pertaining to research, development, and related activities involving fetuses, pregnant women and human in vitro fertilization. Subpart C addresses additional DHHS protections regulations pertaining to biomedical and behavioral research involving incarcerated persons as research subjects. Subpart D addresses additional DHHS protections regulations when children are involved as research subjects. The additional DHHS protections regulations found in Subparts B-D, while not part of the Common Federal Policy, contain basic protection concepts which should be adapted for research that involves protected classes of human subjects. In any case in which requirements of reference (a) and reference (c) differ, the more restrictive requirement shall apply. The Secretaries of the Military Departments or their designee(s) shall ensure that all research, both clinical investigations and research, development,

test and evaluation, involving human subjects, conducted or supported by, or under the auspices of DoD, including DoD supported studies conducted outside the continental United States (OCONUS), and not exempt from compliance with the requirements for protection of human subjects as allowed in Section 101 of reference (a), shall be in full compliance with the Common Federal Policy. The Director, Environmental and Life Sciences, Office of the Director, Defense Research and Engineering is designated policy oversight and responsibility for ensuring DoD compliance with reference (a).

The Office for Protection from Research Risks (OPRR), National Institutes of Health, is responsible for issuing assurances for research supported under the auspices of Agencies of DHHS. These include Cooperative Project Assurances (CPAs) for activities involved in a Cooperative Protocol Research Program, and Single and Multiple Project Assurances (SPAs, MPAs) for other research activities involving human subjects supported by DHHS. DoD Components applying for DHHS funded research support must show evidence of an approved assurance from DHHS prior to award of research funds from DHHS. A DoD issued Assurance Number cannot be accepted at this time by DHHS in requests for DHHS funded research.

In lieu of requiring submission of another assurance, DoD accepts the existence of a current assurance, appropriate for the research in question, on file with the Office for Protection from Research Risks, DHHS, and approved for federal wide use by that office. For DoD sponsored research conducted under a DHHS-approved assurance (in lieu of an approved DoD Assurance) all reports required by Section 103 of References (a) and (b) shall be provided to the appropriate DoD offices as well as to OPRR, DHHS. For DoD sponsored research conducted under a DoD approved assurance, all reports required by Section 103 need only be sent to the appropriate DoD offices. The DoD Components listed below with designated authority to issue numbered Assurances for DoD subordinate activities, contractors and grantees shall acknowledge Assurances issued by other Components of DoD as valid in the review of Service conducted research.

Commencing with all proposals initiated on or after 1 June 1993, all DoD Components conducting human subjects research shall institute a DoD assurance of compliance model as required by reference (a). This suspense applies to all research involving DoD facilities located within CONUS and OCONUS. For DoD funded research in CONUS and OCONUS contractor/grantee facilities, all DoD Components shall implement Assurance requirements for research approved for start on or after 1 June 1993. DoD Components responsible for human subjects research are delegated authority to issue numbered Assurances for all subordinate activities, contractors and grantees as follows:

a. Department of the Army

- (1) U.S. Army Health Services Command (USAHSC):

Clinical Investigation Regulatory Office (CIRO), Health Care Studies and Clinical Investigation Directorate, HSHN-I, Army Medical Department Center and School (AMEDD C&S), Fort Sam Houston, TX 78234-6100; (210) 221-2511 or -0628; DSN 471-2511 or -0628.

(2) U.S. Army Medical Research and Development Command (USAMRDC): Commander, U.S. Army Medical Research and Development Command, ATTN: Human Use Review and Regulatory Affairs Office (HURRAO), SGRD-HR, Fort Detrick, Frederick, MD 21702-5012; (301)-619-2165; DSN 343-2165.

b. Department of the Navy

(1) Naval Health Sciences Education and Training Command (HSETC): Commanding Officer, Naval Health Sciences Education and Training Command, ATTN: Code 2MC, Bethesda, MD. 20889-5022; (301) 295-5769; DSN 295-5769.

(2) Naval Medical Research and Development Command (NMRDC): Commanding Officer, Naval Medical Research and Development Command, National Naval Medical Center, Bethesda, MD. 20889-5606; (301) 295-0287; DSN 295-0287.

c. Department of the Air Force

(1) Clinical Investigations and Life Sciences Division, Headquarters Air Force Medical Operations Agency (HQ AFMOA/SGPT), Office of the Air Force Surgeon General, 170 Luke Avenue, Suite 400, Bolling AFB, DC 20332-5113; (202) 767-5078; DSN 297-5078.

d. Uniformed Services University of the Health Sciences (USUHS):

(1) President, Uniformed Services University of the Health Sciences, ATTN: Executive Secretary, (for Human Use Review Committee), Bethesda, MD 20814-4799; (301) 295-3303; DSN 295-3303.

e. Office of the Chief of Naval Research (OCNR)

(1) Chief of Naval Research, Ballston Center Tower 1, 800 North Quincy Street, Arlington, VA. 22217-5660; (703) 696-4767; DSN 224-4767.

To obtain an approved DoD Single Project Assurance (DSPA), DoD Multiple Project Assurance (DMPA) or DoD Cooperative Project Assurance (DCPA), non-DoD institutions conducting, supporting or collaborating in human subjects research shall provide the required written assurance to their appropriate DoD oversight Office as required by section 219.103 of reference (a). As part

of the protocol submission and prior to funding, contractors and grantees must show evidence of an approved assurance statement (either DoD approved or DHHS approved assurance) from the appropriate oversight office sponsoring the work, including a certification that an IRB has reviewed and approved the work project.

To receive an approved Assurance document for single or multiple projects, a request is executed by an individual authorized to act for the institution and to assume, on behalf of the institution, the obligations imposed in reference (a). The institution must provide to the appropriate DoD oversight office a written statement with the following provisions:

a. A statement that all research involving human subjects is reviewed by the institution's IRB. The research shall be either approved, not approved or is considered exempt under 32 CFR Part 219.101.

b. A statement of principles governing the institution in the discharge of its responsibilities for protecting the rights and welfare of human subjects of research. Each service may choose to accept a statement that the provision governing regulations shall be adopted (for the Army: AR 40-7, "Use of Investigational Drugs and Devices in Humans and the Use of Schedule I Controlled Drug Substances," AR 40-38, "Clinical Investigation Program," and AR 70-25, "Use of Volunteers as Subjects of Research"; for the Navy: SECNAV Instruction 3900.39B, "Protection of Human Subjects, and NAVMEDCOM Instruction 6710.4, "Use of Investigational Agents in Human Beings"; for the Air Force: AFPD 40.4, "Clinical Investigation and Human Use in Medical Research."

c. A statement designating the local name(s) of the committee(s) fulfilling the IRB role (for example, Institutional Review Board, Clinical Investigation Committee, Committee for the Protection of Human Subjects). A statement that provisions have been made for meeting space and sufficient staff to support the IRB's review and record keeping responsibilities shall be included.

d. A list of IRB members identified by name, academic degrees; representative capacity, professional experience (board certifications, licenses, etc.) sufficient to describe each member's professional contributions to IRB deliberations, and any employment or other relationship between each member and the institution (i.e., active or reserve military, paid or unpaid consultant). Changes in IRB membership shall be reported to the appropriate oversight office at the time the changes occur.

e. Written procedures which the IRB will follow for conduct of its research reviews, determinations of frequency and verification of project reviews, and requirements for prompt reporting of changes to previously approved research projects.

f. Written procedures for ensuring prompt reporting to the IRB, and appropriate institutional and agency offices any unanticipated problems involving risk to subjects, any serious noncompliance with this policy, or any suspension or termination of IRB approval.

Assurances for single, multiple or cooperative projects shall be approved by each oversight agency after assuring all regulatory requirements have been met. An Assurance for multiple projects shall expire not later than five years after it is issued. For clarity; Assurance numbers shall be assigned by the DoD Component to subordinate activities in accordance with sections 219.4, 219.5, and 219.6 of Reference (a).

a. Each single or multiple project Assurance number shall consist of an eight alpha-numeric character code. The first three characters shall be "DoD."

b. The next five characters shall be Service specific numbers. The Army shall designate Assurances using numbers

10000 through 29999 (HSC: 10001-19999, USAMRDC: 20000-29999). Assurance number DoD-10000 is reserved for the Army's Human Subjects Research Review Board (HSRRB). The Navy shall designate Assurance numbers 30000 through 39999 as reserved for the Navy Medical Research and Development Command (NMRDC). Assurance number DoD-30000 is reserved for the NMRDC Committee for the Protection of Human Subjects. The Navy shall designate Assurances using numbers 40000 through 49999 to the Health Science Education and Training Command (HSETC). Assurance number DoD-40000 is reserved for HSETC use. The Air Force shall designate Assurance numbers 50000 through 59999. Assurance number DoD-50000 is reserved for the Air Force Surgeon General's Clinical Investigation Committee and DoD-50002 is reserved for the Air Force Human/Animal Review Committee. The Uniformed Services University of the Health Sciences shall designate Assurances using numbers 60000 through 69999. Assurance number DoD-60000 is reserved for the University's Human Use Review Committee. The Office of the Chief of Naval Research (OCNR) shall designate Assurance numbers 70000 through 79999. Assurance number DoD 70000 is reserved for the OCNR Human Use Review Committee.

c. Other numbers shall be made available by the Director, Environmental and Life Sciences or the

appropriate DoD Assurance approval authority, as necessary.

d. The attached Optional Form 310 may be used by DoD subordinate activities or institutions with approved DoD Assurances to certify IRB review and approval. Letters or other modes of written communication may also be used in lieu of Optional Form 310 to provide the same information.

Approval of a written assurance and the assignment of an accompanying Assurance number from the appropriate Assurance approval authority is required before any non-exempt, DoD-funded research involving human subjects may be conducted. All approved, on-going projects shall be reviewed at least annually by the responsible IRB.

Component Activities designated above shall be given delegated Assurance approval and oversight responsibility following submission of an assurance statement to the Director, Environmental and Life Sciences to include: (1) a statement that the Component Activity understands and shall execute the assigned responsibilities imposed by this memorandum; (2) that the Component Activity shall act fairly and impartially to ensure the well-being of all subjects participating in volunteer studies; (3) that all research conducted under the Component Activity's auspices shall be in strict compliance with the provisions of the Federal Policy for the Protection of Human Subjects; and, (4) that any issues that cannot be resolved within this infrastructure shall be referred to that Component's Office of the Surgeon General or to the Director, Environmental and Life Sciences as appropriate for resolution.

Recognizing that there are inherent differences among the various Component activities, the guidance provided in sections 219.1 - 219.7 of reference (a) regarding the protection of human subjects in DoD supported research shall be the common policy within DoD. The approval authority for DoD assurances and subsequent issuance of the reserved assurance numbers shall also be the Director, Environmental and Life Sciences. The Director, Environmental and Life Sciences shall establish a standing committee composed of a representative from each of the Component Activities listed above. The committee shall provide a forum for discussion of Service issues and shall recommend changes to regulations or directives regarding the protection of human subjects as may be required or mandated by law.

Once approved by the Director, Environmental and Life Sciences, each DoD Component with delegated assurance approval authority may begin issuing approved Assurance for those activities under its jurisdiction.

Additional information that may assist in the preparation of the necessary Assurance documents is provided as attachments.

Included is background information regarding informed consent, shared IRBs, and other pertinent documents related to the protection of human subjects.

*Edward D. Martin*

Edward D. Martin  
Acting Assistant Secretary of  
Defense (Health Affairs)

*Joseph V. Osterman*

Joseph V. Osterman  
Director, Environmental and  
Life Sciences

Attachments:

1. Optional Form 310
2. Background Information for U.S. Government and Agency Personnel. Protection of Human Subjects in Studies Conducted Outside the United States
3. Points to Consider: Protection of Human Subjects in International Research and Narrative Format for Providing an Assurance for International Research
4. Format: Assurance of Protection for Human Subjects in International Research
5. World Medical Association Declaration of Helsinki of June 1964, as amended in October 1975, October 1983, and September 1989.
6. Sample DoD Single Project Assurance (DSPA)
7. Modified Sample DoD Single Project Assurance (DSPA) for an Institution utilizing the IRB of another Institution.
8. General Guidance on the Use of Another Institutions's IRB
9. Tips on Informed Consent
10. Department of Defense, Title 32, United States Code of Federal Regulations, Part 219

cc:  
Surgeons General

## Protection of Human Subjects Assurance Identification/Certification/Declaration (Common Federal Rule)

**POLICY:** Research activities involving human subjects may not be conducted or supported by the Departments and Agencies adopting the Common Rule (56FR28003, June 18, 1991) unless the activities are exempt from or approved in accordance with the common rule. See Section 101(b) the common rule for exemptions. Institutions submitting applications or proposals for support must submit certification of appropriate Institutional Review Board (IRB) review and approval to the Department or Agency in accordance with the common rule.

Institutions with an assurance of compliance that covers the research to be conducted on file with the Department, Agency, or the Department of Health and Human Services (HHS) should submit certification of IRB review and approval with each application or proposal unless otherwise advised by the Department or Agency. Institutions which do not have such an assurance must submit an assurance and certification of IRB review and approval within 30 days of a written request from the Department or Agency.

<b>1. Request Type</b> <input type="checkbox"/> ORIGINAL <input type="checkbox"/> FOLLOWUP <input type="checkbox"/> EXEMPTION	<b>2. Type of Mechanism</b> <input type="checkbox"/> GRANT <input type="checkbox"/> CONTRACT <input type="checkbox"/> FELLOWSHIP <input type="checkbox"/> COOPERATIVE AGREEMENT <input type="checkbox"/> OTHER: _____	<b>3. Application or Proposal Identification No. (if known)</b>  
<b>4. Title of Application or Activity</b>  		<b>5. Name of Principal Investigator, Program Director, Fellow, or Other</b>  

**6. Assurance Status of this Project (Respond to one of the following)**

This Assurance, on file with the Department of Health and Human Services, covers this activity:  
 Assurance identification no. M-\_\_\_\_\_ IRB identification no. \_\_\_\_\_

This Assurance, on file with (agency/dept.) \_\_\_\_\_, covers this activity.  
 Assurance identification no. \_\_\_\_\_ IRB identification no. \_\_\_\_\_ (if applicable)

No assurance has been filed for this project. This institution declares that it will provide an Assurance and Certification of IRB review and approval upon request.

Exemption Status: Human subjects are involved, but this activity qualifies for exemption under Section 101 (b), paragraph \_\_\_\_\_.

**7. Certification of IRB Review (Respond to one of the following IF you have an Assurance on file)**

This activity has been reviewed and approved by the IRB in accordance with the common rule and any other governing regulations or subparts on (date) \_\_\_\_\_ by:  Full IRB Review or  Expedited Review.

This activity contains multiple projects, some of which have not been reviewed. The IRB has granted approval on condition that all projects covered by the common rule will be reviewed and approved before they are initiated and that appropriate further certification will be submitted.

**8. Comments**  
 \_\_\_\_\_  
 \_\_\_\_\_  
 \_\_\_\_\_

<b>9. The official signing below certifies that the information provided above is correct and that, as required, future reviews will be performed and certification will be provided.</b>		<b>10. Name and Address of Institution</b>  	
<b>11. Phone No. (with area code)</b>	<b>12. Fax No. (with area code)</b>	<b>14. Title</b>  	
<b>13. Name of Official</b>  			
<b>15. Signature</b>  		<b>16. Date</b>  	

**BACKGROUND INFORMATION FOR U.S. GOVERNMENT  
AND AGENCY PERSONNEL**

**PROTECTION OF HUMAN SUBJECTS IN STUDIES  
CONDUCTED OUTSIDE THE UNITED STATES**

This information package is provided to guide U.S. Government personnel who design, review or carry out research involving human subjects in foreign settings. The purpose of this information is to alert and to inform the reviewing U.S. Government officials of the responsibilities of their Departments and Agencies. The various Federal Departments and Agencies must adhere to the requirements of U.S. law and Federal regulations governing the protection of human subjects involved in research conducted, supported or otherwise subject to regulation by the Federal Government outside the U.S. The Common Rule (Federal Policy for the Protection of Human Subjects, Title 32 Code of Federal Regulations, Part 219 (32 CFR 219)) states that any research involving human subjects, supported or conducted in whole or in part by the Federal Departments or Agencies, in either foreign or domestic settings, is subject to the Common Rule. An additional regulation is also binding for Food and Drug Administration (FDA) regulated research. Foreign clinical studies conducted under an FDA research permit (Investigational New Drug (IND) or Investigational Device Exemption (IDE)) must be reviewed by an Institutional Review Board which meets the organizational and functional requirements specified under 21 CFR Part 56. The FDA may accept studies not conducted under a research permit provided that the studies are well designed, well conducted, performed by qualified investigators, and conducted in accordance with the ethical principles contained in the "Declaration of Helsinki," or the laws and regulation of the country in which the research was conducted, whichever represents the greater level of protection for the research subject (21 CFR 312.120).

In the event that research does not meet the standards of the Common Rule, the Department or Agency must either (1) assure that any deficiency is corrected, (2) obtain a waiver from the official designated by the Common Rule as authorized to grant a waiver. Unless the Common Rule standard can be met, Federal Departments and Agencies will not be able to participate in the research.

Procedures normally followed in foreign countries to protect human subjects may differ from those in the Common Rule. If a Department or Agency Head or designee determines that the procedures prescribed by the foreign institution afford protections that are "at least equivalent" to those in the Common Rule, the Department or Agency Head may approve the substitution of the foreign procedures in lieu of those in the Common Rule.

Several international declarations have been formulated to address the involvement of human subjects in research. These are

often cited in reference material submitted by foreign institutions. These references usually include the Nuremberg Code or the Declaration of Helsinki as Revised in 1982. The first attempt to set international standards was the Nuremberg Code of 1947. This was an outgrowth of the Nuremberg Trials of war criminals who performed experiments on prisoners and detainees during the Second World War. The Nuremberg Code was followed in 1964 by the Declaration of Helsinki, which was itself revised several times by the World Medical Assembly. The most recent internationally recognized document is the proposed International Guidelines for Biomedical Research Involving Human Subjects, which was published in 1982 as a joint project of the World Health Organization and the Council for International Organizations of Medical Science (CIOMS). This document is currently under revision. Another important historical document in the U.S. is the Belmont Report - Ethical Principles and Guidelines for the Protection of Human Subjects of Research, produced by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research in 1979.

Each of these documents contain many laudable policies and principles, and are commendable efforts in the evolution of the concept of human subjects protections. It is important to note, however, that while some international codes contain laudable policies and principles, including ethical review by an appropriate review committee, informed consent and meaningful risk/benefit assessment, none to date clearly delineates a mechanism to implement them. Accordingly, a mechanism needs to be found to supplement international codes to implement these essential principles. It is necessary, therefore, to begin negotiations with foreign collaborators to supplement international codes to meet requirements of the Common Rule which is intended to ensure the protection of human subjects. Careful review is necessary to make certain that procedural requirements under the Common Rule are met and research can go forward.

Attachment 3, "Points to Consider" provide a framework in which appropriate evaluation of research proposals submitted by foreign governments and institutions can be accomplished. The Common Rule requires that entities that receive Federal support to conduct research involving human subjects provide an Assurance document that specifies how the provisions of the Common Rule will be implemented. Attachment 4 is a sample "Assurance of Protection for Human Subjects in International Research" as a model document for foreign governments or institutions involved in research supported by a Federal Department or Agency. This document contains all the essential elements required by the Common Rule and can be used as written to assure acceptable procedures. Many institutions will choose to base their Assurance on this sample document; however, should the institution prefer to develop its own Assurance document, the sample document may be used for a

point by point comparison with the locally-developed document to determine the areas needing further discussion, negotiation, revision or exemption. Attachment 3 also contains a narrative format that alternatively could be used as the basis for preparing an assurance document.

It is important to recognize that the requirements of the Common Rule are minimum standards. The issue of protection of human subjects is one that can not be entirely categorized and addressed by regulations. The principles set down by the policy must be taken into consideration in light of the culture and best interests of the subject. While exemptions from certain requirements of the Common Rule may decrease the cost, difficulty, political or social complexity of performing a study, these considerations do not offer sufficient justification to waive protections afforded the subject.

Although it will be the rare exception, circumstances may exist wherein the best interests of the subject are served by waiver of one or more of the requirements of the Common Rule. Procedures for granting such a waiver must be established by each Department or Agency adopting the Common Rule. The Working Group on International Issues of the Human Subjects Research Subcommittee of the Committee on Life Sciences and Health, Federal Coordinating Council on Science Engineering and Technology, is available to Federal Departments and Agencies to provide consultation concerning the waiver and other interpretation of Federal law and regulation in the area of protections of human subject. The Working Group will offer recommendations to responsible officials regarding any issues or questions that arise in this evolving and complex area. It is important to note that the recommendations of the Working Group are advisory in nature and neither limit nor usurp the authority or responsibility of the Federal Department or Agency officials as designated in the Common Rule. The DoD representative to the Working Group and Committee are appointed by the Director, Environmental and Life Sciences, Office of the Director, Defense Research and Engineering, Pentagon Rm 3D129. Questions or comments should be referred to this office through the appropriate Service Component Activity.

May 1993

PROTECTION OF HUMAN SUBJECTS IN STUDIES  
CONDUCTED OUTSIDE THE UNITED STATES

POINTS TO CONSIDER

A. Are Human Subjects Involvement?

1. Does the proposed research provide a detailed description of the involvement of human subjects/ What are the characteristics of the subject population, including the anticipated age range and health status? What is the gender and racial/ethnic composition? Are fetuses, pregnant women, children, prisoners, institutionalized or other vulnerable persons involved?
2. Are data about living, identifiable individuals involved in the form of specimens, records, or other data?
3. What are the potential physical, psychological, social, legal or other risks? What is the likelihood of these risks occurring?
4. Are there alternative treatments?
5. What procedures are there to minimize risks, including confidentiality? What kind of medical or professional interaction is available in the case of adverse effects to subjects? Are there methods to monitor data collected to ensure safety of participants?
6. Are the risks to subjects reasonable in relation to anticipated benefits to subjects and to knowledge expected to result from the research?

B. Is the Research Exempt? On What Basis?

C. Institutional Review Board (IRB)

1. Is there a domestic institutional review board that will review the research?

and/or

Is there a local group that fulfill the criteria and perform the functions of an institutional review board? If so, where is it located?

2. Who are the members? Can the membership criteria in Sec. 107 of the Common Rule (32 CFR 219.107) be fulfilled?

3. Are there any conflicts of interest? For example, the investigator(s) must not be a member for purposes of his/her research, vote, or be present during IRB proceedings except to present his/her research and to answer questions.
4. Does/will the IRB assess:
  - Risks to subjects and how they can be minimized?
  - Risk/benefit ratios?
  - Equitable selection of subjects?
  - Informed consent process, context and documentation?
  - Confidentiality?
  - Special protections for vulnerable subjects?
  - Does/will the board meet as often as needed and at least annually?
  - Does/will the board keep minutes and records?
  - Does the board have sufficient autonomy and authority to be able to disapprove a protocol or to take action to suspend or terminate a protocol?

D. Reporting

1. How will the research institution report to the sponsor or agency (and to the IRB) unanticipated problems involving risks to human subjects, instances of serious noncompliance or suspension or termination of IRB approval?

E. Informed Consent

1. What is the process to inform subjects about the study?
2. Are all required elements of informed consent included in the process? If not, why not?
3. Is there any exculpatory language?
4. Will a short form or long form be used?
5. Where will documents be kept (if applicable)?
6. Is there a provision to give each participant an informed consent document (if applicable)?

7. If informed consent or parts of it are waived, can this be justified? For example, is the study minimal risk? and will waiver or alteration affect the rights and/or welfare of the subjects? and could the research not be practically carried out without alteration or waiver? and, if appropriate, will subjects be provided with additional information after the study? Clinical research involving Food and Drug Administration (FDA) regulated products must meet the requirements of 21 CFR Part 50, which does not include a waiver provision for informed consent.

F. Documentation/Assurances

Does/will the institution provide accurate documentation addressing the following?

1. A statement of principles governing protection of human subjects in the institution in protecting human subjects?
2. The institutional review board and its membership?
3. The procedures it will follow to conduct initial and continuing review and report findings and noncompliance, and review changes to the protocol?
4. The name of the responsible official who will act for the institution in protecting human subjects?

G. Additional Considerations - Based on Experience in Implementation:

1. It is important to emphasize that human subjects protections are important during the initial formulation of research. Participants need to be aware that there are requirements for descriptions, analysis, review, and documentation.
2. Situations which result in conflicts of interests on an IRB often arise when institutions assemble an IRB with the investigator(s) as a member. Or, if the IRB is the same group that formulates and endorses the scientific approach for the proposed research, there is an inherent conflict of interest. This type of situation should be discussed during initial discussions with foreign collaborators.
3. Informed consent procedures do allow some flexibility in documentation and information given, but justifications for flexibility must be carefully delineated.

4. Permission from community and/or tribal leaders may be necessary for the success of the project, but it must not substitute for individual informed consent. Waiver of individual consent may be made if conditions in 32 CFR 219.116 are met and approved by the IRB.

**QUESTIONS FOR FOREIGN INSTITUTIONS  
NARRATIVE FORMAT FOR PROVIDING AN ASSURANCE OR DETERMINING  
AT LEAST EQUIVALENT PROTECTIONS**

1. Please describe what principles govern your institution that address protecting the rights and welfare of human subjects of research (e.g. Declaration of Helsinki, Council of International Organizations of Medical Sciences Proposed Guidelines).
2. Please describe the institutional review board (IRB; group to protect human subjects) in your institution which can act to review this protocol to protect human subjects? The IRB must be able to address the following concerns: Minimal risk to participants; risks to participants and benefits to participants and others; fair selection of participants; special protections for vulnerable participants; informed consent of participants and how this will be documented; monitoring data for safety; confidentiality of data.
3. Please describe the membership of the IRB. Who serves as chairperson? Who are the members and their educational degrees and affiliations: (The IRB should include at least five persons: at least one unaffiliated with the institution; one scientist; one non-scientist; both men and women; someone with expertise about the research and who knows about the community(ies) from which participants will be drawn.) Note that the principal investigator or family members will not be part of the IRB proceeding or vote.
4. Please describe how the IRB will conduct its initial and continuing review and how the IRB will be informed promptly of any changes contemplated in the protocol.
5. Please describe the informed consent process and provide the document(s) to be used to advise participants about the research and seek their consent.

If informed consent is not obtained via a written document, please describe how the consent will be obtained. There must be a witness to the oral presentation to sign the document containing the information presented to the participant.

If informed consent is not sought or all the required elements are not addressed, please indicate the conditions that the IRB cites that are appropriate to justify waiving consent or specific elements.

6. Please describe how you will maintain the records (copies of research protocols; minutes; review records; correspondence; IRB members, degrees and affiliations; procedures; statements of new findings to give to participants).
7. Please describe how the IRB, your institution, and this research sponsor or U.S. agency will be informed of any serious or continuing noncompliance with human subjects protections or if the IRB has suspended or withdrawn its approval.
8. Please provide the signature of the institutional official responsible for this project and for making sure that human subjects are protected.

May 1993



research subjects who may be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disable persons, or economically or educationally disadvantaged persons.

**PART 2  
HUMAN SUBJECT PROTECTIONS FOR RESEARCH  
SUPPORTED BY THE UNITED STATES GOVERNMENT**

**I. Applicability**

Part 2 of this Assurance applies only to the following research project which is conducted or sponsored by this institution and supported by the United States Government:

Project title: \_\_\_\_\_

Project number: \_\_\_\_\_

Project Investigator/Director \_\_\_\_\_

**II. Institutional Responsibilities**

- A. This institution recognizes that all human subjects research supported by the United States Government, including the project referenced above, must be conducted in accordance with the United States Federal Policy for the Protection of Human Research Subjects.
- B. The Institutional Review Board (IRB) listed in Attachment A has been designated to be responsible for the initial and continuing review of the project referenced above. The IRB includes as least five persons, including at least one scientist, one non-scientist, and one person not otherwise affiliated with the institution. Every nondiscriminatory effort has been made to include both women and men. The IRB also includes persons who are sensitive to the concerns of the population form which subjects will be recruited.
- C. Provisions have been made to provide both meeting space for the IRB and sufficient staff to support the IRB's review and record keeping duties.

**III. IRB Responsibilities**

- A. The project referenced above has been and will be reviewed at convened meetings at which a majority of IRB members are present. A majority vote of those members

present at the meeting is required for approval. The research investigators and their family members may not participate in IRB proceedings except to provide information requested by the IRB.

- B. The IRB used the following criteria to determine that protections for human research subjects in this project are adequate:
  - (1) Risks to subjects are minimized.
  - (2) Risks to subjects are reasonable in relation to anticipated benefits.
  - (3) Selection of subjects is equitable.
  - (4) When appropriate, the data collected will be monitored during the course of the study to ensure safety of subjects.
  - (5) Privacy of subjects and confidentiality of data are protected.
  
- C. The IRB has determined that legally effective informed consent will be obtained under circumstances that provide sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence. Copies of all informed consent documents for this project will be provided.
  
- D. The IRB will review, and have the authority to approve, require modification in, or disapprove project changes.
  
- E. Continuing reviews by the IRB will be conducted at intervals appropriate to the degree of risk, but not less than once per year. The IRB may be called into an interim review session by the Chairperson at the request of any IRB member or Institutional Official to consider any matter concerned with the rights and welfare of any subject.
  
- F. The IRB will maintain documentation of its activities to include copies of research protocols, minutes of IRB meetings and continuing review records, correspondence with investigators, IRB membership with degrees and affiliations, IRB operating procedures, and statements of new findings provided to subjects. This documentation will be retained for at least three years after the completion of the project and will be accessible for inspection and copying by the supporting United States Government Agency.
  
- G. The IRB will report promptly to appropriate institutional officials and to the supporting United States Government Agency:
  - (1) Any unanticipated problems or injuries involving risk

- to subjects or others.
- (2) Any serious or continuing noncompliance with this Assurance or with the requirements or determinations of the IRB.
  - (3) Any changes in this project which are reviewed and approved by the IRB.
  - (4) Any suspension or termination of IRB approval.

#### IV. Responsibilities of Project Investigators/Directors

- A. Project investigators/directors accept their responsibility to comply with the stipulations of the IRB and with the terms of this Assurance.
- B. Project investigators/directors will report promptly to the IRB proposed changes in this project, and changes will not be initiated without IRB review and approval except where necessary to eliminate apparent immediate hazards to the subjects.
- C. Project investigators/directors will report promptly to the IRB any unanticipated problems or injuries involving risks to subjects or others.

**PART 3  
INSTITUTIONAL ENDORSEMENT AND CERTIFICATION**

Project Title: \_\_\_\_\_

Project number: \_\_\_\_\_

Project Investigator/Director: \_\_\_\_\_

Date of IRB Approval: \_\_\_\_\_

The officials signing below assure that the project referenced above was approved by the IRB on the date indicated and that the project will be conducted in accordance with all provision of this Assurance and of the United States Federal Policy for the Protection of Human Research Subjects.

**I. Authorized Official of the Institution Providing This Assurance**

Signature: \_\_\_\_\_ Date: \_\_\_\_\_

Name \_\_\_\_\_

Title \_\_\_\_\_

Address \_\_\_\_\_

\_\_\_\_\_  
\_\_\_\_\_  
Telephone: \_\_\_\_\_

**II. Authorized Official of the Institution with the IRB  
(Required only if different from the institution listed above)**

Signature: \_\_\_\_\_ Date: \_\_\_\_\_

Name \_\_\_\_\_

Title \_\_\_\_\_

Address \_\_\_\_\_

\_\_\_\_\_  
\_\_\_\_\_  
Telephone: \_\_\_\_\_

**III. IRB Chairperson**

Name \_\_\_\_\_

Title \_\_\_\_\_

Address \_\_\_\_\_

\_\_\_\_\_  
\_\_\_\_\_  
Telephone: \_\_\_\_\_

PART 4  
FEDERAL COMPONENT AGENCY APPROVAL

Project Title: \_\_\_\_\_

Project number: \_\_\_\_\_

Project Investigator/Director: \_\_\_\_\_

Date of IRB Approval: \_\_\_\_\_

All parts of this Assurance are in compliance with the requirements of the Federal Policy for the Protection of Human Research Subjects.

**Federal Component Agency Approving Official**

Signature: \_\_\_\_\_ Date: \_\_\_\_\_

Name \_\_\_\_\_

Title \_\_\_\_\_

Address \_\_\_\_\_

\_\_\_\_\_  
\_\_\_\_\_

Telephone: \_\_\_\_\_

ASSURANCE NUMBER \_\_\_\_\_

NOTE: The period for which this document is approved should be defined in accordance with each Department's or Agency's policies.

INSTITUTIONAL REVIEW BOARD (IRB) MEMBERSHIP

NAME OF IRB AGENCY OR COMMAND \_\_\_\_\_

Address and Phone No Chairperson only \_\_\_\_\_  
 \_\_\_\_\_  
 \_\_\_\_\_  
 \_\_\_\_\_

Members' Names			Highest Degree Earned	Scientific Specialty	Affiliation with Institution (Yes or No)
First	MI	Last			
(1)					
(2)					
(3)					
(4)					

- (1) Denotes Chairperson
- (2) Denotes IRB members
- (3) Denotes IRB alternates to member
- (4) Denotes non-voting IRB attendee (expert or technical expertise)

WORLD MEDICAL ASSOCIATION DECLARATION OF HELSINKI  
Recommendations Guiding Physicians  
in Biomedical Research Involving Human Subjects

Adopted by the 18th World Medical Assembly  
Helsinki, Finland, June 1964

and amended by the

29th World Medical Assembly  
Tokyo, Japan, October 1975

35th World Medical Assembly  
Venice, Italy, October 1983  
and the

41st World Medical Assembly  
Hong Kong, September 1989

INTRODUCTION

It is the mission of the physician to safeguard the health of the people. His or her knowledge and conscience are dedicated to the fulfillment of this mission.

The Declaration of Geneva of the World Medical Association binds the physician with the words, "The health of my patient will be my first consideration," and the International Code of Medical Ethics declares that, "A physician shall act only in the patient's interest when providing medical care which might have the effect of weakening the physical and mental condition of the patient."

The purpose of biomedical research involving human subjects must be to improve diagnostic, therapeutic and prophylactic procedures and the understanding of the etiology and pathogenesis of disease.

In current medical practice, most diagnostic, therapeutic or prophylactic procedures involve hazards. This applies especially to biomedical research.

Medical progress is based on research which ultimately must rest in part on experimentation involving human subjects.

In the field of biomedical research a fundamental distinction must be recognized between medical research in which the aim is essentially diagnostic or therapeutic for a patient, and medical research in which the essential object is purely scientific and without implying direct diagnostic or therapeutic value to the person subjected to the research.

Special caution must be exercised in the conduct of research which may affect the environment, and the welfare of animals used for research must be respected.

Because it is essential that the results of laboratory experiments be applied to human beings to further scientific knowledge and to help suffering humanity, the World Medical Association has prepared the following recommendations as a guide to every physician in biomedical research involving human subjects. They should be kept under review in the future. It must be stressed that the standards as drafted are only a guide to physicians all over the world. Physicians are not relieved from criminal, civil, and ethical responsibilities under the laws of their own countries.

## I. BASIC PRINCIPLES

1. Biomedical research involving human subjects must conform to generally accepted scientific principles and should be based on adequately performed laboratory and animal experimentation and on a thorough knowledge of the scientific literature.
2. The design and performance of each experimental procedure involving human subjects should be clearly formulated in an experimental protocol which should be transmitted for consideration, comment and guidance to a specially appointed committee independent of the investigator and the sponsor provided that this independent committee is in conformity with the laws and regulations of the country in which the research experiment is performed.
3. Biomedical research involving human subjects should be conducted only by scientifically qualified persons and under the supervision of a clinically competent medical person. The responsibility for the human subject must always rest with a medically qualified person and never rest on the subject of the research, even though the subject has given his or her consent.
4. Biomedical research involving human subjects cannot legitimately be carried out unless the importance of the objective is in proportion to the inherent risk to the subject.
5. Every biomedical research project involving human subjects should be preceded by careful assessment of predictable risks in comparison with foreseeable benefits to the subject or to others. Concern for the interests of the subject must always prevail over the interests of science and society.
6. the right of the research subject to safeguard his or her integrity must always be respected. Every precaution should be taken to respect the privacy of the subject and to minimize the impact of the study on the subject's

physical and mental integrity and on the personality of the subject.

7. Physicians should abstain from engaging in research projects involving human subjects unless they are satisfied that the hazards involved are believed to be predictable. Physicians should cease any investigation if the hazards are found to outweigh the potential benefits.
8. In publication of the results of his or her research, the physician is obligated to preserve the accuracy of the results. Reports of experimentation not in accordance with the principles laid down in this Declaration should not be accepted for publication.
9. In any research on human beings, each potential subject must be adequately informed of the aims, methods, anticipated benefits and potential hazards of the study and the discomfort it may entail. He or she should be informed that he or she is at liberty to abstain from participation in the study and that he or she is free to withdraw his or her consent to participation at any time. The physician should then obtain the subject's freely-given informed consent, preferably in writing.
10. When obtaining informed consent for the research project, the physician should be particularly cautious if the subject is in a dependent relationship to him or her or may consent under duress. In that case, the informed consent should be obtained by a physician who is not engaged in the investigation and who is completely independent of this official relationship.
11. In case of legal incompetence, informed consent should be obtained from the legal guardian in accordance with national legislation. Where physical or mental incapacity makes it impossible to obtain informed consent, or when the subject is a minor, permission from the responsible relative replaces that of the subject in accordance with national legislation.  
  
Whenever the minor child is in fact able to give a consent, the minor's consent must be obtained in addition to the consent of the minor's legal guardian.
12. The research protocol should always contain a statement of the ethical considerations involved and should indicate that the principles enunciated in the present Declaration are complied with.

## **II. MEDICAL RESEARCH COMBINED WITH PROFESSIONAL CARE (Clinical Research)**

1. In the treatment of the sick person, the physician must be free to use a new diagnostic and therapeutic measure, if in his or her judgement it offers hope of saving life, reestablishing health or alleviating suffering.
2. The potential benefits, hazards and discomfort of a new method should be weighed against the advantages of the best current diagnostic and therapeutic methods.
3. In any medical study, every patient, including those of a control group (if any), should be assured of the best proven diagnostic and therapeutic method.
4. The refusal of the patient to participate in a study must never interfere with the physician-patient relationship.
5. If the physician considers it essential not to obtain informed consent, the specific reasons for this proposal should be stated in the experimental protocol for transmission to the independent committee (Section I.2)
6. The physician can combine medical research with professional care, the objective being the acquisition of new medical knowledge, only to the extent that medical research is justified by its potential diagnostic or therapeutic value for the patient.

## **III. NON-THERAPEUTIC BIOMEDICAL RESEARCH INVOLVING HUMAN SUBJECTS (Non-Clinical Biomedical Research)**

1. In the purely scientific application of medical research carried out on a human being, it is the duty of the physician to remain the protector of the life and health of that person on whom biomedical research is being carried out.
2. The subjects should be volunteers, either healthy persons or patients from whom the experimental design is not related to the patient's illness.
3. The investigator or the investigating team should discontinue the research if in his/her or their judgement it may, if continued, be harmful to the individual.
4. In research on man, the interest of science and society should never take precedence over considerations related to the well-being of the subject.

THIS IS A SAMPLE DoD SINGLE PROJECT ASSURANCE (SPA) FOR AN INSTITUTION WHICH CURRENTLY DOES NOT HAVE A MULTIPLE PROJECT ASSURANCE (MPA) ON FILE WITH OPRR OR DOD COMPONENT ACTIVITY

FULL BOARD REVIEW REQUIRED OF IRB

Using this Sample, type on Organizational Letterhead supplying where indicated, information specific to the proposed research activity and your Organization, including the required certification on the endorsement page.

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(Name of Institution)

Assurance of Compliance with DoD Regulations for Protection of Human Research Subjects

PART 1

(Name of Institution), hereafter known as the "institution", hereby gives assurance that it shall comply with the Department of Defense (DoD) Regulations for the Protection of Human Research Subjects, Title 32, Code of Federal Regulations, Part 219 (32 CFR 219) revised as of July 1, 1993, as specified below.

I. Statement of Principles and Policies

A. Ethical Principles

1. This institution is guided by the ethical principles regarding all research involving humans as subjects as set forth in the report of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research entitled, Ethical Principles and Guidelines for the Protection of Human Subjects of Research (the "Belmont Report"). In addition, the requirements set forth in 32 CFR 219 shall be met for all applicable DoD-supported research.

B. Institutional Policy

1. Except for research in which the only involvement of human subjects is in one or more of the categories exempted or waived under 32 CFR 219.101(b)(1-6) or 219.101(e) of the DoD regulations, this policy is applicable to all research involving human subjects, and all other activities which even in part involve such research, if either:

a. the research is sponsored by this institution, or

- b. the research is conducted by or under the direction of any employee or agent of this institution in connection with his or her institutional responsibilities, or
  - c. the research is conducted by or under the direction of any employee or agent of this institution using any property or facility of this institution, or
  - d. the research involves the use of this institution's non-public information to identify or contact human research subjects or prospective subjects.
2. This institution acknowledges and accepts its responsibilities for protecting the rights and welfare of human subjects or research covered by this policy.
  3. This institution assures that before human subjects are involved in research covered by this policy, proper consideration shall be given to:
    - a. the risks to the subjects,
    - b. the anticipated benefits to the subjects and others
    - c. the importance of the knowledge that may reasonably be expected to result, and
    - d. the informed consent process to be employed.
  4. This institution acknowledges that it bears full responsibility for the performance of all research involving human subjects, covered by this policy.
  5. This institution bears full responsibility for complying with federal, state, or local laws as they may relate to research covered by this policy.
  6. This institution encourages and promotes constructive communication among the research administrator, department heads, research investigators, clinical care staff, human subjects, and institutional officials as a means of maintaining a high level of awareness regarding the safeguarding of the rights and welfare of the subjects.
  7. This institution shall exercise appropriate administrative overview carried out at least annually to ensure that its



review session by the Chairperson at the request of any IRB member or Institutional Official to consider any matter concerned with the rights and welfare of any subject.

- F. The IRB shall prepare and maintain adequate documentation of its activities in accordance with 32 CFR 219.115.
- G. The IRB shall report promptly to institutional officials and the appropriate Service Oversight Office:
  - a. any serious or continuing noncompliance by investigators with the requirements of the IRB, and
  - b. any suspension or termination of IRB approval.
- H. The IRB shall report promptly to institutional officials any information received concerning:
  - a. injuries to human subjects,
  - b. unanticipated problems involving risks to subjects or others, and
  - c. any changes in this research activity which are reviewed and approved by the IRB.

## II. Research Investigator Reporting Responsibilities

- A. Research investigators shall report promptly to the IRB proposed changes in this research activity and the changes shall not be initiated without IRB review and approval except where necessary to eliminate apparent immediate hazards to the subjects.
- B. Research investigators shall report promptly to the IRB any unanticipated problems involving risks to subjects and others.

## III Institutional Responsibilities

- A. This institution has provided and shall continue to provide both meeting space for the IRB and sufficient staff to support the IRB's review and record keeping duties.
- B. This institution shall report promptly to the appropriate Service Oversight Office:





INSTITUTIONAL REVIEW BOARD (IRB) MEMBERSHIP

NAME OF IRB AGENCY OR COMMAND \_\_\_\_\_

Address and Phone No Chairperson only \_\_\_\_\_  
 \_\_\_\_\_  
 \_\_\_\_\_

Members' Names			Highest Degree Earned	Scientific Specialty	Affiliation with Institution (Yes or No)
First	MI	Last			
(1)					
(2)					
(3)					
(4)					

(1) Denotes Chairperson  
 (2) Denotes IRB members

(3) Denotes IRB alternates to member  
 (4) Denotes non-voting IRB attendee (expert or technical expertise)

THIS IS A MODIFIED SAMPLE DoD SINGLE PROJECT ASSURANCE (SPA) FOR AN INSTITUTION UTILIZING THE INSTITUTIONAL REVIEW BOARD (IRB) OF ANOTHER INSTITUTION. THE INSTITUTION WITH AN IRB MUST HAVE A MULTIPLE PROJECT ASSURANCE (MPA) ON FILE WITH OPRR OR DoD COMPONENT ACTIVITY, OR MUST SUBMIT A SINGLE PROJECT ASSURANCE (SPA) FOR OPRR OR DoD COMPONENT APPROVAL

---

(Name of Institution)

Assurance of Compliance with DoD Regulations for  
Protection of Human Research Subjects

PART 1

(Name of Institution), hereafter known as the "institution", hereby gives assurance that it shall comply with the Department of Defense (DoD) Regulations for the Protection of Human Research Subjects, Title 32, Code of Federal Regulations, Part 219 (32 CFR 219) revised as of July 1, 1993, as specified below.

I. Statement of Principles and Policies

A. Ethical Principles

1. This institution is guided by the ethical principles regarding all research involving humans as subjects as set forth in the report of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research entitled, Ethical Principles and Guidelines for the Protection of Human Subjects of Research (the "Belmont Report"). In addition, the requirements set forth in 32 CFR 219 shall be met for all applicable DoD-supported research.

B. Institutional Policy

1. Except for research in which the only involvement of human subjects is in one or more of the categories exempted or waived under 32 CFR 219.101(b)(1-6) or 219.101(e) of the DoD regulations, this policy is applicable to all research involving human subjects, and all other activities which even in part involve such research, if either:
  - a. the research is sponsored by this institution, or

- b. the research is conducted by or under the direction of any employee or agent of this institution in connection with his or her institutional responsibilities, or
  - c. the research is conducted by or under the direction of any employee or agent of this institution using any property or facility of this institution, or
  - d. the research involves the use of this institution's non-public information to identify or contact human research subjects or prospective subjects.
2. This institution acknowledges and accepts its responsibilities for protecting the rights and welfare of human subjects or research covered by this policy.
  3. This institution assures that before human subjects are involved in research covered by this policy, proper consideration shall be given to:
    - a. the risks to the subjects,
    - b. the anticipated benefits to the subjects and others
    - c. the importance of the knowledge that may reasonably be expected to result, and
    - d. the informed consent process to be employed.
  4. This institution acknowledges that it bears full responsibility for the performance of all research involving human subjects, covered by this policy.
  5. This institution bears full responsibility for complying with federal, state, or local laws as they may relate to research covered by this policy.
  6. This institution encourages and promotes constructive communication among the research administrator, department heads, research investigators, clinical care staff, human subjects, and institutional officials as a means of maintaining a high level of awareness regarding the safeguarding of the rights and welfare of the subjects.
  7. This institution shall exercise appropriate administrative overview carried out at least annually to ensure that its



shall be obtained in a manner and method which meets the requirements of 32 CFR 219, and in cases of research involving protected classes of individuals 45 CFR 46, Subparts B,C, and D.

- E. The IRB shall review, and have the authority to approved, require modification in, or disapprove changes proposed in this research activity.
- F. The next scheduled meeting of the IRB for review of this activity shall be (insert date no later than one year from last review). The IRB may be called into an interim review session by the Chairperson at the request of any IRB member or Institutional Official to consider any matter concerned with the rights and welfare of any subject.
- G. The IRB shall prepare and maintain adequate documentation of its activities in accordance with 32 CFR 219.115.
- H. The IRB shall report promptly to institutional officials and the appropriate Service Oversight Office:
  - a. any serious or continuing noncompliance by investigators with the requirements of the IRB, and
  - b. any suspension or termination of IRB approval.
- I. The IRB shall report promptly to institutional officials any information received concerning:
  - a. injuries to human subjects,
  - b. unanticipated problems involving risks to subjects or others, and
  - c. any changes in this research activity which are reviewed and approved by the IRB.

## II. Research Investigator Reporting Responsibilities

- A. Research investigators shall report promptly to the IRB proposed changes in this research activity and the changes shall not be initiated without IRB review and approval except where necessary to eliminate apparent immediate hazards to the subjects.
- B. Research investigators shall report promptly to the IRB any unanticipated problems involving risks to subjects and others.





Service/DoD Approving Official

Signature \_\_\_\_\_ Date \_\_\_\_\_

Name and Title \_\_\_\_\_

Service/DoD Address \_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

Phone number \_\_\_\_\_

ASSURANCE NO. \_\_\_\_\_

**INSTITUTIONAL REVIEW BOARD (IRB) MEMBERSHIP**

NAME OF IRB AGENCY OR COMMAND \_\_\_\_\_

Address and Phone No Chairperson only \_\_\_\_\_  
 \_\_\_\_\_  
 \_\_\_\_\_  
 \_\_\_\_\_

Members' Names			Highest Degree Earned	Scientific Specialty	Affiliation with Institution (Yes or No)
First	MI	Last			
(1)					
(2)					
(3)					
(4)					

(1) Denotes Chairperson  
 (2) Denotes IRB members

(3) Denotes IRB alternates to member  
 (4) Denotes non-voting IRB attendee (expert or technical expertise)

## GENERAL GUIDANCE ON THE USE OF ANOTHER INSTITUTION'S IRB

Each approved Single Project Assurance (SPA) designates an Institutional Review Board (IRB) which is authorized to review and approve cooperative protocols. However, though it may be permissible under 32 CFR 219.114 for an institution to rely on an IRB of another DoD Component Agency approved institution for protocol review, institutions planning such an arrangement should seek prior guidance from the appropriate DoD Component Agency to avoid unnecessary delays. It is in the best interests of institutions to appreciate that review by another's qualified IRB (i.e. DoD Component agency approved) raises questions about membership qualifications that would likely be inherently satisfied when reviews are confined to protocols conducted in the IRB's own institution. Local laws, institutional policies and constraints, professional and community standards, and population differences are examples of pertinent local factors that can influence the setting of research (refer 32 CFR 219.103(d), 219.107(a), and 219.111(a)(3)). For example, the considered opinion of an IRB of one institution may be blind to information that would alter its decision for another where:

- institutions draw from culturally dissimilar patient populations;
- institutions are located in different states or other geographical subdivision with varied legal or regulatory constraints;
- institutions are not accustomed to each other Services operational policies, constraints, procedures, or commitments; or
- there is uncertain satisfaction of drug control responsibilities, or other FDA requirements.

Apparent efficiencies of such review to avoid perceived duplication of effort may be shortsighted if detached from concomitant review of the setting in which such protocols are to be conducted. Accordingly, reliance on another IRB should not be considered lightly. In spite of a joint willingness between institutions, DoD Component agencies may not approve a proposed arrangement if there are circumstances that are not appropriate. Therefore, such plans should include consultation with the appropriate DoD Component agency(s) to avoid delays.

Several options for IRB arrangements are available which comply with the letter and intent of both 32 CFR 219.114 and the regulations as a whole.

Institutional sites that are geographically close enough to comfortably contribute membership to a common IRB can share in bearing the costs of operations while simultaneously providing reviews for protocols that may be used by physicians at some or all of the sites. This approach results in one IRB that can be equally cited as their own IRB of record by all sites that contribute to its membership.

A second approach is for one IRB with unique expertise, a legal or administrative preference for involvement, or otherwise to host reviews for other nearby institutional sites with consultant representation from each site present for all initial and continuing reviews of protocols jointly used by these sites. In this approach only the hosting institution has its own IRB. The other sites rely on another's IRB but in such a way as not to defeat the intent of 32 CFR 219.

The most obvious way to fully comply with the regulations is for each site to host its own IRB. An institution that has a standing IRB which is qualified to perform reviews for a specified research activity would be expected to do or justify not doing so before approval would be considered for other options. If a local hospital or research facility exists with an applicable DoD Component agency approved Assurance for the research in question, a second institution may seek permission to rely upon such an IRB when justified. DoD Component agencies should understand the propriety of considering and approving reliance on another's IRB when a plausible case is made apparent. For example, an IRB with a suitably diversified membership might exist at one site to host IRB reviews for another side due to: (1) the cosmopolitan nature of the host site; (2) a wide catchment area from which patients and subjects are referred to it, (3) or reasons as may otherwise be of a compelling and pertinent nature. However, institutional constraints are less easily accounted for between institutions when there is little or no intimate understanding of each other's staff, procedures, policy, practices, and legal issues. Each case deserves individual consideration.

## TIPS ON INFORMED CONSENT

The process of obtaining informed consent must comply with the requirements of 32 CFR 219.116. The documentation of informed consent must comply with 32 CFR 219.116. The following comments may help in the development of an approach and proposed language by investigators for obtaining consent and its approval by Institutional Review Boards (IRBs).

Informed consent is a process, not just a form. Information must be presented to enable persons to voluntarily decide whether or not to participate as a research subject. It is a fundamental mechanism to ensure respect for persons through provisions of thoughtful consent for a voluntary act. The procedures used in obtaining informed consent should be designed to educate the subject population in terms that they can understand. Therefore, informed consent language and its documentation (especially explanations of the study's purpose, duration, experimental procedures, alternatives, risks, and benefits) must be written in "lay language", (i.e. understandable to the people being asked to participate). The written presentation of information is used to document the basis for consent and for the subjects' future reference. The consent document should be revised when deficiencies are noted or when additional information will improve the consent process.

Avoid first person (e.g., "I understand that ... "). This phraseology can be interpreted as suggestive, may be relied upon as a substitution for sufficient factual information, and can constitute coercive influence over a subject. Use of scientific jargon and legalese is not appropriate. Think of the document primarily as a teaching tool and not as a legal instrument.

Describe the overall experience that will be encountered. Explain the research activity, how it is experimental (e.g., a new drug, extra tests, separate research records, or nonstandard means of management, such as flipping a coin for random assignment or other design issues). Inform the human subjects of the reasonably foreseeable harms, discomforts, inconvenience and risks that are associated with the research activity. If additional risks are identified during the course of the research, the consent process and documentation will require revisions to inform subjects as they are recontacted and/or newly contacted. Individuals enrolled in a study must be informed of any new information, risk assessment, etc and given the opportunity to reevaluate their continued participation in the study.

Describe the benefits that subjects may reasonably expect to encounter. There may be none other than a sense of helping the public at large. If payment is given to defray the incurred expense for participation, it must not be coercive in amount or method of distribution.

Describe any alternatives to participating in the research project. For example, in drug studies the medication(s) may be available through their family doctor or clinic without the need to volunteer for the research activity.

32 CFR 219 insist that the subject be told the extent to which their personally identifiable private information will be held in confidence. For example, some studies require disclosure of information to other parties. Some studies inherently are in need of a Certificate of Confidentiality which protects the investigator from subpoena of research records. The IRB will determine the level of adequate requirements for confidentiality in light of its mandate to ensure minimal risk and determination that the residual risks warrant involvement of subjects.

If research-related injury (i.e. physical, psychological, social, financial, or otherwise) is possible in research that is more than minimal risk (see 32 CFR 219.102(g)), an explanation must be given of whatever voluntary compensation and treatment will be provided. Note that the regulations do not limit injury to "physical injury". This is a common misinterpretation.

The regulations prohibit waiving or appearing to waive any legal rights of subjects. Therefore, for example, consent language must be carefully selected that deals with what the institution is voluntarily willing to do under circumstances, such as providing for compensation beyond the provisions of immediate or therapeutic intervention in response to a research-related injury. In short, subjects should not be given the impression that they have agreed to and are without recourse to seek satisfaction beyond the institution's voluntarily chosen limits.

The regulations provide for the identification of contact persons who would be knowledgeable to answer questions of subjects about the research, rights as a research subject, and research-related injuries. These three areas must be explicitly stated and addressed in the consent process and documentation. Furthermore, a single person is not likely to be appropriate to answer questions in all areas. This is because of potential conflicts of interest or the appearance of such. Questions about the research are frequently best answered by the investigator(s). However, questions about the

rights of research subjects or research-related injuries (where applicable) may best be referred to those not on the research team. These questions could be addressed to the IRB, an ombudsman, an ethics committee, or other informed administrative body. Therefore, each consent document can be expected to have at least two names with local telephone numbers for contacts to answer questions in these specified areas.

The statement regarding voluntary participation and the right to withdraw at any time can be taken almost verbatim from the regulations (32 CFR 219.116(a)(8)). It is important not to overlook the need to point out that no penalty or loss of benefits will occur as a result of both not participating or withdrawing at any time. It is equally important to alert potential subjects to any foreseeable consequences to them should they unilaterally withdraw while dependent on some intervention to maintain normal function.

Don't forget to ensure provision for appropriate additional requirements which concern consent. Some of these requirements can be found in sections 32 CFR 219.116(b). Additional Department of Health and Human Services (DHHS) human subject protection requirements for research involving pregnant women, prisoners, children, etc are found in 45 CFR 46.205(a)(2), 46.207(b), 46.208(b), 46.209(d), 46.305(a)(5-6), 46.408(c), and 46.409(b). The IRB may impose additional requirements that are not specifically listed in the regulations to help ensure that adequate information is presented in accordance with institutional or Service policy and local law.

May 93

# code of federal regulations

National Defense

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PARTS 190 TO 399  
Revised as of July 1, 1991



§ 219.101

- Sec. 219.110 Expedited review procedures for certain kinds of research involving no more than minimal risk, and for minor changes in approved research.
- 219.111 Criteria for IRB approval of research.
- 219.112 Review by institution.
- 219.113 Suspension or termination of IRB approval of research.
- 219.114 Cooperative research.
- 219.115 IRB records.
- 219.116 General requirements for informed consent.
- 219.117 Documentation of informed consent.
- 219.118 Applications and proposals lacking definite plans for involvement of human subjects.
- 219.119 Research undertaken without the intention of involving human subjects.
- 219.120 Evaluation and disposition of applications and proposals for research to be conducted or supported by a Federal Department or Agency.
- 219.121 (Reserved)
- 219.122 Use of Federal funds.
- 219.123 Early termination of research support: Evaluation of applications and proposals.
- 219.124 Conditions.

AUTHORITY: 5 U.S.C. 301; 42 U.S.C. 300v-1(b).

SOURCE: 56 FR 28012, 28021, June 18, 1991, unless otherwise noted.

§ 219.101 To what does this policy apply?

- (a) Except as provided in paragraph (b) of this section, this policy applies to all research involving human subjects conducted, supported or otherwise subject to regulation by any Federal department or agency which takes appropriate administrative action to make the policy applicable to such research. This includes research conducted by federal civilian employees or military personnel, except that each department or agency head may adopt such procedural modifications as may be appropriate from an administrative standpoint. It also includes research conducted, supported, or otherwise subject to regulation by the federal government outside the United States.
- (1) Research that is conducted or supported by a federal department or agency, whether or not it is regulated as defined in § 219.102(e), must comply with all sections of this policy.
- (2) Research that is neither conducted nor supported by a federal depart-

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sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

(5) Research and demonstration projects which are conducted by or subject to the approval of department or agency heads, and which are designed to study, evaluate, or otherwise examine:

- (i) Public benefit or service programs; (ii) procedures for obtaining benefits or services under those programs; (iii) possible changes in or alternatives to those programs or procedures; or (iv) possible changes in methods or levels of payment for benefits or services under those programs.

(6) Taste and food quality evaluation and consumer acceptance studies, (i) if wholesome foods without additives are consumed or (ii) if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

(c) Department or agency heads retain final judgment as to whether a particular activity is covered by this policy.

(d) Department or agency heads may require that specific research activities or classes of research activities conducted, supported, or otherwise subject to regulation by the department or agency but not otherwise covered by this policy, comply with some or all of the requirements of this policy.

(e) Compliance with this policy requires compliance with pertinent federal laws or regulations which provide additional protections for human subjects.

(f) This policy does not affect any state or local laws or regulations which may otherwise be applicable and which provide additional protections for human subjects.

(g) This policy does not affect any foreign laws or regulations which may

otherwise be applicable and which provide additional protections to human subjects of research.

(h) When research covered by this policy takes place in foreign countries, procedures normally followed in the foreign countries to protect human subjects may differ from those set forth in this policy. [An example is a foreign institution which complies with guidelines consistent with the World Medical Assembly Declaration (Declaration of Helsinki) amended (1989) issued either by sovereign states or by an organization whose function for the protection of human research subjects is internationally recognized.] In these circumstances, if a department or agency head determines that the procedures prescribed by the institution afford protections that are at least equivalent to those provided in this policy, the department or agency head may approve the substitution of the foreign procedures in lieu of the procedural requirements provided in this policy. Except when otherwise required by statute, Executive Order, or the department or agency head, notices of these actions as they occur will be published in the FEDERAL REGISTER or will be otherwise published as provided in department or agency procedures.

(i) Unless otherwise required by law, department or agency heads may waive the applicability of some or all of the provisions of this policy to specific research activities or classes of research activities otherwise covered by this policy. Except when otherwise required by statute or Executive Order, the department or agency head shall forward advance notices of these actions to the Office for Protection from Research Risks, Department of Health and Human Services (HHS), and shall also publish them in the FEDERAL REGISTER or in such other manner as provided in department or agency procedures.

<sup>1</sup> Institutions with HHS-approved assurances on file will abide by provisions of title 45 CFR part 46 subparts A-D. Some of the other Departments and Agencies have incorporated all provisions of title 45 CFR part 46 into their policies and procedures as

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ment or agency but is subject to regulation as defined in § 219.102(e) must be reviewed and approved. In compliance with § 219.101, § 219.102, and § 219.107 through § 219.117 of this policy, by an institutional review board (IRB) that operates in accordance with the pertinent requirements of this policy.

(b) Unless otherwise required by department or agency heads, research activities in which the only involvement of human subjects will be in one or more of the following categories are exempt from this policy:

- (1) Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as (i) research on regular and special education instructional strategies, or (ii) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.
- (2) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless: (i) Information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and (ii) any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.
- (3) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under paragraph (b)(2) of this section, if: (i) The human subjects are elected or appointed public officials or candidates for public office; or (ii) federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.
- (4) Research, involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these

[56 FR 28012, 28021, June 18, 1991, as amended at 56 FR 29756, June 28, 1991]

§ 219.102 Definitions.

(a) *Department or agency head* means the head of any federal department or agency or any other officer or employee of any department or agency to whom authority has been delegated.

(b) *Institution* means any public or private entity or agency (including federal, state, and other agencies).

(c) *Legally authorized representative* means an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research.

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

(e) *Research subject to regulation*, and similar terms are intended to encompass those research activities for which a federal department or agency has specific responsibility for regulating as a research activity, (for example, Investigational New Drug requirements administered by the Food and Drug Administration). It does not include research activities which are incidentally regulated by a federal department or agency solely as part of the department's or agency's broader responsibility to regulate certain types

well. However, the exemptions at 45 CFR 46.101(b) do not apply to research involving prisoners, fetuses, pregnant women, or human in vitro fertilization, subparts B and C. The exemption at 45 CFR 46.101(b)(2), for research involving survey or interview procedures or observation of public behavior, does not apply to research with children, subpart D, except for research involving observations of public behavior when the investigator(s) do not participate in the activities being observed.

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of activities whether research or non-research in nature (for example, Wage and Hour requirements administered by the Department of Labor).

(f) *Human subject* means a living individual about whom an investigator conducting research obtains

(1) Data through intervention or interaction with the individual, or

(2) Identifiable private information. *Intervention* includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes. *Interaction* includes communication or interpersonal contact between investigator and subject. "Private information" includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects.

(g) *IRB* means an institutional review board established in accordance with and for the purposes expressed in this policy.

(h) *IRB approval* means the determination of the IRB that the research has been reviewed and may be conducted at an institution within the constraints set forth by the IRB and by other institutional and federal requirements.

(i) *Minimal risk* means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

(j) *Certification* means the official notification by the institution to the supporting department or agency, in

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accordance with the requirements of this policy, that a research project or activity involving human subjects has been reviewed and approved by an IRB in accordance with an approved assurance.

§ 219.103 Assuring compliance with this policy—research conducted or supported by any Federal Department or Agency.

(a) Each institution engaged in research which is covered by this policy and which is conducted or supported by a federal department or agency shall provide written assurance satisfactory to the department or agency head that it will comply with the requirements set forth in this policy. In lieu of requiring submission of an assurance, individual department or agency heads shall accept the existence of a current assurance, appropriate for the research in question, on file with the Office for Protection from Research Risks, HHS, and approved for federalwide use by that office. When the existence of an HHS-approved assurance is accepted in lieu of requiring submission of an assurance, reports (except certification) required by this policy to be made to department and agency heads shall also be made to the Office for Protection from Research Risks, HHS.

(b) Departments and agencies will conduct or support research covered by this policy only if the institution has an assurance approved as provided in this section, and only if the institution has certified to the department or agency head that the research has been reviewed and approved by an IRB provided for in the assurance, and will be subject to continuing review by the IRB. Assurances applicable to federally supported or conducted research shall at a minimum include:

(1) A statement of principles governing the institution in the discharge of its responsibilities for protecting the rights and welfare of human subjects of research conducted at or sponsored by the institution, regardless of whether the research is subject to federal regulation. This may include an appropriate existing code, declaration, or statement of ethical principles, or a statement formulated by the institu-

tion itself. This requirement does not preempt provisions of this policy applicable to department- or agency-supported or regulated research and need not be applicable to any research exempted or waived under § 219.101 (b) or (l).

(2) Designation of one or more IRBs established in accordance with the requirements of this policy, and for which provisions are made for meeting the IRB's review and recordkeeping duties.

(3) A list of IRB members identified by name; earned degrees; representative capacity; indications of experience such as board certifications, licenses, etc., sufficient to describe each member's chief anticipated contributions to IRB deliberations; and any employment or other relationship between each member and the institution; for example: full-time employee, part-time employee, member of governing panel or board, stockholder, paid or unpaid consultant. Changes in IRB membership shall be reported to the department or agency head, unless in accordance with § 219.103(a) of this policy, the existence of an HHS-approved assurance is accepted. In this case, change in IRB membership shall be reported to the Office for Protection from Research Risks, HHS.

(4) Written procedures which the IRB will follow (i) for conducting its initial and continuing review of research and for reporting its findings and actions to the investigator and the institution; (ii) for determining which projects require review more often than annually and which projects need verification from sources other than the investigators that no material changes have occurred since previous IRB review; and (iii) for ensuring prompt reporting to the IRB of proposed changes in a research activity, and for ensuring that such changes in approved research, during the period for which IRB approval has already been given, may not be initiated without IRB review and approval except when necessary to eliminate apparent immediate hazards to the subject.

(5) Written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, and the

department or agency head of (1) any unanticipated problems involving risks to subjects or others or any serious or continuing noncompliance with this policy or the requirements or determinations of the IRB and (ii) any suspension or termination of IRB approval.

(c) The assurance shall be executed by an individual authorized to act for the institution and to assume on behalf of the institution the obligations imposed by this policy and shall be filed in such form and manner as the department or agency head prescribes.

(d) The department or agency head will evaluate all assurances submitted in accordance with this policy through such officers and employees of the department or agency and such experts or consultants engaged for this purpose as the department or agency head determines to be appropriate. The department or agency head's evaluation will take into consideration the adequacy of the proposed IRB in light of the anticipated scope of the institution's research activities and the types of subject populations likely to be involved, the appropriateness of the proposed initial and continuing review procedures in light of the probable risks, and the size and complexity of the institution.

(e) On the basis of this evaluation, the department or agency head may approve or disapprove the assurance, or enter into negotiations to develop an approvable one. The department or agency head may limit the period during which any particular approved assurance or class of approved assurances shall remain effective or otherwise condition or restrict approval.

(f) Certification is required when the research is supported by a federal department or agency and not otherwise exempted or waived under § 219.101 (b) or (l). An institution with an approved assurance shall certify that each application or proposal for research covered by the assurance and by § 219.103 of this Policy has been reviewed and approved by the IRB. Such certification must be submitted with the application or proposal or by such later date as may be prescribed by the department or agency to which the ap-

plication or proposal is submitted. Under no condition shall research covered by § 219.103 of the Policy be supported prior to receipt of the certification that the research has been reviewed and approved by the IRB. Institutions without an approved assurance covering the research shall certify within 30 days after receipt of a request for such a certification from the department or agency, that the application or proposal has been approved by the IRB. If the certification is not submitted within these time limits, the application or proposal may be returned to the institution.

(Approved by the Office of Management and Budget under control number 9999-0020)

[56 FR 28012, 28021, June 18, 1991, as amended at 56 FR 29756, June 28, 1991]

§§ 219.104—219.106 [Reserved]

§ 219.107 IRB membership.

(a) Each IRB shall have at least five members, with varying backgrounds to promote complete and adequate review of research activities commonly conducted by the institution. The IRB shall be sufficiently qualified through the experience and expertise of its members, and the diversity of the members, including consideration of race, gender, and cultural backgrounds and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects. In addition to possessing the professional competence necessary to review specific research activities, the IRB shall be able to ascertain the acceptability of proposed research in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice. The IRB shall therefore include persons knowledgeable in these areas. If an IRB regularly reviews research that involves a vulnerable category of subjects, such as children, prisoners, pregnant women, or handicapped or mentally disabled persons, consideration shall be given to the inclusion of one or more individuals who are knowledgeable about and experienced in working with these subjects.

(b) Every nondiscriminatory effort will be made to ensure that no IRB consists entirely of men or entirely of women, including the institution's consideration of qualified persons of both sexes, so long as no selection is made to the IRB on the basis of gender. No IRB may consist entirely of members of one profession.

(c) Each IRB shall include at least one member whose primary concerns are in scientific areas and at least one member whose primary concerns are in nonscientific areas.

(d) Each IRB shall include at least one member who is not otherwise affiliated with the institution and who is not part of the immediate family of a person who is affiliated with the institution.

(e) No IRB may have a member participating in the IRB's initial or continuing review of any project in which the member has a conflicting interest, except to provide information requested by the IRB.

(f) An IRB may, in its discretion, invite individuals with competence in special areas to assist in the review of issues which require expertise beyond or in addition to that available on the IRB. These individuals may not vote with the IRB.

§ 219.108 IRB functions and operations.

In order to fulfill the requirements of this policy each IRB shall:

(a) Follow written procedures in the same detail as described in § 219.103(b)(4) and, to the extent required by, § 219.103(b)(5).

(b) Except when an expedited review procedure is used (see § 219.110), review proposed research at convened meetings at which a majority of the members of the IRB are present, including at least one member whose primary concerns are in nonscientific areas. In order for the research to be approved, it shall receive the approval of a majority of those members present at the meeting.

§ 219.109 IRB Review of Research.

(a) An IRB shall review and have authority to approve, require modifications in (to secure approval), or disapprove all research activities covered by this policy.

(b) An IRB shall require that information given to subjects as part of informed consent is in accordance with § 219.116. The IRB may require that information, in addition to that specifically mentioned in § 219.116, be given to the subjects when in the IRB's judgment the information would meaningfully add to the protection of the rights and welfare of subjects.

(c) An IRB shall require documentation of informed consent or may waive documentation in accordance with § 219.117.

(d) An IRB shall notify investigators and the institution in writing of its decision to approve or disapprove the proposed research activity, or of modifications required to secure IRB approval of the research activity. If the IRB decides to disapprove a research activity, it shall include in its written notification a statement of the reasons for its decision and give the investigator an opportunity to respond in person or in writing.

(e) An IRB shall conduct continuing review of research covered by this policy at intervals appropriate to the degree of risk, but not less than once per year, and shall have authority to observe or have a third party observe the consent process and the research.

(Approved by the Office of Management and Budget under control number 9999-0020)

§ 219.110 Expedited review procedures for certain kinds of research involving no more than minimal risk, and for minor changes in approved research.

(a) The Secretary, HHS, has established, and published as a Notice in the FEDERAL REGISTER, a list of categories of research that may be reviewed by the IRB through an expedited review procedure. The list will be amended, as appropriate after consultation with other departments and agencies, through periodic republication by the Secretary, HHS, in the FEDERAL REGISTER. A copy of the list is available from the Office for Protection from Research Risks, National Institutes of Health, HHS, Bethesda, Maryland 20892.

§ 219.111

(b) An IRB may use the expedited review procedure to review either or both of the following:

- (1) Some or all of the research appearing on the list and found by the reviewer(s) to involve no more than minimal risk,
- (2) Minor changes in previously approved research during the period (of one year or less) for which approval is authorized.

Under an expedited review procedure, the review may be carried out by the IRB chairperson or by one or more experienced reviewers designated by the chairperson from among members of the IRB. In reviewing the research, the reviewers may exercise all of the authorities of the IRB except that the reviewers may not disapprove the research. A research activity may be disapproved only after review in accordance with the non-expedited procedure set forth in § 219.108(b).

- (c) Each IRB which uses an expedited review procedure shall adopt a method for keeping all members advised of research proposals which have been approved under the procedure.
- (d) The department or agency head may restrict, suspend, terminate, or choose not to authorize an institution's or IRB's use of the expedited review procedure.

§ 219.111 Criteria for IRB approval of research.

(a) In order to approve research covered by this policy the IRB shall determine that all of the following requirements are satisfied:

- (1) Risks to subjects are minimized:
  - (i) By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and
  - (ii) whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.
- (2) Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result. In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive

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even if not participating in the research). The IRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.

(3) Selection of subjects is equitable. In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons.

(4) Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by § 219.116.

(5) Informed consent will be appropriately documented, in accordance with, and to the extent required by § 219.117.

(6) When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.

(7) When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

(b) When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.

§ 219.112 Review by institution.

Research covered by this policy that has been approved by an IRB may be subject to further appropriate review and approval or disapproval by officials of the institution. However, those officials may not approve the research if it has not been approved by an IRB.

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§ 219.113 Suspension or termination of IRB approval of research.

An IRB shall have authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to subjects. Any suspension or termination of approval shall include a statement of the reasons for the IRB's action and shall be reported promptly to the investigator, appropriate institutional officials, and the department or agency head.

(Approved by the Office of Management and Budget under control number 9999-0020)

§ 219.114 Cooperative research.

Cooperative research projects are those projects covered by this policy which involve more than one institution. In the conduct of cooperative research projects, each institution is responsible for safeguarding the rights and welfare of human subjects and for complying with this policy. With the approval of the department or agency head, an institution participating in a cooperative project may enter into a joint review arrangement, rely upon the review of another qualified IRB, or make similar arrangements for avoiding duplication of effort.

§ 219.115 IRB records.

(a) An institution, or when appropriate an IRB, shall prepare and maintain adequate documentation of IRB activities, including the following:

- (1) Copies of all research proposals reviewed, scientific evaluations, if any, that accompany the proposals, approved sample consent documents, progress reports submitted by investigators, and reports of injuries to subjects.
- (2) Minutes of IRB meetings which shall be in sufficient detail to show attendance at the meetings; actions taken by the IRB; the vote on these actions including the number of members voting for, against, and abstaining; the basis for requiring changes in or disapproving research; and a written summary of the discussion of controverted issues and their resolution.

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(3) Records of continuing review activities.

(4) Copies of all correspondence between the IRB and the investigators.

(5) A list of IRB members in the same detail as described in § 219.103(b)(3).

(6) Written procedures for the IRB in the same detail as described in § 219.103(b)(4) and § 219.103(b)(5).

(7) Statements of significant new findings provided to subjects, as required by § 219.116(b)(5).

(b) The records required by this policy shall be retained for at least 3 years, and records relating to research which is conducted shall be retained for at least 3 years after completion of the research. All records shall be accessible for inspection and copying by authorized representatives of the department or agency at reasonable times and in a reasonable manner.

(Approved by the Office of Management and Budget under control number 9999-0020)

§ 219.116 General requirements for informed consent.

Except as provided elsewhere in this policy, no investigator may involve a human being as a subject in research covered by this policy unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative. An investigator shall seek such consent only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence. The information that is given to the subject or the representative shall be in language understandable to the subject or the representative. No informed consent, whether oral or written, may include any exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence.

(a) Basic elements of informed consent. Except as provided in paragraph

(c) or (d) of this section, in seeking informed consent the following information shall be provided to each subject:

- (1) A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental;
- (2) A description of any reasonably foreseeable risks or discomforts to the subject;
- (3) A description of any benefits to the subject or to others which may reasonably be expected from the research;
- (4) A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;
- (5) A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained;
- (6) For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained;
- (7) An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject; and
- (8) A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

(b) Additional elements of informed consent. When appropriate, one or more of the following elements of information shall also be provided to each subject:

- (1) A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable;
- (2) Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent;
- (3) Any additional costs to the subject that may result from participation in the research;
- (4) The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject;
- (5) A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject; and
- (6) The approximate number of subjects involved in the study.

(c) An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth above, or waive the requirement to obtain informed consent provided the IRB finds and documents that:

- (1) The research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine:
  - (i) Public benefit of service programs;
  - (ii) procedures for obtaining benefits or services under those programs; (iii) possible changes in or alternatives to those programs or procedures; or (iv) possible changes in methods or levels of payment for benefits or services under those programs; and
- (2) The research could not practicably be carried out without the waiver or alteration.
- (d) An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth in this section, or waive the requirements to obtain informed consent provided the IRB finds and documents that:
  - (1) The research involves no more than minimal risk to the subjects;
  - (2) The waiver or alteration will not adversely affect the rights and welfare of the subjects;
  - (3) The research could not practicably be carried out without the waiver or alteration; and

(4) Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

(e) The informed consent requirements in this policy are not intended to preempt any applicable federal, state, or local laws which require additional information to be disclosed in order for informed consent to be legally effective.

(f) Nothing in this policy is intended to limit the authority of a physician to provide emergency medical care, to the extent the physician is permitted to do so under applicable federal, state, or local law.

(Approved by the Office of Management and Budget under control number 9999-0020)

§ 219.117 Documentation of informed consent.

(a) Except as provided in paragraph (c) of this section, informed consent shall be documented by the use of a written consent form approved by the IRB and signed by the subject or the subject's legally authorized representative. A copy shall be given to the person signing the form.

(b) Except as provided in paragraph (c) of this section, the consent form may be either of the following:

(1) A written consent document that embodies the elements of informed consent required by § 219.116. This form may be read to the subject or the subject's legally authorized representative, but in any event, the investigator shall give either the subject or the representative adequate opportunity to read it before it is signed; or

(2) A short form written consent document stating that the elements of informed consent required by § 219.116 have been presented orally to the subject or the subject's legally authorized representative. When this method is used, there shall be a witness to the oral presentation. Also, the IRB shall approve a written summary of what is to be said to the subject or the representative. Only the short form itself is to be signed by the subject or the representative. However, the witness shall sign both the short form and a copy of the summary, and the person actually obtaining consent shall sign a copy of

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the summary. A copy of the summary shall be given to the subject or the representative, in addition to a copy of the short form.

(c) An IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects if it finds either:

(1) That the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern; or

(2) That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.

In cases in which the documentation requirement is waived, the IRB may require the investigator to provide subjects with a written statement regarding the research.

(Approved by the Office of Management and Budget under control number 9999-0020)

§ 219.118 Applications and proposals lacking definite plans for involvement of human subjects.

Certain types of applications for grants, cooperative agreements, or contracts are submitted to departments or agencies with the knowledge that subjects may be involved within the period of support, but definite plans would not normally be set forth in the application or proposal. These include activities such as institutional type grants when selection of specific projects is the institution's responsibility; research training grants in which the activities involving subjects remain to be selected; and projects in which human subjects' involvement will depend upon completion of instruments, prior animal studies, or purification of compounds. These applications need not be reviewed by an IRB before an award may be made. However, except for research exempted or waived under § 219.101 (b) or (l), no human subjects may be involved in

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any project supported by these awards until the project has been reviewed and approved by the IRB, as provided in this policy, and certification submitted, by the institution, to the department or agency.

§ 219.119 Research undertaken without the intention of involving human subjects.

In the event research is undertaken without the intention of involving human subjects, but it is later proposed to involve human subjects in the research, the research shall first be reviewed and approved by an IRB, as provided in this policy, a certification submitted, by the institution, to the department or agency, and final approval given to the proposed change by the department or agency.

§ 219.120 Evaluation and disposition of applications and proposals for research to be conducted or supported by a Federal Department or Agency.

The department or agency head will evaluate all applications and proposals involving human subjects submitted to the department or agency through such officers and employees of the department or agency and such experts and consultants as the department or agency head determines to be appropriate. This evaluation will take into consideration the risks to the subjects, the adequacy of protection against these risks, the potential benefits of the research to the subjects and others, and the importance of the knowledge gained or to be gained.

(b) On the basis of this evaluation, the department or agency head may approve or disapprove the application or proposal, or enter into negotiations to develop an approvable one.

§ 219.121 [Reserved]

§ 219.122 Use of Federal funds.

Federal funds administered by a department or agency may not be expended for research involving human subjects unless the requirements of this policy have been satisfied.

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§ 219.123 Early termination of research support: Evaluation of applications and proposals.

(a) The department or agency head may require that department or agency support for any project be terminated or suspended in the manner prescribed in applicable program requirements, when the department or agency head finds an institution has materially failed to comply with the terms of this policy.

(b) In making decisions about supporting or approving applications or proposals covered by this policy the department or agency head may take into account, in addition to all other eligibility requirements and program criteria, factors such as whether the applicant has been subject to a termination or suspension under paragraph (a) of this section and whether the applicant or the person or persons who would direct or have directed the scientific and technical aspects of an activity has have, in the judgment of the department or agency head, materially failed to discharge responsibility for the protection of the rights and welfare of human subjects (whether or not the research was subject to federal regulation).

§ 219.124 Conditions.

With respect to any research project or any class of research projects the department or agency head may impose additional conditions prior to or at the time of approval when in the judgment of the department or agency head additional conditions are necessary for the protection of human subjects.

**EFFECTIVE DATE NOTE:** At 56 FR 28012, 28021, July 6, 1991, part 219 was revised, effective Aug. 19, 1991. For the convenience of the user of this volume, the superseded text appears as follows:

## PART 219—PROTECTION OF HUMAN SUBJECTS IN DOD-SUPPORTED RESEARCH

Sec.

219.1 Purpose.

219.2 Applicability and scope.

219.3 Definition.

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Sec.

219.4 Policy.

219.5 Responsibilities.

219.6 Procedure.

219.7 Information requirements.

**AUTHORITY:** 5 U.S.C. 301, sec. 474(a).

**SOURCE:** 48 FR 35400, Aug. 4, 1983, unless otherwise noted.

§ 219.1 Purpose.

This rule, under 45 CFR part 46 and 21 CFR parts 1-82, 300-460, and 800-895 establishes policy; assigns responsibilities; and specifies authority for protecting the rights and welfare of humans used as subjects of study in DoD-supported research, development, test, and evaluation (RDT&E) and clinical investigation activities (hereafter referred to as "research").

§ 219.2 Applicability and scope.

(a) This rule applies to the Office of the Secretary of Defense (OSD), the Military Departments, the Organization of the Joint Chiefs of Staff, the Unified and Specified Commands, the Defense Agencies, and the Uniformed Services University of the Health Sciences (USUHS) (hereafter referred to as "DoD Components") and to contractor or grantee activities supported by the Department of Defense.

(b) Its provisions encompass the following:

- (1) Clinical investigations as established by DoD Directive 6000.4, bio-medical research, and behavioral studies.

- (2) RDT&E involving new drugs, vaccines, biologicals, or investigational medical devices.

- (3) Inclusion of human subjects, whether as the direct object of research or as the indirect object of research involving more than minimal risk in the development and testing of military weapon systems, vehicles, aircraft, and other materiel. The determination of whether a research protocol involves more than minimal risk shall be made by review committees established in accordance with § 219.6, below. Nothing in this rule is intended to supersede requirements for health hazard or other safety reviews required by other DoD issuances or other DoD Component regulations.

- (c) Its provisions do not apply to epidemiological surveys that are of no more than minimal risk as set forth in the human protection regulations issued by the Department of Health and Human Services (45 CFR part 46).

- (d) Nothing in this rule is intended to limit the authority of a health care practitioner to provide emergency medical care under applicable law of the jurisdiction in which the care is provided or of commanders in the discharge of assigned duties or responsibilities.

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§ 219.3 Definitions.

Terms used in this rule are as defined in 45 CFR part 46 except for the following:

- (a) *Human subject.* A living individual about whom an investigator conducting research obtains data through interaction with the individual, including both physical procedures and manipulations of the subject or the subject's environment. The term does not include military or civilian personnel who are qualified to test by assignment to duties that call specifically for such qualifications such as test pilots and test engineers.

- (b) *Non-U.S. citizens.* Foreign nationals, excluding, for the purposes of this rule, personnel on active duty.

- (c) *Research.* A systematic investigation as described in § 219.2(b) (1), (2) and (3), above, that is designed to develop or contribute to generalizable knowledge. The term does not include individual or group training of military personnel such as combat readiness, effectiveness, proficiency, or fitness exercises.

§ 219.4 Policy.

- (a) It is the policy of the Department of Defense that:

- (1) The fundamental rights and welfare of human subjects in research funded by DoD Components shall be protected to the maximum extent possible. This protection is meant to encompass basic respect for human dignity and to protect subjects from actual harm. Responsibility for the protection of human subjects is a command responsibility.

- (2) Except as provided elsewhere in this rule the human protection regulations issued by the Department of Health and Human Services (45 CFR part 46) shall apply to research supported by the Department of Defense.

- (3) Contractors or grantees (and elements of DoD Components) holding an assurance of compliance with the Human use regulations of the Department of Health and Human Services (45 CFR part 46) shall be considered in compliance with the terms of this rule. In the absence of such an assurance, a special assurance that meets the minimum requirements of 45 CFR part 46 shall be negotiated between the contractor or grantee and the DoD Component concerned.

- (4) Only persons who are informed fully and voluntarily agree to participate may be used as human subjects in research. The only exception to the policy is that consent to participate may be obtained from a legal representative of the subject when the measures used are intended to be beneficial to the subject.

- (5) In research conducted outside the United States involving non-U.S. citizens as human subjects, the laws, customs, and

practices of the country in which the research is conducted, or those required by this rule, whichever are more stringent, shall take precedence. The research shall meet the same standards of ethics and safety that apply to research conducted within the United States involving U.S. citizens.

(4) The use of prisoners of war as human subjects of research is prohibited.

(5) For any research involving human subjects, a medical monitor shall be appointed by name if the approving official determines that the risk is more than minimal.

(6) Requests for exceptions to policy as stated above shall be submitted with full justification to the Under Secretary of Defense for Research and Engineering (USDR&E) by heads of DoD Components.

#### § 219.5 Responsibilities.

(a) The Under Secretary of Defense for Research and Engineering, or designee, shall:

(1) Develop policies in coordination with the Assistant Secretary of Defense (Health Affairs) (ASD(HA)) to protect human subjects in DoD-funded research.

(2) Coordinate DoD Component activities in the protection of human subjects.

(3) Serve as the point of contact within the Department of Defense and act as the principal DoD liaison with civil or federal agencies outside the Department of Defense on matters pertaining to protection of humans in research.

(4) Serve as the final DoD approval authority for all research involving actual exposure of human subjects to nuclear weapons effect or chemical warfare agents.

(b) The Assistant Secretary of Defense (Health Affairs) shall:

(1) Provide policy guidance regarding medical safety and standards of professional medical care and conduct as they relate to the use of humans in research.

(2) Serve as the DoD representative on matters relating to implementation of Food and Drug Administration (FDA) regulatory requirements.

(c) The Heads of DoD Components, or designees, shall:

(1) Protect the rights and welfare of human subjects in research sponsored or conducted by or among the members of the respective DoD Components.

(2) When more than one DoD Component is involved, determine primary responsibility based upon consideration of whether the subjects are inpatients or outpatients of a DoD medical treatment facility (MTF); whether the research is conducted in-house or by contract; or whether the prospective human subjects are members of a DoD Component.

(3) When the research, regardless of in-house or contract status, involves use of patients of a DoD MTF, the Component to

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which the MTF belongs organizationally shall have primary responsibility, except as provided in § 219.5(e).

(4) For research not involving the use of patients at a DoD MTF, primary responsibility rests as follows:

(A) If the research is done on grant or contract, primary responsibility rests with the DoD Component providing funds.

(B) If the research is conducted in-house, primary responsibility rests with the DoD Component to which the principal investigator is assigned.

(C) If the research is not funded by a DoD Component and there is no DoD principal investigator, primary responsibility rests with the DoD Component to which the prospective human subject is assigned.

(3) Establish procedures to maintain adequate documentation of human subjects used in research, including resulting adverse reactions.

(4) Establish procedures for responding to reports of improper use of human subjects.

(5) Establish review committees as provided for in § 219.6(b), of this part.

(d) The Secretaries of the Military Departments shall approve in-house and contract research involving human subjects, conducted at or funded by a DoD Component for which the Military Department has been designated executive agent. This responsibility includes research that is classified for reasons of national security. When more than one Military Department is involved in the same research, the first review committee to which the research is submitted shall perform the human use review and make recommendations to the Military Department Secretaries concerned. Each Secretary may accept these recommendations or may require additional reviews.

(e) The President, Uniformed Services University of the Health Sciences, and the Director, Defense Nuclear Agency (DNA), shall have primary responsibility for research by their respective DoD Components when the research does not also involve patients of a DoD MTF. The President, USUHS, shall have additional responsibility for research conducted in-house or by contract when the research involves patients of a DoD MTF or other U.S. Government health care facility, and USUHS directly funds the research, has received a grant or gift, or has received some other non-DoD form of support for the research. However, in these instances, the MTF review committee shall perform the human use review and make recommendations to the President, USUHS, and to the DoD Component or other U.S. Government institution concerned. The President, USUHS, may accept these recommendations or may require additional reviews.

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#### § 219.6 Procedures.

(a) *Delegation of Authority.* (1) The Secretaries of the Military Departments are authorized to delegate all or part of their authority under § 219.5, of this part, within the military chain of command to the lowest level operating a human-subjects review process.

(2) In addition, the Secretaries of the Military Departments are authorized to make the determination that unique military requirements dictate the use of drugs or devices not officially approved by the FDA. The Secretaries of the Military Departments may delegate this authority to the respective Surgeons General or designees.

(3) The President, USUHS, may delegate the authority specified in § 219.5(e), of this part, to the Dean or Associate Deans.

(4) Requests for approval of the use of human subjects in research funded by DoD Components other than the Military Departments, DNA, and USUHS shall be submitted to the USDR&E for final determination.

(5) Authority not delegated above to specific officials is retained by the Secretary of Defense.

(b) *Review Committees.* Each official having approval authority for research involving human subjects shall establish one or more committees to provide initial and continuing review of the use of human subjects in such research.

(1) The review committees is similar functionally to the Institutional Review Board (IRB) established under 45 CFR part 46. The IRB performs protocol review and protocol approval. Within the Department of Defense these functions are separated. Review committees exercise only protocol review and recommend approval, modification, or disapproval to an approving authority. Approval authority is vested in the approving official to whom the review committee reports.

(2) The review committee shall be constituted in accordance with 45 CFR part 46 standards for IRBs and § 219.5(c)(5), of this part, with the following exceptions:

(i) The prohibition in 45 CFR part 46 of all-male or all-female membership may be waived by the approving official when compliance is impractical.

(ii) The requirement in 45 CFR part 46 for a nonaffiliated member may be met by appointment of a member of an institution or organizational unit not subject to the immediate authority of the approving official.

(iii) When the approving authority, or the review committee itself, has reason to believe a given proposal includes more than minimal risk, a physician shall be included as an *ad hoc* member of the committee (see also § 219.4(a)(6), of this part).

(iv) The approving official may not be a member.

(3) The review committee shall retain records of research reviewed for at least 3 years after the completion of the research, or at the option of the approving official, shall forward records to that official for longer retention.

(4) An approving official may not approve research for which the official is also a principal or coinvestigator. Such research shall be reviewed and approved at a higher echelon of command.

(5) Research that involves the use of human subjects may not be initiated until all necessary approvals and the informed consent of the subjects have been obtained.

(6) If a review committee recommends safeguards or special conditions to a protocol it is recommending for approval, the approving official may not reduce the safeguards or conditions upon approving the protocol. The approving official may require additional safeguards, may disapprove the protocol, or may refer it to a higher approving authority and review committee.

#### § 219.7 Information requirements.

The memorandum of understanding between the FDA and the Department of Defense requires that the FDA be informed whenever the use of human subjects in new drug or device research that is classified for reasons of national security has been approved. The FDA also shall be informed when a determination has been made that unique military requirements dictate the use of drugs or devices that have not been approved by the FDA. Such notification also shall be provided to the USDR&E and ASD(HA).